ABSTRACT
E-BOOK

8TH Congress of the Macedonian Neurological Society

From theory to therapy

9-12 October 2025 Ohrid, North Macedonia
Hotel Inex Olgica

МАКЕДОНСКО ЗДРУЖЕНИЕ НА НЕВРОЛОЗИ

ean european academy of neurology

SPINRAZA
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КЛИНИЧКИТЕ ИСПИТУВАЊА И ИСПИТУВАЊАТА ОД РЕАЛНИОТ СВЕТ ПОКАЖАЛЕ ДЕКА

МОЖНО Е ПОВЕЌЕ

MORE IS POSSIBLE

SPINRAZA ИМ ПОМАГА НА ПАЦИЕНТИТЕ ДА НАПРАВАТ ПОВЕЌЕ, ВО СПОРЕДБА СО ПЛАЦЕБО И ПРИРОДНИОТ ТЕК НА БОЛЕСТА[1, 2]

Лекот Spinraza е индициран за лекување на спинална мускулна атрофија предизвикана од мутација на хромозомот 5q.[1]

Во клучни, рандомизирани, контролирани испитувања, лекот SPINRAZA покажа клинички и статистички значајни подобрувања на моторните функции во споредба со плацебо постапката.[1]

Испитувањата од реалниот живот ги подржуваат подобрувањата во однос на природниот тек на болеста, од пресиптоматски па се до возрасни пациенти.[1, 2]

Резултатите може да варираат од пациент до пациент зависно од напредување на болеста и времетраење на лекувањето.
Прикажаните слики се инспирирани од вистински луѓе кои живеат со СМА и служат само за илустративни цели.

Начин на издавање на лекот: Лекот може да се употребува само во здравствена установа.
Пред препишување на лекот SPINRAZA, за повеќе информации Ве молиме да го прочитате последниот одобрен Збирен извештај за особините на лекот и Упатството за употреба на лекот, кои можете да ги добиете од носителот на решението за ставање во промет на лекот во РСМ, Медис Македонија ДООЕЛ Скопје, е-пошта: medis.mk@medis.com, или со скенирање на QR кодот.

Литература: 1. SPINRAZA Збирен извештај за особините на лекот **2.** Coratti G, et al. Orphanet J Rare Dis. 2021;16:430.

Датум на добивање на одобрение за ставање во промет: Септември 2021 година
Датум на припрема: Септември 2025 година

MK-SPI-0925-001 САМО ЗА СТРУЧНА ЈАВНОСТ
Медис Македонија ДООЕЛ Скопје, Наум Наумовски Борче 50/2-11, 1000 Скопје, РСМ

SPINRAZA SmPC

MEDIS Therapeutics

ДАЛИ ВАШИОТ ПАЦИЕНТ МОЖЕ ДА ИМА ФРИДРАЈХОВА АТАКСИЈА (ФА)?

“Фактот дека имав проблеми и со рамнотежата, особено додека трчав или кога бев во слабо осветлена средина, ги натера лекарите кои ме прегледаа да помислат дека можеби има невролошки проблем зад ортопедскиот, па отидов кај невролог.“

Филипо*, 45 години

Што претставува ФА?

ФА е ретка, наследна форма на прогресивна невродегенеративна атаксија поврзана со оштетување на мускулната координација и губење на функцијата со текот на времето, што често доведува до зависност од инвалидска количка во рок од 10 до 20 години кај повеќето пациенти, а дури и до 3 години кај тешки случаи.[1-3]

ФА е **најчестата наследна атаксија**, затоа е од **суштинско значење да се има предвид при толкување на симптомите** и поставување на **почетната диференцијална дијагноза**.[4]

Подетален преглед на вообичаените невролошки симптоми кај ФА

Паѓања
(атаксија при одење)[2,5]

Историја на сопнувања или несмасност, губење на координацијата

Губење на рамнотежа
(слаба проприоцепција)[2,5]

Тешкотии при одење во права линија, зависност од помагала за одење

Исцрпеност
(замор)[1,6]

Исцрпеност по рутинска физичка активност, мускулна слабост во карлицата и долните екстремитети

Нејасен говор
(дизартрија)[1,2]

Потешкотии при зборување, нејасна артикулација, со намалена разбирливост во напредни случаи.

Кога ќе забележите било која комбинација од овие симптоми, прво помислете на ФА, Побарајте генетски тест штом се посомневате на ФА.[2,4]

Други симптоми што треба да се бараат а не се невролошки:

Кардиомиопатија
(срцева болест)[2,7]

Нарушена срцева функција што предизвикува замор, отежнато дишење и едем

Речиси сите пациенти со ФА ќе развијат кардиомиопатија.

Сколиоза[1,2]

Абнормална странична кривина на ‘рбетот

Многу честа, иако може да биде блага.

Колку побрзо се потврди ФА, толку побрзо вашите пациенти ќе имаат пристап до оптимална нега.

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*Прикажаното лице е вистински пациент.

Овој материјал е креиран и финансиран од Biogen.

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ЛЕКУВАЈТЕ СО ЕФИКАСНОСТА И ИСКУСТВОТО НА ЛЕКОТ

ПОМОШ НА КОЈА И ВЕРУВАТЕ

ВО БОРБАТА ПРОТИВ РРМС

Литература: **1.** Tysabri, Збирен извештај за особините на лекот **2.** Податоци од компанијата Biogen за бројот на лекувани пациенти од клинички испитувања и пост-маркетинг следење, 2025.

Начин на издавање на лекот: Лекот може да се употребува само во здравствена установа.
Пред препишување на лекот TYSABRI, за повеќе информации Ве молиме да го прочитате последниот одобрен Збирен извештај за особините на лекот и Упатството за употреба на лекот, кои можете да ги добиете од носителот на решението за ставање во промет на лекот во РСМ, Медис Македонија ДООЕЛ Скопје, е-пошта: medis.mk@medis.com, или со скенирање на QR кодот.
Датум на добивање на одобрение за ставање во промет: Февруари 2022 година
Датум на припрема: Септември 2025 година

TYSABRI SmPC

MK-TYS-0925-002 | Само за стручна јавност
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KRKA

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- Безбедносниот профил на лекот е споредлив со плацебо [3,4]

*AJOVY® е индициран за профилакса на мигрена кај возрасни кои имаат мигрена најмалку четири дена во месецот[1]
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PLIVA | teva

Референци
1. Збирен извештај за особините на лекот AJOVY®, одобрен декември 2023; 2. Goadsby PJ et al.Neurology 2020; 95(18);
3. Dodick DW et al. JAMA 2018; 319(19): 1999-2008.; 4. Silberstein SD et al. N Engl J Med 2017; 377(22):2113-2122.

Напомена: Збирен извештај за особините на лекот AJOVY® е достапен на сајтот на Агенцијата за лекови и медицински средства (www.malmed.gov.mk). **Датум на последна ревизија на текстот:** AJOVY®, декември 2023 год. **Број на Одобрението за ставање на лекот во промет:** AJOVY® (11-4355/1). **Начин и место на издавање:** на лекарски рецепт, во аптека. **Носител на одобрение:** ПЛИВА дооел Скопје, Никола Парапунов бб, Скопје. Тел. 02/3062-702. **Датум на подготовка:** септември 2024. CNS-MK-00159.

▼ Лекот е предмет на дополнително следење. Ова ќе овозможи брза идентификација на нови безбедносни информации. Од здравствените работници се бара да ги пријават сите сомнителни несакани реакции. Несаканите реакции од лековите може да бидат пријавени во Националниот центар за фармаковигиланца при Агенцијата за лекови и медицински средства (www.malmed.gov.mk).

САМО ЗА ЗДРАВСТВЕНИ РАБОТНИЦИ

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Напомена: Збирен извештај за особините на лековите Memantin PLIVA и Memantine Pliva е достапен на барање и на сајтот на Агенцијата за лекови и медицински средства МАЛМЕД (www.malmed.gov.mk). Датум на последна ревизија на текстот: декември 2018 (Мемантин Плива) и февруари 2020 (Мемантине Плива). Одобренија за ставање на лекот во промет: 11-100/2 (Мемантин Плива) и 11-240/2 (Мемантине Плива). Начин и место на издавање: на лекарски рецепт, во аптека. Носител на одобрение: ПЛИВА дооел Скопје, Никола Парапунов б.б., Скопје. Тел. 02/3062-702. Датум на подготовка: јуни 2024. CNS-MK-00142

PLIVA | teva

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2. Податоци на Рош. Пресек на податоци: јуни 2025 г.

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Датум и место на подготовка: август 2025 г., Скопје

M-MK-0000985

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Evrysdi е иновативен модификатор за врзување на *SMN2* со докажана ефикасност, на кој му веруваат повеќе од 21 000 лица со СМА ширум светот.[1,2]

Evrysdi▼ risdiplam

Континуирана **експресија на SMN протеин во ЦНС и периферните ткива,** со **висока комплијанса** од >99%

Животот со СМА бара терапија на која можеш да се потпреш секој ден.

Evrysdi (risdiplam) е прва и единствена орална терапија за СМА со неинвазивно дозирање во домашни услови[1], нудејќи голема флексибилност за пациентите и нивните семејства. Клиничките податоци покажуваат **висока ефикасност** и **добар безбедносен профил**[1], овозможувајќи слободно секојдневие исполнето со движење и удобност.

Индикација:
Evrysdi е индициран за третман на 5q спинална мускулна атрофија (СМА) кај пациенти со клиничка дијагноза на СМА тип 1, тип 2 или тип 3 или со една до четири *SMN2* копии.

Референци:
1. Збирен извештај за особините на лекот Evrysdi (risdiplam), број на одобрение за ставање на лек во промет: 11-6730/1 од 06.07.2021 г., последна ревизија: август 2024 г.; **2.** Податоци на Рош, пациенти на комерцијален лек, учесници во клинички студии и пациенти во Програми за помош од сочувство. Пресек на податоци: август 2025 г

СМА, спинална мускулна атрофија.

▼Овој лек подлежи на дополнително следење. Со ова се овозможува брзо откривање на нови информации за безбедноста на лекот. Од здравствените работници се бара да пријават секаква сомнителна несакана реакција од овој лек.

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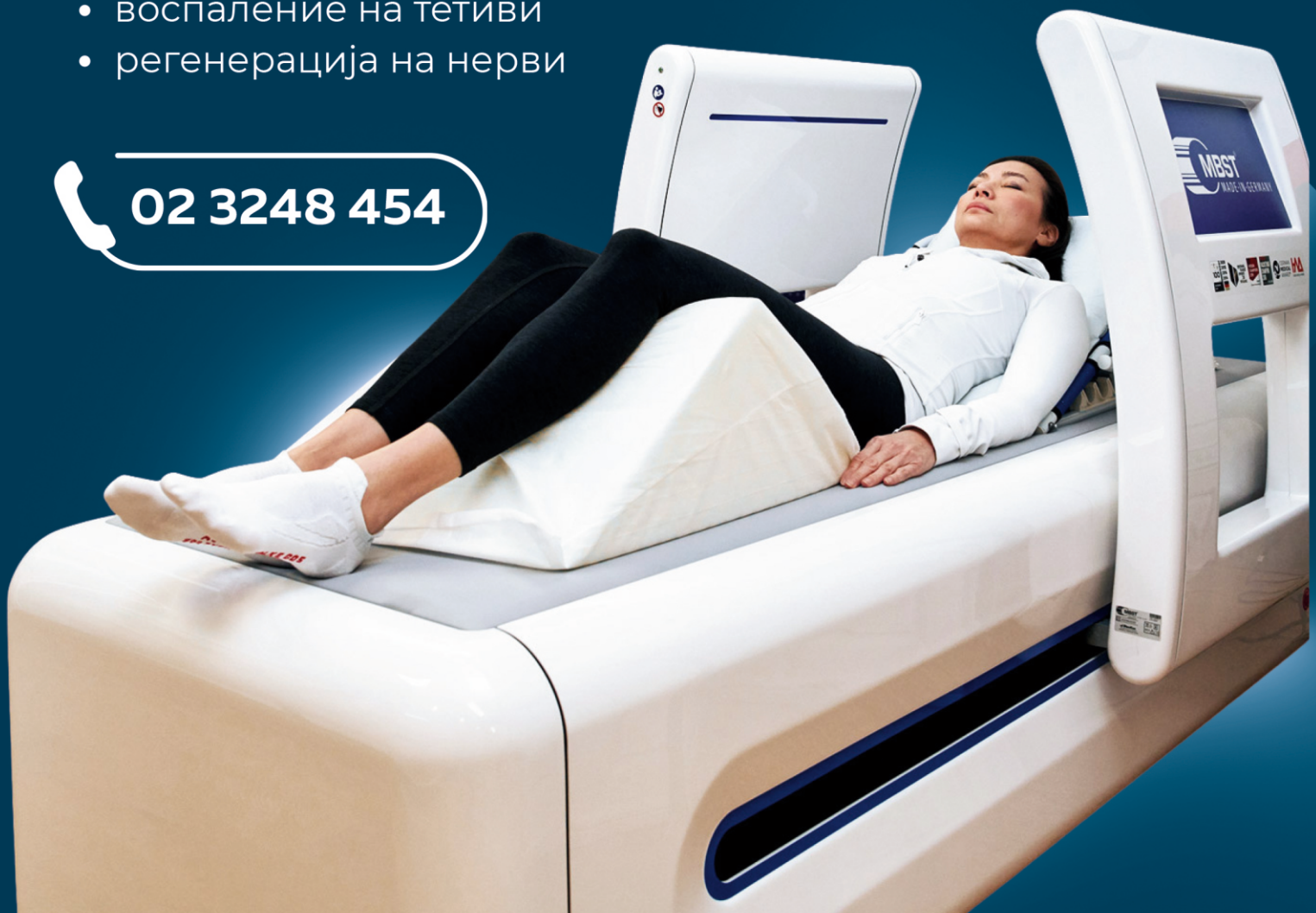

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- *New onset epileptic seizures, altered behavior or confusional states in elderly – Case report*

19. **Learta Ademi**
    - *Multiple cavernoma syndrome – A clinical case report*
    - *CASPR2 antibody-associated autoimmune encephalitis and epilepsy: A rare case report in a 5-year-old child*
    - *Neurological assessment and sequelae of pediatric cerebral ischemic stroke: Case series in a tertiary care hospital*
20. **Marija Babunovska** – *Double trouble: DCX mutation-associated subcortical band heterotopia – A case report*
21. **Marija Stojanovska** – *Single-image EEG interpretation: Multimodal large language models rival expert neurophysiologists*
22. **Maja Bozinovska Smicevska** – *Familial case report – Spinal muscular atrophy – Intrafamilial phenotypic variability and treatment response*
23. **Nikolina Tanovska**
    - *Current landscape of neuromyelitis optica spectrum disorder (NMOSD) management in North Macedonia: A real-world overview*
24. **Petar Kuzmanovski** – *Chorea as neurological manifestation of systemic lupus erythematosus – A case report*
25. **Simona Jovska** – *Gaps and opportunities in adult SMA care in North Macedonia: Insights from the SMA adult care benchmarking initiative*
26. **Simona Perchakovska** – *Fabry disease – Case report*
27. **Slobodanka Sazdova Burnevska** – *Association of HLA Alleles with Oligoclonal Band Status in Multiple Sclerosis Patients -- Association of Vitamin D Levels with Oligoclonal Band Status in Multiple Sclerosis Patients*
28. **Tatjana Petkovska Boshkova**
    - *Real-world outcomes of a complete transition to subcutaneous ocrelizumab in multiple sclerosis: A single-center study on efficacy, safety, and patient experience*
    - *A single-center real-world experience with subcutaneous ocrelizumab: Transition outcomes and healthcare benefits*
29. **Teodora Kukoska** – *Central pontine myelinolysis in a 30-year-old male with chronic alcohol use and hyponatremia*
30. **Tina Petrunova** – *Difficulties in attention and concentration among patients with degenerative and vascular dementia*
31. **Tanja Deleva Stosevska** – *Burning mouth syndrome and diabetic polyneuropathy – Coincidence or correlation? Case report*
32. **Vasilka Nikolovska** – *Epilepsy associated with right frontal subcortical heterotopia: A 14-year case history with favorable medical response*
33. **Lirim Shabani –** *Importance of medication therapy management for neurological patients with polytherapy*

ORAL PRESENTATIONS

COGNITIVE HEALTH AND THE ROLE OF BRAINVIT IN MENTAL CLARITY – AN ADJUVANT APPROACH IN SUPPORTING MENTAL HEALTH AND COGNITIVE FUNCTIONS

Doneva Ana [1]

Department of Neurology GCH 8th of September Skopje, Macedonia

Cognitive health is a vital component of overall well-being, yet in recent decades the world has faced a dramatic increase in cognitive disorders and neurodegenerative diseases. According to the World Health Organization, the number of people with dementia will exceed 150 million by 2050, posing a serious medical, social, and economic challenge. This highlights the urgent need of effective strategies for prevention and brain function support.

This presentation focuses on neurodegeneration, including oxidative stress, mitochondrial dysfunction, impaired synaptic plasticity, accumulation of amyloid-beta, tau proteins and neuroinflammation. At the same time it explores the potential of Brainvit – a specialized formula containing plant extracts (ginkgo biloba, bacopa monnieri, gotu kola), phospholipids, coenzyme Q10, B vitamins, and essential amino acids.

The components of Brainvit act synergistically by improving cerebral circulation, enhancing mitochondrial bioenergetics, reducing oxidative stress, stimulating neuroplasticity and supporting cholinergic and dopaminergic neurotransmission. Clinical research demonstrates that these effects lead to improvements in memory, attention, mental performance, and clarity across different age groups.

Particularly noteworthy are the positive results in individuals with mild cognitive impairment and patients in early stages of neurodegenerative diseases. Moreover, combining Brainvit with a Mediterranean diet, physical activity, and cognitive stimulation creates an integrated approach to preserving cognitive health.

In conclusion, Brainvit represents an effective adjuvant tool for supporting brain functions, capable of delaying cognitive decline and improving quality of life.

Keywords: Cognitive health, Brainvit, mental clarity, neurodegeneration, neuroplasticity

NEW TREATMENT OPTIONS IN INTRACEREBRAL HAEMORRHAGE

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Abstract: Spontaneous intracerebral haemorrhage (ICH) is a non-traumatic intraparenchymal bleed, often extending into the ventricles, and usually linked to cerebral small vessel disease when no macrovascular, neoplastic, infectious, inflammatory, or haemodynamic cause is found. In 2019, the global incidence was estimated at 3.41 million cases (95% CI 2.97–3.91), accounting for nearly 29% of all strokes. Major risk factors include ageing, hypertension, and air pollution. Evidence from randomized controlled trials and high-quality observational studies has shaped modern management.

The European Stroke Organisation (ESO), in collaboration with the European Association of Neurosurgical Societies (EANS), recently updated clinical guidelines. Patients with ICH should be admitted to organized stroke units to improve survival and functional outcome. Diagnostic algorithms such as DIAGRAM help identify the underlying cause. For secondary prevention, early initiation of antihypertensive therapy–ideally within 2 hours–is crucial. Target systolic blood pressure is <140 mmHg with minimized variability. Tranexamic acid may reduce haematoma expansion. Specific reversal agents are recommended for anticoagulant-related ICH: four-factor PCC plus vitamin K for VKA; andexanet alfa for factor Xa inhibitors; and idarucizumab for dabigatran. Surgical interventions may be beneficial in selected cases. Hematoma evacuation, decompressive surgery, and external ventricular drainage (EVD) should be considered depending on hematoma size, location, neurological status, and timing. For cerebellar hemorrhage, evacuation of hematomas >15 mL improves survival.

Guideline-based acute care, rapid blood pressure control, anticoagulant reversal, and timely surgical strategies are essential to reduce mortality and disability in ICH.

Key words: intracerebral haemorrhage, guidelines, stroke units, haematoma expansion, hematoma evacuation.

LONG-TERM OUTCOMES OF SURGICAL MANAGEMENT OF PHARMACORESISTANT FOCAL EPILEPSY: FIFTEEN YEARS OF EXPERIENCE AT A TERTIARY CARE CENTER IN SERBIA

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Introduction: Epilepsy surgery is an established therapeutic option for patients with pharmacoresistant focal epilepsy, aiming to achieve long-term seizure freedom and improvement in quality of life. Evaluating long-term results provides important insights into the effectiveness and sustainability of surgical management.

Methods: Between January 1, 2008 and December 31, 2020, a total of 179 patients with pharmacoresistant epilepsy underwent surgical treatment. Patients were prospectively followed until January 2025 (mean follow-up 9 years). Multiple postoperative outcomes were assessed, including seizure remission, discontinuation of antiseizure medication, changes in sociodemographic variables, neuropsychological outcomes, and overall quality of life.

Results: A total of 134 standardized anterior temporal lobectomies with amygdalohippocampectomy and 45 lesionectomies were performed, including 23 extratemporal resections. Persistent complications were recorded in 2.2% of patients. The most common histopathological substrate was hippocampal sclerosis (55%), followed by malformations of cortical development (26%) and tumors (21%). At the end of the follow-up, 100 patients achieved ILAE Class 1a outcome, 50 patients Class 1, while 26 patients were distributed across the remaining classes. Antiseizure medications were successfully discontinued in 27% of patients. There was a statistically significant increase in the number of employed patients, as well as in the number of disability pension recipients and divorce rates. The proportion of patients holding a driver's license also increased significantly. Postoperative decline on neuropsychological tests was observed in 29% of patients, while 28% showed improvement. Quality of life improved substantially following surgery, as measured by both general and epilepsy-specific quality-of-life questionnaires.

Conclusion: The results of our long-term follow-up cohort are comparable to those reported by other European centers in terms of seizure remission rates, complication frequency, and the proportion of patients in whom antiseizure medication was discontinued. Differences in sociodemographic outcomes reflect the cultural specificities of the local population.

Keywords: surgery, remission, temporal lobe, quality of life

WHEN NOTHING ADDS UP – PUT THE PIECES TOGETHER: REVISITING HISTORY AND NEUROLOGICAL EXAM

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Introduction: Hereditary spastic paraplegias (HSP) are a clinically and genetically heterogeneous group of motor neurodegenerative disorders characterized by a progressive pyramidal syndrome. They are classified into *pure* forms, and *complex* forms, which present with additional neurological or systemic manifestations which increases the overall complexity of the clinical presentations. We report a case of delayed diagnosis due to complex symptoms overshadowing the progressive spasticity, the key clue to HSP.

Case presentation: A 54-year-old male was admitted for reevaluation of a long-standing undiagnosed neurological disorder. His symptoms began 15 years earlier with impaired gait, lower limb stiffness and difficulty lifting his legs, soon followed by vertiginous episodes. Initial investigations, including brain MRI, carotid ultrasound, and EEG were unremarkable, and he was discharged with a diagnosis of vertigo-atactic syndrome. Over the years, his condition progressively worsened. Detailed anamnesis revealed additional symptoms, including distal paresthesia, urinary urgency and incontinence, memory problems, and further gait deterioration. Family history was notable for a sister with similar symptoms, undiagnosed yet. Neurological examination showed horizontal nystagmus, impaired gaze fixation, upper motor neuron signs (spasticity, hyperreflexia, positive Babinski), distal leg hypotrophy, decreased light touch and deep sensation in distal extremities, truncal ataxia, pes cavus, scoliosis, and distal epilation in both legs. Paraclinical investigations revealed peripheral sensorimotor demyelinating neuropathy on EMG, multidomain cognitive impairment on neuropsychological testing, cerebellar atrophy on head CT, and thoracic spinal cord thinning on MRI, while cervical and lumbosacral spine MRIs were normal. The patient was referred for genetic testing, including HSP and spinocerebellar ataxia panels.

Conclusion: Rare diagnoses are not always as rare as they seem. HSP exhibits remarkable genetic and clinical heterogeneity and ranks among the most diverse neurological conditions, alongside peripheral neuropathies. In this case, only a thorough clinical evaluation and careful synthesis of findings pointed toward a probable diagnosis of complex HSP, most likely HSP type 7.

Key words: Hereditary Spastic Paraparesis, Complex form, Pure form

ASSESSMENT OF VISUOSPATIAL DEFICITS IN DEGENERATIVE AND VASCULAR ETIOLOGIES THROUGH THE REY-OSTERRIETH COMPLEX FIGURE

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Objectives: Cognitive impairment and dementia arise from multiple etiologies, most commonly degenerative and cerebrovascular. Beyond aging, risk factors include genetic predisposition, sex, education, physical activity and exposure to toxins and substances. This study examined whether age and education are associated with performance on the Rey-Osterrieth Complex Figure (ROCF) among patients with degenerative and vascular etiologies.
Methods: A total of 62 participants were divided into two groups according to etiology (degenerative vs. vascular). Performances were compared on the ROCF copy trial and delayed (30-minute) recall trial. ROCF is designed to assess visuoconstructional ability, visual memory, planning, and organizational skills. It involves copying a complex geometric figure, followed by recalling it after a period of time (30 minutes). Performance is scored both quantitatively (accuracy and completeness) and qualitatively (organization, strategy, and error patterns). Correlations between participants' age, educational level, and test performance were analyzed. Additionally, qualitative features of ROCF protocols were explored to evaluate their potential utility in differentiating between the groups.
Results: Neither age nor the level of education have a statistically significant correlation to the performance on ROCF (copy trial or recall trial) of both groups. Regarding age, a slightly negative trend was observed without any statistical significance on the copy trial ($p=0.387$) and the 30-minute recall trial ($p=0.580$). No statistical significance was found comparing the education levels either ($p=0.347$). Despite this, the degenerative group had a lower average delayed recall score. The qualitative analysis indicated that distortions, dislocations and confabulations are more common among the degenerative group, whereas omissions were more notable in the vascular group.
Conclusion: Although, age and education did not significantly influence performance, ROCF commonly reveals impairments in both degenerative and vascular cases. Qualitative analysis may still provide additional clinical value in differentiating etiologies.
Keywords: Degenerative dementia, Vascular dementia, Rey-Osterrieth Complex Figure, age, education.

DYSTONIA: 40 YEARS LATER

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Dystonia is a variable movement disorder that can present as the sole motor manifestation of a disease or as a symptom within another disease process (ie, Parkinson disease), and is characterized by sustained or intermittent abnormal movements, postures, or both. They are typically patterned and repetitive and may be tremulous or jerky. They are often initiated or worsened by voluntary action and frequently associated with overflow movements. The two-axis structure for classification of the many different presentations of dystonia was also retained, with some revision. Axis I summarizes key clinical characteristics of dystonia (age at onset, family history, body distribution, temporal dimensions, phenomenology, and whether dystonia is isolated or combined with other neurological or medical problems). Axis II organizes information regarding its etiological basis, including genetic, acquired, and anatomical, and common disease mechanisms. Genetic dystonias are linked to several genes (exceeding 400 by 2024, with approximately 76.6% linked to neurodevelopmental disorders), including pathogenic variations of VPS16, TOR1A, THAP1, GNAL, and ANO3. On the molecular level, several, often intertwined pathways have been linked to pathogenic variants in dystonia genes, including gene transcription during neurodevelopment (e.g., *KMT2B*, *THAP1*), calcium homeostasis (e.g., *ANO3*, *HPCA*), striatal dopamine signaling (e.g., *GNAL*), endoplasmic reticulum stress response (e.g., *EIF2AK2*, *PRKRA*, *TOR1A*), autophagy (e.g., *VPS16*), and others. Advances in neuroimaging have improved our understanding of dystonia-related brain networks. Pharmacological agents, such as oral anticholinergic administration and botulinum toxin injection, play a major role in the initial treatment of patients. In more severe and/or refractory cases, focal areas for neurosurgical intervention are identified and targeted to improve quality of life. Deep brain stimulation (DBS) targets these anatomical locations to minimize dystonia symptoms.

DISTONIJA: 40 GODINA KASNIJE

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Distonija se može ispoljiti kao jedina, izolovana motorna manifestacija ili kao simptom unutar drugog patogenog procesa (npr. Parkinsonova bolest). Karakteriše se intermitentnim ili protrahovanim abnormalnim pokretima, položajima ili oba. Oni se tipično javljaju po istom obrascu, repetitivni su i mogu biti tremulozni ili trzajni. Često ih izazivaju ili pogoršavaju voljni pokreti, a odlikuje ih i fenomen prelivanja pokreta. Predložena je i delom izmenjena 2025. godine klasifikacija koja se zasniva na dve osovine. Osovina I obuhvata ključne kliničke karakteristike (starost na početku simptoma, porodična anamneza, distribucija distonije, vremenske dimenzije pokreta, fenomenologija, kao i to da li je distonija izolovana ili kombinovana sa drugim neurološkim ili medicinskim problemima). Osovina II obuhvata informacije koje se tiču etiološke osnove, uključujući genetske, stečene i anatomske aspekte, kao i zajedničke mehanizme bolesti. Genetske distonije su povezane sa brojnim genima (>400 u 2024. godini sa oko 76,6% povezanih sa neurorazvojnim bolestima), uključujući patogene varijante VPS16, TOR1A, THAP1, GNAL, i ANO3. Na molekularnom nivou se uključuje nekoliko, često isprepletanih puteva koji su povezani sa patogenim varijantama gena distonije, uključujući transkripciju gena tokom neurorazvojnog perioda (npr., *KMT2B*, *THAP1*), homeostazu kalcijuma (npr., *ANO3*, *HPCA*), dopaminsku transmisiju u strijatumu (npr., *GNAL*), odgovor na stres u endoplatičnom retikulumu (npr., *EIF2AK2*, *PRKRA*, *TOR1A*), autofagiju (npr., *VPS16*), i drugo. Napredak neuroimidžinga poboljšava naše razumevanje moždanih mreža relevantnih za distoniju. Farmakološka sredstva, tipa antiholinergičkih lekova i injiciranja botulinskog toksina, imaju značajnu ulogu u ranim fazama lečenja. Kod težih i/ili refraktornih bolesnika identifikovane su morfološke strukture mozga čije oštećenje poboljšava klinički status distonije. Duboka moždana stimulacija ovih struktura smanjuje simptome distonije.

FRIEDREICH'S ATAXIA: FIRST EXPERIENCES WITH OMAVELOXOLONE (SKYCLARYS) IN NORTH MACEDONIA

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Background: Friedreich's ataxia (FRDA) is a rare autosomal recessive, progressive neurodegenerative disorder caused by GAA trinucleotide repeat expansion in the FXN gene, leading to frataxin deficiency and mitochondrial dysfunction. Clinical manifestations include progressive gait and limb ataxia, dysarthria, cardiomyopathy, and systemic complications.
Objective: To present therapeutic advances with omaveloxolone (Skyclarys), the first disease-modifying therapy for FRDA, and to describe the implementation of treatment in the Republic of North Macedonia.
Methods: Review of published clinical trial data, long-term extension studies, real-world safety evidence, and national regulatory documents. Presentation of initial local experience in North Macedonia through the Program for Rare Disease Treatment.
Results:Omaveloxolone was approved by the U.S. FDA in 2023 and by the European Commission in 2024. Clinical studies demonstrated significant slowing of disease progression, measured by the modified Friedreich's Ataxia Rating Scale (mFARS). Real-world evidence supports its favorable safety and tolerability profile, with the most common adverse effects being mild to moderate increases in liver enzymes, headache, nausea, and fatigue. In 2025, the Republic of North Macedonia published the first official national protocol for FRDA treatment in the Official Gazette, defining strict admission and monitoring criteria. Since August 2020, three patients at the PHI University Clinic of Neurology in Skopje have been treated under the state Program for Rare Disease Treatment.
Conclusion: Omaveloxolone represents a milestone in the management of Friedreich's ataxia, offering clinically meaningful benefits in disease progression and quality of life. North Macedonia is the first country in the region to implement a national protocol and initiate therapy, ensuring structured and earlier access for affected patients.

Keywords: Friedreich's ataxia, omaveloxolone, Skyclarys, frataxin, neurodegenerative disease, rare diseases, North Macedonia

Фридрајхова атаксија: Први искуства со омавелоксолон (Skyclarys) во Северна Македонија

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Вовед: Фридрајховата атаксија (ФРА) е ретко, автозомно рецесивно, прогресивно невродегенеративно заболување предизвикано од GAA триплет-експанзија во FXN генот, што доведува до недостаток на фратаксин и митохондријална дисфункција. Клиничките манифестации вклучуваат прогресивна атаксија на одење и екстремитети, дизартрија, кардиомиопатија и системски компликации.
Цел: Да се прикажат терапевтските напредоци со омавелоксолон (Skyclarys), првиот лек што модифицира тек на болеста кај ФРА, и да се опише имплементацијата на третманот во Република Северна Македонија.

Методи: Преглед на достапни клинички испитувања, долгорочни студии, реални податоци за безбедност, како и национални регулаторни документи. Презентација на првични локални искуства преку Програмата за ретки болести.
Резултати: Омавелоксолон беше одобрен од Американската ФДА во 2023 година и од Европската комисија во 2024 година. Клиничките студии покажаа значајно забавување на прогресијата на болеста, мерено со модифицираната скала за Фридрајхова атаксија (mFARS). Реалните студии ја потврдуваат добрата безбедносна и толерантна профила, при што најчести несакани ефекти се умерено покачување на ензимите на црниот дроб, главоболка, мачнина и замор. Во 2025 година, во Службен весник на РСМ беше објавен првиот официјален национален протокол за третман на ФРА, со строго дефинирани критериуми за прием и следење. Од август 2020 година, на Универзитетската клиника за неврологија во Скопје започна третман на тројца пациенти преку Државната програма за ретки болести.
Заклучок: Омавелоксолон претставува значаен терапевтски пробив во лекувањето на Фридрајховата атаксија, со клинички значајни придобивки во забавување на прогресијата и подобрување на квалитетот на живот. Северна Македонија е прва земја во регионот што воведе национален протокол и започна со терапија, овозможувајќи структурирана и навремена грижа за пациентите.

Клучни зборови: Фридрајхова атаксија, омавелоксолон, Skyclarys, фратаксин, невродегенеративни болести, ретки болести, Северна Македонија

THE INFLUENCE OF ATHEROSCLEROTIC CHANGES AND RISK FACTORS ON THE COGNITIVE STATUS OF PATIENTS WITH ASYMPTOMATIC CAROTID ARTERY STENOSIS

Author Elena Joveva[7]

Background
Carotid atherosclerosis is a major risk factor for cognitive decline. Carotid artery stenosis and intima-media thickness (IMT) indicate disease severity, while vascular and inflammatory factors further influence dementia risk.
Methods
In a prospective study, 180 patients aged 50–70 years were divided into three groups: (1) asymptomatic carotid stenosis without transient ischemic attack (TIA) or infarction, (2) symptomatic stenosis with TIA or infarction, and (3) controls with normal carotid findings. Vascular risk factors, diabetes, hypercholesterolemia, and inflammatory markers (tumor necrosis factor-α, C-reactive protein, fibrinogen, leukocyte sedimentation) were assessed. Carotid ultrasound evaluated stenosis, cognitive function was measured with the Addenbrooke's Cognitive Examination-Revised (ACE-R), and brain CT/MRI identified ischemic lesions.
Results
Asymptomatic carotid stenosis was independently associated with cognitive impairment. Severe right-sided stenosis increased the risk of severe cognitive decline 14-fold, while severe left-sided stenosis raised the risk nearly 20-fold.
Conclusion
Carotid stenosis strongly correlates with cognitive dysfunction, even in the absence of clinical cerebrovascular events. Early detection and monitoring of inflammatory activation may help prevent cognitive decline and improve long-term neurological outcomes.
Key words: atherosclerosis, carotid artery stenosis, cognitive impairment, vascular risk factors.

SEIZURES AND SHRINKING BRAIN: AN ADULT CASE OF RASMUSSEN ENCEPHALITIS

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Introduction

Progressive focal epilepsy accompanied by unilateral hemispheric atrophy in adults presents a complex diagnostic challenge, frequently mimicking more common conditions such as vascular lesions, mitochondrial diseases, autoimmune encephalitis, or cortical malformations.

Rasmussen encephalitis (RE), rarely seen in adults, progresses slowly, often resulting in delayed recognition. We present a challenging adult-onset RE case that underscores the need to consider this disorder in adults with focal epilepsy and worsening neurological deficits.

Case Presentation

We present a 38-year-old female patient with recurrent seizures, right-sided weakness, and motor dysphasia. Brain MRI revealed a left temporal cortical lesion interpreted initially as possible ischemic infarct with a hemorrhagic component. Multiple EEGs were obtained and left temporal slowing was observed. Neuropsychological testing revealed deficits in attention, visuospatial skills, and language. Over the subsequent year, the patient experienced repeated focal seizures with evolving neurological deterioration, including right hemiparesis and speech difficulties, resulting in several hospitalizations.

Serial MRI scans demonstrated progressive unilateral cortical and subcortical atrophy with laminar necrosis and contrast enhancement consistent with ongoing inflammation. Genetic testing excluded mitochondrial disorders such as MELAS. Extensive autoimmune, paraneoplastic, and thrombophilia work-up was negative except heterozygosity for MTHFR, MTRR, MTP, and SERPINE1 variants. Brain biopsy revealed focal cortical dysplasia type IB, indicating dual pathology.

Discussion & Conclusion

The evolving clinical, radiological findings of progressive uni-hemispheric destruction, despite the inconclusive biopsy fulfilled the updated diagnostic criteria for Rasmussen Encephalitis (RE). [2,3] She was treated with azathioprine, plasma exchange, corticosteroids and anticonvulsive therapy and showed mild improvement of neurological symptoms.

This case underlines the importance of considering RE in adult patients (accounting for approximately 10% of the cases) with progressive focal epilepsy and unilateral neurological decline. The absence of specific biomarkers and overlapping features with strokes, vasculitis and mithochondrial disorders can delay diagnosis. Early recognition is crucial as immunomodulatory therapies may slow disease progression, and timely hemispherotomy can improve long-term outcomes.[2,3]

Keywords: Rasmussen encephalitis, adult-onset, seizures, hemispheric atrophy, immunotherapy, plasmapheresis

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STATUS EPILEPTICUS AND HYPERAMMONEMIC TOPIRAMATE-INDUCED ENCEPHALOPATHY IN A YOUNG PATIENT WITH REFRACTORY EPILEPSY – A CASE REPORT

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Introduction:
Status epilepticus is a neurological emergency, defined as a seizure lasting more than 5 minutes or recurrent seizures without return to baseline consciousness. It is associated with significant morbidity and mortality, particularly in patients with refractory epilepsy. Topiramate, commonly used as an antiepileptic drug, can rarely induce encephalopathy due to metabolic disturbances and neurotransmitter imbalance.

Case Presentation:
A 34-year-old male with childhood-onset refractory epilepsy, on multiple antiepileptic drugs (levetiracetam, valproate, topiramate, clonazepam), presented with frequent generalized tonic-clonic seizures progressing to SE. He exhibited confusion, lethargy, weakness, speech difficulties, and focal right-sided tonic seizures. Laboratory results showed hypokalemia, hyponatremia, hyperammonemia, and metabolic acidosis. EEG showed diffuse slowing with generalized slow-wave activity. Brain MRI revealed a chronic periventricular vascular lesion. CSF analysis was sterile; autoimmune markers (anti-MOG, anti-AQP4) were negative.

Management:
Topiramate-induced encephalopathy was suspected. The presumed mechanism involved carbonic anhydrase inhibition leading to acidosis, electrolyte imbalance, and GABA/glutamate dysregulation. Topiramate was tapered and discontinued, while valproate and levetiracetam doses were adjusted. Supportive care included sedation with propofol, intubation, and mechanical ventilation.

Outcome:
Seizures resolved after six days of intensive management. The patient was extubated and discharged in stable condition.

Discussion:
This case highlights the importance of considering topiramate-induced encephalopathy in patients presenting with status epilepticus and unexplained neurological deterioration. Hyperammonemia, although rare, is a serious adverse effect that requires prompt recognition and management to prevent long-term neurological sequelae.

Conclusion:
This case highlights the importance of recognizing topiramate-induced encephalopathy in patients with SE. Early identification, appropriate adjustment of antiepileptic drugs, and monitoring of metabolic parameters are crucial to improving patient outcomes.

Keywords: status epilepticus, encephalopathy, topiramate, metabolic disturbances

POST-STROKE SPASTICITY PATIENT EXPERIENCE JOURNEY MAP (PSS-PEJM): BRIDGING CLINICAL CARE AND LIVED EXPERIENCE

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Word count: 258/300

Background:
Post-stroke spasticity (PSS) is a common complication following stroke that significantly impacts motor function, quality of life, and caregiver burden. Despite advances in acute stroke care, the recognition and management of PSS remain inconsistent, resulting in unmet rehabilitation needs. The PSS Patient Experience Journey Map (PSS-PEJM) was developed to systematically capture the experiences of patients, caregivers, and healthcare professionals across Europe, with the aim of providing actionable insights to improve clinical care pathways.

Methods:
Using a combined multimodal, experience-based co-design qualitative methodology, a multi-stakeholder working group–including patients with PSS, caregivers, neurologists, rehabilitation specialists, and patient representatives from nine European countries–collated and analyzed patient experience data from multiple sources. The PSS-PEJM was developed and iteratively refined through workshops and validated by an independent panel (n=23) via anonymous surveys.

Results:
The PSS-PEJM provides a comprehensive view of the patient journey, capturing clinical, emotional, and social dimensions. Insights from the PEJM reveals significant gaps in the post-stroke care pathway, including delayed diagnosis, unclear referral processes, and fragmented long-term support. The journey map identifies key areas for intervention to enhance early detection, coordinated multidisciplinary management, and patient-centered rehabilitation, and provides a practical framework to improve spasticity care by incorporating patient experiences into clinical decision-making.

Conclusion:
The PSS-PEJM represents an innovative, patient-centered methodology bridging the gap between clinical practice and the lived experience of PSS. By incorporating patient and caregiver perspectives, it provides a strategic tool to redesign care pathways, improve communication, guide health policy and ultimately improve long-term outcomes and quality of life for stroke survivors affected by spasticity.

Keywords: post-stroke spasticity, patient experience journey map, stroke rehabilitation, multidisciplinary care, patient-centered care.

Study funding: This study was funded by Ipsen.

BEYOND SEIZURES: BONE MINERAL DISORDERS IN CHRONIC EPILEPSY–A CROSS-SECTIONAL STUDY

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Background: Patients with epilepsy have an increased risk of fractures, partly due to antiepileptic therapy (AET) through reduced bone mineral density (BMD). Although bone loss is multifactorial, AET may play a significant role, but the exact mechanisms remain unclear.

Aim: To investigate the association between AET use and decreased BMD in an unselected population of Macedonian patients with epilepsy. Internationally accepted guidelines for bone health monitoring in epilepsy are lacking, and in our country there are no standardized recommendations. Identifying high-risk groups is essential for the prevention of osteoporosis and fractures.

Methods: A cross-sectional study was conducted on 95 patients older than 20 years, treated with AET for more than 2 years, who attended the Epilepsy Outpatient Department at the University Clinic of Neurology between January 1st, 2021 and January 31st, 2024. Data included DXA scan results and demographic information. Logistic regression and other statistical analyses were applied.

Results: Osteopenia was present in 50.5% and osteoporosis in 20.0% of patients. Independent risk factors for reduced BMD were female sex, polytherapy with AET, comorbidities, menopause, older age, and longer epilepsy duration. Age >50 years and depression were significant in univariate analysis but not confirmed in multivariate analysis.

Conclusion: Independent risk factors such as female sex, menopause, older age, lower BMI, polytherapy, epilepsy duration, and comorbidity were associated with decreased BMD in epilepsy patients. These findings emphasize the importance of using known risk factors as guidance to identify patients at high risk of osteoporosis and fractures.

Keyword: bone health, ASM, comorbidity of epilepsy

Oral presentation
Author: Sanja Djambazovska Zikova
CGH "8 th September" – Skopje, N.Macedonia

A MISSED CONNECTION BETWEEN PFO AND STROKE IN OLDER PATIENTS. DOES AGE STILL MATTER?

Introduction: The clinical importance of PFO, serving as a conduit for right to left shunt has been associated with cryptogenic stroke, platipnea otrhodeoxia syndrome and recurrent decompression illness in divers which represents well established indications for percutaneous closure. No randomized controlled trials have been conducted comparing the effects of PFO closure versus medical therapy in patients >60 years of age. On the other hand, age play critical role in evaluating the relevance of PFO in cryptogenic stroke because the likelihood of causality validated through scoring system decreases with age.
Aim: This study aims to evaluate the impact of patients age on the significance and causality of PFO in cryptogenic stroke through a review of current data, and to compare these insights with our findings.
Methods: We extracted data from previously published studies to compare the association between PFO and stroke across different age groups. A scoring system was applied within age groups to determine the likelihood of causal relationship and its clinical and therapeutic relevance.
Results: The contribution of PFO to stroke appears to vary by age. In older patients, the association remains clinically relevant and diagnostic interpretation as well as scoring application may vary, leading to district clinical and therapeutic considerations.
Conclusion: Age is important when evaluating the role of PFO in stroke, highlighting the need for careful evaluating regardless of age.
Keywords: PFO, cryptogenic stroke, older age.

Note: The data presented in this oral presentation are derived from previously published studies included in the author's doctoral dissertation. This analysis synthesized existing findings to provide new insights into the association between PFO and stroke across different age groups and application of scoring system for therapeutic decision.

ДИФЕРЕНЦИЈАЛНИ НАРУШУВАЊА ВО СТРУКТУРНАТА МОЗОЧНА МРЕЖНА ПОВРЗАНОСТ КАЈ ПАЦИЕНТИ СО ПАРКИНСОНОВА БОЛЕСТ СО И БЕЗ КОГНИТИВНО НАРУШУВАЊЕ: СТУДИЈА БАЗИРАНА НА ГРАФ-ТЕОРЕТСКА АНАЛИЗА НА МРИ ПОДАТОЦИ

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Апстракт

Цел:
Целта на оваа студија е да ги испита промените во структурната поврзаност на мозокот кај пациенти со Паркинсонова болест (ПБ), со посебен фокус на разликувањето помеѓу пациенти со благо когнитивно нарушување (ПБ-БКН) и оние без такво нарушување (ПБ-без-БКН).

Методи:
Со примена на граф-теорија, беа анализирани мозочните мрежи добиени од структурни МРИ снимки. Се користеа метрики како што се јачина на нодус, глобалната ефикасност на мрежата и коефициентот на групирање. Во студијата беа вклучени три групи: здрави контролни испитаници (КГ), пациенти со ПБ-ЛКД и пациенти со ПБ-без-ЛКД. За статистичка споредба помеѓу групите се користеше Mann-Whitney -U тестот.

Резултати:
Пациентите со ПБ-БКН покажаа значително намалување на јачината на нодус, глобалната ефикасност и локалниот коефициент на групирање во споредба со здравите испитаници, особено во региони како што се таламусот, каудатусот и десниот супериорен фронтален кортекс. И пациентите со ПБ-без-БКН покажаа нарушувања во поврзаноста, но во помал обем, што укажува на континуум на мрежна дисфункција во согласност со когнитивниот статус. Специфични структурни разлики помеѓу групите со и без ЛКД беа забележани во региони како што се десниот енторинален кортекс и левиот парахипокампан гирус, што укажува на нивната потенцијална улога во напредувањето на когнитивното нарушување кај пациентите со ПБ.

Заклучок:
Резултатите ја потенцираат вредноста на граф-теоретските анализи во идентификувањето и карактеризирањето на структурните мрежни нарушувања кај Паркинсонова болест. Истото укажува на можноста за користење на мрежни биомаркери за рано откривање и следење на когнитивниот пад, со потенцијал за развој на насочени терапевтски интервенции.

Клучни зборови:
Паркинсонова болест, благо когнитивно нарушување, структурна мозочна поврзаност, МРИ, граф-теорија, анализа на мрежа

"DIFFERENTIAL STRUCTURAL BRAIN NETWORK DISRUPTIONS IN PARKINSON'S DISEASE WITH AND WITHOUT COGNITIVE IMPAIRMENT: A GRAPH-THEORETICAL MRI STUDY"

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ABSTRACT

Objective:
This study aims to explore changes in structural brain connectivity in individuals with Parkinson's Disease (PD), with an emphasis on distinguishing between patients exhibiting mild cognitive impairment (MCI) and those without.

Methods:
Graph theory was employed to analyze structural MRI-based brain networks, examining metrics such as strength of a node, network efficiency and clustering coefficients. The study cohort included healthy controls (HC), PD patients with MCI (PD-MCI), and PD patients without MCI (PD-non-MCI). Statistical comparisons were performed using the Mann-Whitney- U test to identify significant differences in structural connectivity measures across groups.

Results:
Compared to healthy individuals, PD-MCI patients showed marked reductions in node strength, global efficiency and local clustering, particularly in the thalamus, caudate, and right superior frontal cortex. PD-non-MCI patients also exhibited changes in connectivity, though to a lesser extent, indicating a continuum of network disruption aligned with cognitive status. Notable distinctions between PD-MCI and PD-non-MCI groups were observed in areas including the right entorhinal and left parahippocampal regions, suggesting that specific structural connectivity alterations may be linked to the onset and advancement of cognitive decline in PD.

Conclusion:
Our results reinforce the value of graph-theoretical approaches for characterizing brain network alterations in Parkinson's Disease and underscore their potential in identifying early markers of cognitive impairment. These insights may inform future therapeutic strategies aimed at maintaining cognitive function and slowing disease progression.

Keywords:
Parkinson's Disease, mild cognitive impairment, structural brain connectivity, MRI, graph theory, network analysis.

TITLE: INITIAL EVALUATION OF THE RESULTS OF VAGUS NERVE STIMULATION IN PATIENTS WITH DRUG-RESISTANT EPILEPSY IN ADULTS

Introduction/Objectives:
Vagus nerve stimulation (VNS) is a widely accepted adjunctive therapy for patients with drug-resistant epilepsy, offering an alternative when pharmacological options are exhausted. Although its mechanism remains incompletely understood, VNS has demonstrated favorable effects on seizure control and quality of life. The objective of this study was to retrospectively assess the initial outcomes of VNS in adult patients with pharmacoresistant epilepsy treated at our center.
Methods:
We retrospectively analyzed 21 adult patients with drug-resistant epilepsy who underwent VNS implantation at the University Clinic for Neurosurgery, Skopje, between 2019 and 2023. Postoperative management and follow-up were performed by neurologists at the University Clinic for Neurology, including optimization of antiepileptic drug (AED) regimens and VNS parameters. Clinical outcomes were assessed using seizure frequency, seizure severity and duration, AED load and quality of life.
Results:
Results: Eleven patients were female and ten patients were male. The median age at implantation was 30 years, and the median duration of epilepsy was 15 years. The overall response rate after 2 years was 61.9% (13 of 21 patients), defined as patients with $\geq$ 50% reduction in seizure frequency after VNS implantation. Patients in the group with all types of epileptic seizures, as well as those with partial type of epileptic seizures, showed a significant reduction in seizure frequency after 2 years, compared to the preoperative period before VNS implantation ($p<0.05$). In the total postoperative evaluation period of 2 years, improvements in seizure duration were also detected in 85.7% of patients and in seizure severity in 66.7%; The number of antiepileptic drugs (AEDs) was reduced in 61.9% of patients, and 90.5% reported improved quality of life.
Conclusions:
This initial clinical experience confirms that VNS is a safe and effective adjunctive therapy in adults with refractory epilepsy, leading to meaningful reductions in seizure burden and improvements in quality of life. Long-term follow-up and larger patient cohorts are warranted to further evaluate sustained outcomes.
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WHAT IS IN A NAME AND WHAT IS IN THE BRAIN? -CLINICIANS' DILEMMAS IN THE BIOMARKER ERA

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This viewpoint draws analogy from Shakespeare's query, "What's in a name?" and explores what defines neurodegenerative diseases such as Parkinson's (PD) and Alzheimer's (AD) and what clinicians understand by that name in relation to the underlying brain pathology and disease biology. The inspiration comes from the latest biological definitions of PD revealing significant similarities with the biological definition of AD.

The first act: W*alking straight into circles*, reflects on the slight imperfections of these concepts, keeping us walking in circles while thinking we are moving forward, towards clinically meaningful treatment. Even though biological definitions of NDDs are paving the way for future breakthroughs in neurodegenerative disease management, slight misinterpretations as equating pathology and biology of a disease could be misleading in defining treatment targets.

The second act, *"What's in a Name and What's in the Brain",* presents few dementia case studies, each one posing a question in search of an answer regarding genotype/phenotype and underling pathology/biology correlation. A novel c.2158T>G (p.Leu720Val) APP mutation in EOAD with marked parkinsonism and visual hallucinations; SQSTM1 mutation in bv FTD associated with amyloid β proteinopathy; phenotypic variability in C9orf72 expansion mutation. The emerging questions aim to understand the correlation between observed phenotype, genotype and (un)expected underlying protein aggregation, to understand occurrence and significance of co-pathologies, and to explore drivers of phenotypic variability. In the era of biologically defining NDDs, we are undoubtedly moving to a direction where clinicians have the mindset of both a researcher and a pathologist. However, on this challenging path, we must ensure that clinicians are not "lost in translation" while coding and decoding NDDs, striving to align clinical diagnoses with the underlying brain pathology and biology, to ensure more effective treatment outcomes in the future.

ВОЗРАСТ И КОМОРБИДИТЕТИ – ПРЕДИЗВИК КАЈ БОЛНИТЕ СО МИЈАСТЕНИЈА ГРАВИС

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Мијастенија гравис (МГ) е автоимуна болест која се карактеризира со слабост и патолошка заморливост на скелетните мускули.
Тоа е хетерогено заболување со различни возраст на почеток, клинички манифестации, имунолошки профил и промени на тимусот.
Во зависност од тоа кога се појавуваат иницијалните симптоми, МГ може да биде со ран почеток-под 50 год. возраст и доцен почеток-над 50 год. возраст.
Епидемиолошките истражувања укажуваат на пораст на инциденцата и преваленцата кај повозрасната популација над 50 год. возраст, што делумно се објаснува со продолжување на животиот век, препознавање и побрза дијагноза, поширок избор на ефикасни третмани. Но, не се исклучува и вистински пораст на стапката на инциденца меѓу највозрасната популација над 65 год. возраст-МГ со многу доцен почеток.
Возраста и коморбидитетите кај болните со МГ значително влијаат на начинот на лекување.
Повозрасната популација болни со МГ е дополнително оптоварена со коморбидитети, кои можат да бидат поврзани со самата болест-други автоимуни заболувања кои се јавуваат заедно со МГ почесто отколу во општата популација, заболувања кои се јавуваат или влошуваат како последица од лекувањето на МГ, и различни други коморбидни состојби.
Повеќето од болните со доцен почеток на МГ покажуваат позитивни ефекти од лекувањето кое треба да биде прилагодено и на возраста и на придружните заболувања кои ја следат. Несоодветната контрола и лекување ќе имаат сериозни последици и на општата состојба и квалитетот на живот.

Клучни зборови: Мијастенија гравис, возраст, коморбидитети, лекување.

PREGNANCY IN PATIENTS WITH MULTIPLE SCLEROSIS: A FOCUS ON OCRELIZUMAB

Authors:
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INTRODUCTION:
Multiple sclerosis (MS) predominantly affects women of childbearing potential, mostly diagnosed between ages 20 and 40. In North Macedonia, approximately 66% of MS patients are female, with an average age of 32 years. While pregnancy is typically associated with reduced relapse activity, the postpartum period carries an increased risk of disease reactivation. Historically, high-efficacy therapies (HET) were not recommended during pregnancy. This created a therapeutic gap, increasing the risk of disease reactivation in women with highly active MS. However, emerging evidence suggests that ocrelizumab, the only studied HET, may offer a new treatment paradigm in this context.

OBJECTIVE:
To review recent data on the safety and potential use of ocrelizumab during pregnancy and breastfeeding in MS women.

METHODS:
A comprehensive literature review was conducted, focusing on data from recent studies, and the ongoing Ocrelizumab Pregnancy Registry. Real-world post-marketing safety data were also reviewed. Data from prospective studies (MINORE and SOPRANINO) and post-marketing surveillance were analyzed. Outcome measures included maternal relapse rates, obstetric and neonatal outcomes, drug transfer across placenta and into breastmilk, and B-cell status in infants.

RESULTS:
Real-world studies show overall low relapse activity and no increase in postpartum disease activity in women receiving ocrelizumab prior to conception. The MINORE prospective, Phase IV study demonstrated low (<5%) placental transfer of ocrelizumab when administered >3 months prior to delivery and no infant B-cell depletion. The SOPRANINO prospective study confirmed minimal ocrelizumab transfer into breastmilk, and no adverse effects observed in breastfed infants. Interim data from the Ocrelizumab Pregnancy Registry and pharmacovigilance programs report reassuring outcomes. From >3,989 pregnancies by March 2024, 84.4% live births were reported, with no increased risk of miscarriage or congenital anomalies. Additionally, 13 ocrelizumab trials and non-interventional data noted that women with live births had minimal peripartum disease activity.

CONCLUSION:
Ocrelizumab has a potential for a paradigm shift in managing MS in women planning pregnancy. Emerging evidence supports that ocrelizumab administered preconception or early pregnancy offers effective relapse protection with minimal fetal or infant exposure and favorable safety profile. This supports its consideration as a peripartum treatment strategy. Ongoing studies are essential to further define its role and strengthen confidence in long-term maternal and neonatal outcomes.

Keywords: pregnancy, preconception, relapse, ocrelizumab, MS, multiple, sclerosis, female

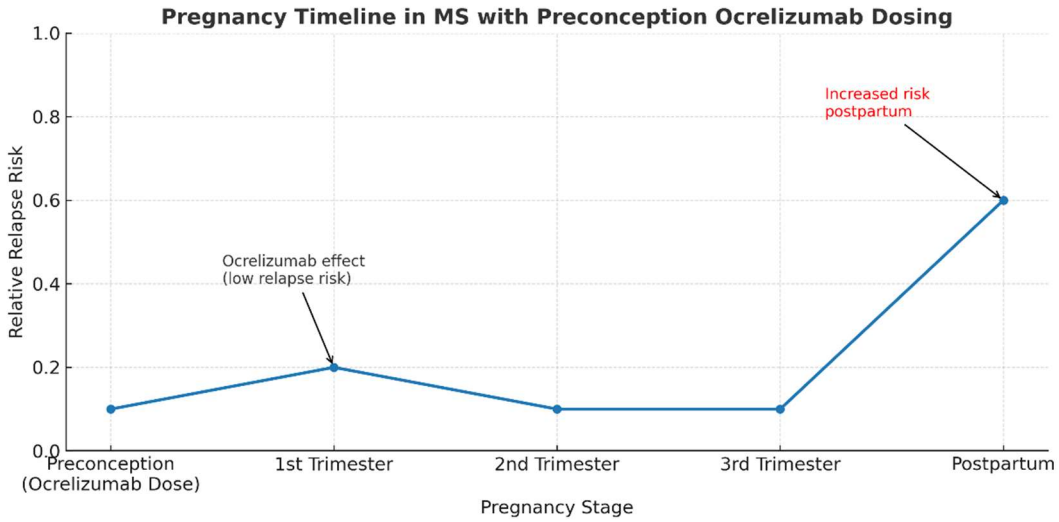

Table 1. The pregnancy timeline with the last dose of ocrelizumab before conception, the relative risk of relapse in different trimesters, and the characteristic increase in risk in the postpartum period.

ГЛАВОБОЛКА ВО ДЕТСКАТА И АДОЛЕСЦЕНТНАТА ВОЗРАСТ

Дума Ф.
Неуромедика Скопје

Главоболката е едно најчестите нарушувања во склоп на различни состојби и заболувања. Листата со диференцијални дијагнози се состои од 13 големи категории и 129 поткатегории. Постконтузиона главоболка, мигрената, тензиона главоболка, синузитис, интракранијална маса, напрегнат вид, откажување од кофеин, псеудотумор церебри, нарушувања на сонот, хипертироидизам, хипертензија и заболувања на темпоро-мандибуларниот зглоб, се дел од категориите. Главоболката и алергискиот ринитис се чести коморбидитети кај децата.

Преваленцата на силна повторувачка главоболка е 10/1000 кај деца до 10 години и 46/1000 за возрасти од 10-17 години, и во просек е причина за отсуство од училиште за 3,3 денови по ученик секоја училиштна година.

Мигрена, кластер и тензионите главоболки се примарни (идиопатски) главоболки, а помалку од 10% од главоболките се секундарни (симптоматски).

Главоболките се причина за ограничено учество во социјални активности, семејни настани и школски активности. Пред пубертетот нема разлика во половата дистрибуција, по пубертетот женскиот пол е двојно позастапен од машкиот пол.

Листата на моќни причини за мигрена е претставена од:

1. фактори од околината (на пр., сонце, бучава, застоен воздух, мириси),
2. храна (на пр., одредени сирења, чоколада, конзерванси за храна, лоша хидратација),
3. животен стил (на пр., промена на ритамот на спиење, пропуштени оброци),
4. психосоцијален стрес,
5. алергиски ринитис, хронична уртикарија, синузитис, одредени алергии на храна.

Главоболките кај децата и адолесцентите се чести и често може ефикасно да се контролираат со соодветни стратегии. Родителите треба да ги следат симптомите на своето дете и да се консултираат со здравствен работник ако главоболките се чести, силни или придружени со загрижувачки симптоми. Раната интервенција може да помогне во подобрувањето на квалитетот на животот и намалувањето на влијанието на главоболките врз секојдневните активности.

HEADACHES IN CHILDHOOD AND ADOLESCENCE

Duma F.
Neuromedika Skopje

Headaches are one of the most common and wide-ranging disorders. The list of differential diagnoses for headaches is divided into 13 major categories and 129 subcategories. They include post-concussion headaches, migraines, tension headaches, sinusitis, intracranial mass, eye strain, caffeine withdrawal, pseudotumor cerebri, sleep disorders, hyperthyroidism, hypertension, and temporomandibular joint disease. Headaches and allergic rhinitis (AR) are common in children and often co-occur.

The prevalence of severe recurrent headaches in those under the age of 10 is almost 10 per 1,000; it is approximately 46 per 1,000 for those aged 10 to 17, and the cause of an average of 3.3 missed school days per child each year.

Primary headache: includes migraine, cluster, and tension headaches. Less than 10% of patients presenting with a headache have a secondary headache.

Children with headaches may be forced to limit participation in social activities, family events, and school activities. Children's headaches (e.g., migraine) exhibit no gender variation before puberty. In late adolescence, however, twice as many females report recurrent headaches.

The list of potential migraine triggers includes:

1. environmental factors (e.g., sunlight, loud noises, stagnant air, odors),
2. foods (e.g., some cheeses, chocolate, food preservatives, poor hydration),
3. lifestyle choices (e.g., changing one's sleep patterns, missing a meal),
4. psychosocial stress,
5. allergic rhinitis, chronic urticaria, sinusitis, certain food allergies.

Headaches in children and adolescents are common and can often be managed effectively with appropriate strategies. Parents should monitor their child's symptoms and consult a healthcare provider if headaches are frequent, severe, or accompanied by concerning symptoms. Early intervention can help improve the child's quality of life and reduce the impact of headaches on daily activities.

NEURO-FORENSIC ASPECTS OF CRIMINAL BEHAVIOR IN PATIENTS WITH EPILEPSY

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Patients with various neurological disorders, including epilepsy, may occasionally appear in criminal courtrooms. In such cases, the court expects neurologists to provide answers to complex medico-legal questions.

Key issues for neurologists include whether violent behavior can be a manifestation of epilepsy, whether it can be induced by epileptic seizures, or whether epileptogenic lesions themselves may influence a predisposition to violence. Violent behavior in epilepsy can be categorized into periictal violence (preictal, ictal, and postictal), which occurs in close temporal relation to seizures, and interictal violence, which lacks such direct association. The legal defense of innocence can be applied only in patients with epilepsy who, at the time of committing an offense, experience a seizure or an associated mental disorder.

Seizures may contribute to a legal defense of innocence through the occurrence of involuntary behavior in the form of epileptic automatisms, or through impaired reasoning caused by psychotic symptoms during the postictal period. Epileptic automatisms are involuntary, stereotyped, and often complex motor activities that may resemble purposeful behavior but are contextually inappropriate and lack conscious intent.

Although individuals with epilepsy who commit serious crimes may attempt to base their defense on such involuntary behavior, violations occurring under these conditions are usually minor, without evidence of planning or deliberate postictal concealment of the act.

Key words: epilepsy - crime - law

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KNOWLEDGE, AWARENESS AND SOCIAL ATTITUDES TOWARDS EPILEPSY AMONG NURSES IN NORTH MACEDONIA

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Abstract

Objective
This study aims at assessing the knowledge, awareness and social attitudes towards epilepsy and people with epilepsy (PWE), among nurses in North Macedonia (NM).
Methods
284 nurses employed in different departments of the City General Hospital in Skopje, NM were surveyed using an anonymous, self-administered questionnaire, which consisted of several sections: demographic data, general knowledge, social attitudes and practices related to epilepsy. The scale used to assess knowledge was: low knowledge was defined as the proportion of correctly answered knowledge questions < 50%, moderate knowledge level 50-75%, high knowledge level > 75%.
Results
All surveyed nurses reported being familiar with epilepsy. Their knowledge about epilepsy symptoms, causes, and treatment options, was moderate. The most commonly recognized symptom of epilepsy was convulsions, identified by 91.2% of respondents. Nurses identified "brain disease" as a possible epilepsy etiology significantly more often compared to other response options ($p < .0000$). When asked how they would respond to an epileptic seizure, nurses across all departments demonstrated a moderate level of knowledge. However, emergency center nurses had the highest percentage of correct responses compared to others ($p < .000$). Positive attitudes toward PWE were dominant among the respondents.
Conclusion: Continuing education and epilepsy certification programs are essential to improve the knowledge, awareness, and practices of nurses, enabling them to provide better care for people with epilepsy. It will also have a stimulating effect on strengthening positive social attitudes among them.
Key words: Knowledge, Social attitudes; Epilepsy, Nurses

POSTER PRESENTATIONS

ANTIPHOSPHOLIPID SYNDROME REVEALED THROUGH SEQUENTIAL ARTERIAL THROMBOTIC EVENTS: MESENTERIC ISCHEMIA PRECEDING MULTIFOCAL EMBOLIC STROKE

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Introduction: Antiphospholipid Syndrome (APS) is an autoimmune disorder with recurrent arterial or venous thrombosis. Sequential involvement of distinct vascular territories remains rare and diagnostically challenging.

Case Presentation: A 47-year-old man, without known vascular risk factors, presented with acute right-sided hemisyndrome, dysarthria, and moderate aphasia (NIHSS 15). MRI revealed multifocal ischemic infarcts in the left hemisphere. CT angiography revealed a floating thrombus in the left ICA with associated high-grade stenosis, as well as wall-adherent thrombi at the origin of the left subclavian artery and additional thrombi in the aortic arch. Dual antiplatelet therapy and Enoxaparin were initiated, followed by extracranial ICA stenting. Neurological status improved to NIHSS 3 at discharge. Several weeks earlier, the patient had undergone small-bowel and ileocecal resection for mesenteric ischemia with perforation.

Results: Serology revealed positive anticardiolipin antibodies, confirming APS as the underlying etiology of both gastrointestinal and cerebral thrombotic events. The simultaneous detection of thrombi in subclavian artery, ICA, and aortic arch highlighted the diffuse systemic nature of APS. The patient was discharged on oral anticoagulation with Phenprocoumon.

Conclusion: Our case emphasizes the need to consider APS in patients with recurrent unexplained arterial thrombosis, where early multidisciplinary management and sustained anticoagulation are essential.

Keywords: antiphospholipid syndrome, embolic stroke, mesenteric ischemia, systemic thrombosis, anticoagulation.

AUDIT OF ACUTE STROKE CARE PROCESSES AT THE DEPARTMENT FOR URGENT NEUROLOGY AT THE UNIVERSITY CLINIC OF NEUROLOGY-SKOPJE: FINDINGS FROM THE FIRST QUARTER OF 2025

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Introduction: Rapid reperfusion in acute stroke improves functional outcomes. Guidelines stipulate door-to-needle (DTN) times under 60 minutes for intravenous thrombolysis and door-to-groin puncture times under 90 minutes for endovascular therapy. Brain imaging should be completed within 25 minutes and interpreted within 45 minutes. This study assessed compliance with these benchmarks during January-March 2025.
Aim: To evaluate process metrics, reperfusion rates and early outcomes for acute stroke patients treated during the first quarter in 2025 at the Department for Urgent Neurology at the University Clinic of Neurology - Skopje and compare them with national averages and guideline targets.
Materials and Methods: A retrospective review of hospital information system data from 1 January to 31 March 2025 was conducted. Variables included patient demographics, stroke subtype, onset-to-door time, imaging and treatment times, use of intravenous thrombolysis and mechanical thrombectomy, and discharge metrics. Medians and percentages were calculated.
Results: Seventy-nine stroke cases were recorded (70 ischemic, 9 intracerebral haemorrhages). Median age was 71 years; 53 % were male. Pre-hospital EMS pre-notification occurred in only 7 %, and median onset-to-door time was 180 minutes. All patients underwent brain imaging; median door-to-imaging time was 26 minutes, achieving the < 25-minute target in 48 %. Occlusion was detected in all ischemic strokes. Intravenous thrombolysis was administered to 29 % of patients with a median DTN time of 53 minutes; 57 % of treated patients met the 60-minute benchmark. Mechanical thrombectomy was used in 1 %, with a median door-to-groin time of 194 minutes. Anticoagulation and antithrombotic prescription rates at discharge were 92 % and 100 %, respectively. Median discharge mRS was 5, and median discharge NIHSS was 6.
Conclusion: During the first quarter in 2025, the department achieved universal imaging and reasonable DTN times; however, pre-hospital notification and endovascular therapy uptake were low. Targeted interventions to shorten onset-to-door and door-to-groin times and increase reperfusion therapy use are needed to align fully with international standards.
Keywords: acute ischemic stroke; quality of care; door-to-needle time; intravenous thrombolysis; hospital audit.

IMPROVEMENTS AND CHALLENGES IN ACUTE STROKE CARE AT THE DEPARTMENT FOR URGENT NEUROLOGY AT THE UNIVERSITY CLINIC OF NEUROLOGY-SKOPJE: RESULTS FROM THE SECOND QUARTER 2025

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Introduction: Continuous monitoring of stroke care processes is essential to ensure timely reperfusion. Following baseline evaluation in the first quarter in 2025, targeted process improvements were introduced. This study reviews performance during April–June 2025, with an emphasis on imaging efficiency, reperfusion therapy use and patient outcomes.
Aim: To assess acute stroke care metrics in the second quarter of 2025 and determine how process measures and outcomes have evolved compared with the first quarter of 2025 at the Department for Urgent Neurology at the University Clinic of Neurology - Skopje.
Materials and Methods: A retrospective analysis of hospital information system data from 1 April to 30 June 2025 was performed. Variables included patient demographics, stroke subtype, onset-to-door time, imaging and treatment times, use of intravenous thrombolysis and mechanical thrombectomy, and discharge metrics. Data were summarised using medians and percentages and compared with earlier performance and national benchmarks.
Results: Twenty-eight stroke cases were treated (21 ischemic, 6 intracerebral haemorrhage, 1 subarachnoid haemorrhage). Median admission NIHSS was 13. EMS pre-notification remained absent; however, median onset-to-door time improved to 105 minutes and door-to-imaging time to 20 minutes. Occlusions were identified in 67 % of cases. Intravenous thrombolysis was administered to 35 % of patients and mechanical thrombectomy to 15 %, with an additional 5 % receiving combined therapy. Recanalization was achieved in 55 %. Despite increased reperfusion rates, median DTN time lengthened to 87 minutes, and only about half of treated patients met the $\leq$60-minute goal. Median door-to-groin puncture time improved substantially to 93 minutes, meeting guideline recommendations. Post-acute care indicators improved: carotid imaging was performed in 83 % of ischemic patients; anticoagulants were prescribed in 100 % of atrial fibrillation cases and antithrombotics in 82 % of non-atrial fibrillation cases. Median discharge mRS decreased to 4.5 and discharge NIHSS to 4, though median hospital stay increased slightly to 14 days.
Conclusion: The second quarter in 2025 showed enhanced imaging timeliness and a notable rise in mechanical thrombectomy use, with improved functional outcomes at discharge. However, prolonged DTN times and persistent absence of EMS pre-notification highlight ongoing challenges. Efforts should focus on refining intravenous thrombolysis workflows and strengthening pre-hospital coordination to sustain gains and meet international standards.
Keywords: stroke process improvement; mechanical thrombectomy; door-to-imaging time; reperfusion therapy; quality metrics.

NEONATAL NEUROPROTECTION

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Newborn deaths account for nearly half of all deaths in children under five, with 2.7 million lives lost each year. This represents a critical global health challenge, as most of these deaths are preventable, and inequities in access to care mean that newborns in fragile and vulnerable settings are disproportionately affected. Hypoxic-ischaemic encephalopathy (HIE) is a major contributor to this burden and remains a leading cause of neonatal death and long-term disability. Therapeutic hypothermia is the only proven therapy, though its benefits are not universal and its reach remains uneven across health systems. These combined limitations have accelerated research into novel and complementary neuroprotective strategies.

The purpose of this narrative review is to synthesise evidence on both established and emerging therapies for neonatal neuroprotection. Adjunctive care bundles that stabilise physiological parameters, control seizures, and optimise nutrition contribute to both short and long-term outcomes. Pharmacological agents such as erythropoietin and melatonin have demonstrated anti-inflammatory and antioxidant potential, whereas stem cell-based therapies are characterised by regenerative and immunomodulatory effects. Other experimental approaches, including magnesium sulphate, cannabinoids, and polyphenols such as curcumin and resveratrol, are under investigation but remain largely in preclinical or early clinical stages. Non-pharmacological measures, including family-centred developmental care and kangaroo mother care, further enhance neuroplasticity and cognitive outcomes. Neonatal neuroprotection is evolving toward integrated multimodal and holistic approaches that unite medical innovation with family-centred care. Future research must refine these strategies, close evidence gaps, and expand global accessibility to reduce disparities in neonatal survival and long-term neurological health.

PATIENT-REPORTED OUTCOMES SUPPORTING DECENTRALIZED ACCESS TO THERAPY IN NORTH MACEDONIA

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INTRODUCTION
Access to disease-modifying therapies (DMTs) is essential in managing multiple sclerosis (MS). However, the need to travel to the Neurology clinic in Skopje, to collect/receive the treatment creates significant challenges for patients and caregivers. So far, no one has assessed the extent and impact of these challenges.

OBJECTIVE
To gather data on the experiences of MS patients and caregivers in collecting/receiving the treatment, to support the Association's advocacy for making treatment available at healthcare institutions closer to patients' homes.

METHODOLOGY
An anonymous survey was conducted and involved 92 participants, from different regions across the country. The 13-question survey was designed to capture demographic data, the burden of traveling, and financial and personal impact associated with the current treatment model.

RESULTS
The results show that 90% of respondents were MS patients, remaining caregivers. 57% of respondents stated that they need assistance to travel to Skopje to receive/collect their treatment, whereas only 42% reported being able to do so independently. More than half of the patients (54%) travel to the Neurology Clinic once monthly, while 31% visit every six months. 44% of respondents need <1 hour to reach Skopje, but nearly 30% require >2 hours for a one-way trip. While 38% of patients manage to complete the therapy collection/administration process in <1 hour (excluding travel time), 20% reported that this process takes between 2-4 hours, and 25% require >4 hours to complete it. Over one-third of respondents reported spending <500 MKD per visit for transportation and a snack; however, 27% stated that their costs ranged from 1,000 - 3,000 MKD, and 18% reported spending >3,000 MKD per visit. Nearly 70% of patients reported experiencing fatigue and physical exhaustion after the trip, 56% lost a workday or had to take time off, 40% identified the associated costs as a financial strain, and 32% reported difficulties in organizing the trip to the Neurology Clinic.

Most significantly, 85% of respondents expressed strong willingness and preference for receiving or collecting therapy at a healthcare institution closer to their home. Furthermore, more than 80% believed that such a change would improve their quality of life.

CONCLUSION
This work provides clear evidence that the current centralized model for MS treatment presents substantial logistical, physical, and financial burdens for most patients and caregivers. Many rely on support from others to travel, lose valuable time, and experience exhaustion and financial strain. The overwhelming preference for decentralized treatment access highlights a crucial opportunity for

improving outcomes and quality of life. Facilitating access to MS treatments through regional healthcare institutions would not only alleviate these burdens but also align care delivery with the real-life needs of MS patients.

Keywords: MS, multiple sclerosis, care, decentralization, treatment, need, patient

UNDERSTANDING THE DIAGNOSTIC JOURNEY OF PEOPLE LIVING WITH MULTIPLE SCLEROSIS IN NORTH MACEDONIA

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INTRODUCTION

Multiple Sclerosis (MS) is a chronic, progressive neurological disease that significantly impacts patients' quality of life. Early diagnosis and timely initiation of disease-modifying therapies (DMTs) are crucial for delaying disease progression. In North Macedonia, the diagnostic journey for MS remains underexplored. Understanding this pathway can help identify delays and barriers in accessing care.

OBJECTIVE

This research aims to understand the diagnostic journey of people living with MS in North Macedonia. The study seeks to identify key challenges and barriers to diagnosis and treatment, and to raise awareness of the unmet needs among this patient population.

METHODOLOGY

An anonymous, online questionnaire was developed specifically for this study. It included 8 targeted questions and a consent question. The survey was shared through email and completed by 104 participants.

RESULTS

Among respondents, 95.2% were people living with MS, the rest were caregivers. Regarding the first symptom experienced, 52.9% reported vision problems, 36.5% difficulties with walking, 36.5% numbness, 19.2% fatigue, and 8.7% pain. From symptom onset to seeing a specialist: 38.5% sought care in under a month, while 32.7% waited over a year. The first specialist seen was most commonly a neurologist (60.6%) or ophthalmologist (27.9%). Time to diagnosis: 52.9% were diagnosed within 3 months, but 12.5% waited over 5 years. Time from diagnosis to treatment initiation varied: 27.9% waited more than a year, while only 15.4% began treatment within a month, 17.3% of participants reported not receiving DMTs. Reasons included: use of alternative therapy/Vitamin D (66.6%), being on a waiting list (27.7%), or participation in a clinical trial (5.6%).

CONCLUSION

This research highlights important delays and gaps in the MS care pathway in North Macedonia. Streamlining referral processes, enhancing early recognition, and expanding access to timely treatment are crucial to improving outcomes for individuals with MS.

Keywords: MS, multiple sclerosis, diagnosis, symptom, challenges, access

PSEUDOPARATHYROID SYNDROME AND NEUROLOGICAL MANIFESTATIONS – A CASE REPORT

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Abstract:

Introduction: Pseudoparathyroid syndrome is a rare endocrine disorder caused by genetic mutations that result in tissue resistance to parathyroid hormone (PTH). The most common mutation is in the GNAS gene, which leads to impaired signaling of the Gsα protein and a clinical picture with hypocalcemia, hyperphosphatemia and secondary skeletal and cognitive changes.

Material and methods: We present a case of a 17-year-old patient with neurological manifestations in the form of cognitive impairment and pronounced forgetfulness. Laboratory analyses revealed biochemical abnormalities characteristic of pseudoparathyroidism, and radiological bone examinations showed changes consistent with the diagnosis. Neurological diagnostic procedures performed included: MRI with TOF, Evoked Potentials, neuropsychological testing, and more.

Conclusion: Based on clinical, laboratory, and genetic findings, patient was diagnosed with pseudoparathyroid syndrome, and he was referred for further treatment by an endocrinologist. This case highlights the importance of early recognition of endocrine disorders in adolescents with cognitive impairment and neurological symptoms, as well as the role of genetic testing in confirming the diagnosis and guiding therapy.

Keywords: pseudoparathyroid syndrome, GNAS mutation, cognitive disorders, hypocalcemia, adolescent

ПСЕВДОПАРАТИРОИДЕН СИНДРОМ И НЕВРОЛОШКИ МАНИФЕСТАЦИИ- ПРИКАЗ НА СЛУЧАЈ

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Универзитетска Клиника за Неврологија, Клинички центар Скопје

Абстракт:
Вовед: Псевдопаратироидниот синдром е ретко ендокрино нарушување предизвикано од генетски мутации кои резултираат со отпорност на ткивата кон паратироидниот хормон (ПТХ). Најчесто се работи за мутација во GNAS генот, што доведува до нарушена сигнализација на Gsα протеинот и клиничка слика со хипокалцемија, хиперфосфатемија и секундарни скелетни и когнитивни промени.
Материјал и методи: Прикажуваме случај на 17-годишен пациент со невролошки манифестации во вид на когнитивно страдање и изразена заборавност. Лабораториските анализи откриј биохемиски нарушувања карактеристични за псевдопаратироидизам, а радиолошките испитувања на коските покажаа промени конзистентни со дијагнозата. Во невролошките дијагностички процедури направени се: МРИ со ТОФ, Евоцирани потенцијали, невропсихолошко тестирање и друго.
Заклучок: Врз основа на клиничките, лабораториските и генетските наоди беше поставена дијагноза псевдопаратироиден синдром и упатен е за пнатамошен третман од страна на ендокринолог. Овој случај ја нагласува важноста на навременото препознавање на ендокрините нарушувања кај адолесценти со когнитивни потешкотии и невролошки симптоми, како и улогата на генетското тестирање во потврдувањето на дијагнозата и водењето на терапијата.
Клучни зборови: псевдопаратироиден синдром, GNAS мутација, когнитивни
Keywords: pseudohypoparathyroidism, GNAS mutation, cognitive impairment, hypocalcemia, adolescent

EPILEPSY ASSOCIATED WITH RIGHT FRONTAL SUBCORTICAK HETEROTOPIA: A 14-YEAR CASE HISTORY WITH FAVORABLE MEDICAL RESPONSE

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Background:
Subcortical heterotopia represents a neuronal migration disorder frequently associated with focal epilepsy. Clinical presentation and seizure control vary depending on the size, location, and extent of the heterotopic tissue.

Purpose:
To present a case of focal epilepsy associated with right frontal subcortical nodular heterotopia and discuss the clinical features, imaging findings, and therapeutic response.

Results:
We report a 36-year-old male, active in football training, with a 14-year history of epileptic seizures. The seizures typically occurred during sleep, often preceded by an indistinct aura. Heteroanamnestic data suggested tonic-clonic episodes with preserved auditory perception but inability to respond. Routine and sleep-deprived EEG were normal. MRI revealed disturbed gyral and sulcal architecture of the right frontal lobe with a subcortical nodular heterotopia extending to the frontal horn of the right lateral ventricle, associated with mild ventricular asymmetry. A 2.3 cm arachnoid cyst was also noted in the left posterior cranial fossa. The patient was initially treated with carbamazepine, later switched to oxcarbazepine, achieving seizure stability after dose adjustment.

Conclusion:
This case illustrates epilepsy secondary to right frontal subcortical heterotopia, underlining the diagnostic significance of MRI in patients with normal EEG findings. Adequate antiseizure therapy with oxcarbazepine led to clinical stabilization, highlighting the potential for favorable outcomes with optimized medical management.

Keywords: Epilepsy, Subcortical nodular heterotopia, Right Frontal Lobe, Aura, Nocturnal Seizures.

DIAGNOSTIC CHALLENGE: CNS VASCULITIS DUE TO HEPATITIS C PRESENTING WITH MULTIFOCAL DEFICITS

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Background
Hepatitis C virus (HCV) affects over 170 million people worldwide and can cause both hepatic and extra-hepatic manifestations. Up to 10% of patients develop conditions such as mixed cryoglobulinemia or lymphoproliferative disorders. Rarely, HCV can trigger cryoglobulinemic vasculitis involving the central nervous system (CNS), which may present with acute neurological deficits and mimic cerebrovascular disorders, delaying diagnosis.

Case Presentation
A 46-year-old man with no prior medical history presented with four days of dysarthria and dysphagia, preceded by one month of gait disturbance and clumsiness. Family history was notable for paternal stroke.
Neurological examination revealed dysarthria, dysphagia with left uvular deviation, paresis of the soft palate, diminished pharyngeal and palatal reflexes, latent left hemiparesis with brisk reflexes, and bilateral Babinski signs.
CT showed venous sinus enhancement with periventricular and subcortical hypodensities. MRI revealed widespread periventricular and deep white matter lesions in the corona radiata, centrum semiovale, internal/external capsules, and brainstem. Some lesions displayed diffusion restriction (acute lacunes), others contained hemosiderin deposits.
Extensive evaluation – including CT venography, cervical and intracranial Doppler, and bubble test – was unremarkable. Lumbar puncture revealed intrathecal immune activity. Echocardiography and cardiology assessment excluded cardiac sources. Genetic testing for thrombophilia was negative. Routine bloodwork, tumor markers, endocrine, and rheumatological studies were normal. Viral serology was positive for anti-HCV antibodies, confirming HCV-associated CNS vasculitis.

Discussion
Although initial findings suggested venous sinus thrombosis or ischemic stroke, systematic exclusion of cardiac and thrombophilic causes, along with intrathecal immune activity, redirected attention to inflammatory and infectious etiologies. The diagnosis of HCV-related CNS vasculitis explained the multifocal lesions and progressive course.

Conclusion
CNS vasculitis secondary to HCV can present with acute neurological deficits in adults younger than the typical cerebrovascular population. A broad, multidisciplinary work-up – including viral serology – is essential for timely recognition of this rare but treatable condition.

Keywords
Hepatitis C; CNS vasculitis; Dysarthria; White matter lesions

SWIFT BRIDGING THERAPY: ACHIEVING FULL REPERFUSION IN MCA STROKE

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Background:
Acute ischemic stroke due to large vessel occlusion remains a leading cause of disability and mortality. Early recanalization by intravenous thrombolysis (IVT) and/or mechanical thrombectomy (MT) significantly improves outcomes. We present a case of successful reperfusion after bridging therapy in a patient with middle cerebral artery (MCA) occlusion.
Case presentation:
A 61-year-old female with arterial hypertension, hypercholesterolemia, and a 30-year smoking history presented with sudden-onset right-sided hemiparesis and speech disturbance. Neurological examination revealed severe deficit with NIHSS 10 and pre-stroke mRS 0, current mRS 5. Non-contrast CT showed no acute ischemic changes. The patient underwent IVT within the therapeutic time window. Shortly after thrombolysis, her neurological status improved transiently (NIHSS decreased to 2-4), followed by rapid deterioration back to NIHSS 10. Emergency mechanical thrombectomy was performed, achieving complete recanalization (TICI 3) of the right MCA (M1 segment).
Conclusion:
This case highlights the importance of early recognition and prompt escalation from IVT to MT in acute ischemic stroke due to large vessel occlusion. Bridging therapy allowed successful reperfusion and a favorable neurological outcome (NIHSS 0, mRS 0). Such cases emphasize the need for multidisciplinary collaboration and streamlined stroke pathways to ensure optimal patient care.
Keywords:
Intravenous thrombolysis, Mechanical thrombectomy, Stroke

BRAIN HEALTH PROTECTION FOR DISABILITY PREVENTION IN NEUROLOGICAL DISEASES

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Introduction:
Brain health (BH) promotion and prevention of neurological disorders (ND) are important tasks for the health care system. Timely diagnosis, treatment, care, rehabilitation, and research of ND are for the benefit of healthier future. BH is a state in which every individual, regardless of whether healthy or diseased, can realize his/her own abilities and optimize cognitive, emotional, psychological, and behavioral functioning to cope with life situations. ND are the leading cause of disability and disability adjusted life-years (DALYs), and second largest contributors to mortality worldwide. The global burden of ND of 43% is growing with the growing and aging of the world population.
Methods: Cognitive functioning was evaluated in 553 patients with ND with standardized neuropsychological tests in longitudinal study at the University clinic for neurology, from 2018-2022
Results: Cognitive disability, regardless of physical disability, was found in 78% of 60 stroke patients, in 52,7% of 91 epilepsy patients, in 31 of 32 patients with parkinsonism and in all 17 patients with multiple sclerosis and 353 patients with dementia. Cognitive disability plays important role in the loss of their independent functioning. ND prevention and early detection, treatment and rehabilitation will reduce the burden of the ND on the family members, caregivers and society, and will improve the health and life quality in society.
Conclusion: Screening for BH risk factors and targeting BH risk factors: traumatic brain injury, smoking, excessive alcohol use, air pollution, infections, high blood sugar, dyslipidemia, high blood pressure, obesity, lack of physical, mental and societal activity, depression, less education, hearing and visual impairment, sleep disorders, lack of dental health, unhealthy diet and many other risk factors from preconception to elderly, and building strategy for BH promotion, prevention, treatment, care, rehabilitation, and research of ND will reduce the burden of ND, building a healthier future for our brains.
Keywords: brain health, neurological diseases, neurocognitive evaluation

CEREBRAL ATROPHY AND EPILEPSY – A TWO-WAY STREET: A CASE REPORT

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Introduction: The relationship between the epilepsy which contributes to the atrophy, and the damaged brain (specifically cerebellum) that loses its ability to inhibit epileptic activity, potentially worsening the condition.

Objective: structural abnormalities and epilepsy

Methods: clinical records, neuroimaging findings, EEG, laboratory test findings

Case report : 23 years old female patient complains of a left-sided headache and quick jerks in her left arm (dropping objects from her hand, hitting objects) after waking up for more then 4 years. She fell several times but did not lose consciousness. Treated under the diagnosis of phobic disorders with Escitalopram. At 14 years, examined at the Children's Clinic for obesity. According to heteroanamnestic data she once had a seizure at the age of 6 (no medical data). EEG performed in support of generalized epilepsy and brain MRI - brain stem, cerebellum and cerebrum with atrophic changes, with consecutive dilatation of the ventricular system and marked subarachnoid spaces. Widened Virchow-Robin spaces at the level of the anterior commissures and centrum semiovale bill. Treatment was started with Levetiracetam 2x250 mg for 2 weeks, during which time she had no seisures and she feels better.

Conclusion : Atrophy at age 23 with epilepsy is a red flag that epilepsy may not be just "idiopathic" and it suggests an underlying pathology affecting brain health more globally. The most likely considerations are progressive myoclonic epilepsies (such as Lafora, Unverricht-Lundborg, MERRF) or a metabolic/genetic cause – rather than idiopathic epilepsies like JME. To conduct further investigations: genetic testing, metabolic panels, neurocognitive assessments, and possibly advanced MRI sequences, she was referred to the Neurology Clinic.

Keywords: brain atrophy, epilepsy

CAMPTOCORMIA – BENT SPINE SYNDROME (BSS), IN A PATIENT WITH PARKINSON'S DISEASE

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Introduction: Parkinson's disease is a neurodegenerative disorder with a wide range of clinical features that include both motor and nonmotor symptoms. Because of its diversity, the progression of the disease may be different from one person to another.

Objective: Camptocormia is abnormal thoracolumbal spinal flexion, which is a forward bending of the lower joints of the spine, occurring in a standing position, increasing during walking and abating in supine position. There are two common origins: neurological and muscular, Now it is recognized in addition to psychiatric syndromes. Camptocormia in Parkinsonism is caused by axial dystonia, which is the hallmark of Parkinson's disease.

Methods: We analyzed medical records, radiographical and neuroimaging findings.

Case presentation: A 67-year-old female diagnosed 5 years ago with Parkinson's disease was examined due to difficulty moving, significantly reduced dexterity of the right hand, painful muscle cramps throughout the body during the night. Urinary incontinence is present.

Neurologic examination:The examination was demonstrated diminished facial expressivity,"masked facies", hypophonia, bradilalia, swallowing is preserved. Neck with minimal rigidity. Generally bradykinetic active movements with extrapyramidal type hypertonia of the upper limbs, especially the right upper limb. Dystonia of the right hand. Generally more lively MTR. Hypodiadochokinesia of both hands. Coordination tests are performed slowly without dysmetria, no intention tremor. Tremor is not registered. Lost synkinetic movements of the upper extremities during movement, with anteflexed body position, drop head is present. Dragging of both legs. Camptocormia phenomenon is present. Urinary incontinence.

Results: The CT scans of the brain showed diffuse cortical reduction, radiographic images of the spine cord were normal.

The patient was treated with antiparkinsonian, substitution, and symptomatic therapy.

Conclusion: Our patient described a reduction in movements and difficulty associated with rigidity, gait impairment as well as cognitive changes and autonomic dysfunction.

Keywords: Camptocormia, Axial myopathy, Muscular dystrophies, Parkinson's disease.

HOMOZYGOUS ALS2 PATHOGENIC VARIANT IN A PEDIATRIC PATIENT: A CASE REPORT

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Background
Recent studies reported an incidence of ALS between 0.6 and 3.8 per 100,000 and estimated prevalence of 0.008 cases per 100,000 inhabitants with onset of symptoms before age 18, representing less than 0.1% of all ALS cases are pediatric. Mutations in the ALS2 gene, encoding the alsin protein, are associated with a spectrum of autosomal recessive motor neuron disorders, including juvenile amyotrophic lateral sclerosis (ALS2), infantile ascending hereditary spastic paralysis, and primary lateral sclerosis. These conditions manifest in early childhood with progressive motor impairment, spasticity, and developmental delay.
Objective
To present a case of a pediatric patient with ALS2-associated disorder identified through whole-exome sequencing (WES) and to emphasize the role of genomic analysis in rare disease diagnosis and management.
Case Presentation
A 13-year-old male was evaluated for motor developmental delay, hypotonia, and progressive motor dysfunction initially suspected to represent infantile cerebral palsy. Whole-exome sequencing revealed a homozygous pathogenic nonsense variant in ALS2: NM_020919.4:c.4261C>T (p.Arg1421Ter). Parental testing confirmed heterozygosity in both parents, consistent with autosomal recessive inheritance. No additional pathogenic variants or ACMG secondary findings were detected.
Results
Genetic Analysis: Homozygous ALS2 pathogenic variant confirmed. Chromosomal Findings: Continuous regions of homozygosity on chromosome 2, suggesting possible parental consanguinity.
Management
The patient is currently under multidisciplinary care, including neurology follow-up, physiotherapy, and genetic counseling for recurrence risk assessment.
Conclusion
This case underscores the importance of genomic testing in children presenting with early-onset motor impairment resembling spastic cerebral palsy. Identification of ALS2 mutations enables accurate diagnosis, appropriate management, and targeted family counseling.
Keywords
ALS2, amyotrophic lateral sclerosis, infantile cerebral palsy, whole-exome sequencing, pediatric neurology, genetic diagnosis.

ADDRESSING THE UNMET MEDICAL NEEDS IN DUCHENNE MUSCULAR DYSTROPHY: THE CASE FOR EARLY INTRODUCTION OF INNOVATIVE THERAPIES IN NORTH MACEDONIA

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INTRODUCTION:
Duchenne muscular dystrophy (DMD) is a rare, X-linked neuromuscular disorder caused by mutations in the *DMD* gene, leading to absent or non-functional dystrophin protein. This results in progressive muscle degeneration, severe physical disability, diminished quality of life, and premature death. Although affecting approximately 1 in 5,000 newborn boys worldwide, the therapeutic landscape remains limited, especially in countries like North Macedonia, where only corticosteroids and physiotherapy are currently available.

OBJECTIVE:
To outline the current treatment challenges for DMD patients in North Macedonia and emphasize the urgent need for the introduction of innovative therapies that modify disease progression by targeting its underlying cause.

METHODS:
A comprehensive review of clinical literature, treatment guidelines, and real-world management practices was combined with local experts' insights into the treatment of DMD in North Macedonia.

RESULTS:
The standard of care in North Macedonia is limited to corticosteroids, which only slow disease progression without restoring dystrophin or preventing irreversible muscle damage. In contrast, recent EMA approvals offer new hope. These include novel steroidal anti-inflammatory agent (vamorolone) associated with less side effects compared to traditional corticosteroids, making is a promising alternative for long-term use; histone deacetylase inhibitor (givinostat) that modulates gene expression to reduce inflammation, fibrosis and muscle degeneration. Additionally, dystrophin-restoring gene therapy (delandistrogene moxeparvovec) targeting the underlying genetic cause became recently available. Its clinical data shows durable improvements in motor function for up to 5 years, demonstrating the potential to significantly modify the disease course. Crucially, none of these advanced, disease-modifying treatments are available in North Macedonia, resulting in a significant gap in care.

CONCLUSION:
There is an urgent need to accelerate access to innovative disease-modifying therapies for DMD patients in North Macedonia. Early intervention with modern treatments that target the root cause of the disease, supported by multidisciplinary care, is essential to improve long-term outcomes and quality of life for this vulnerable patient population.

Keywords: DMD, Duchenne, neuromuscular, treatment, patients

IMPROVING TREATMENT CONVENIENCE FOR SMA PATIENTS: THE POTENTIAL OF RISDIPLAM TABLET FORMULATION IN NORTH MACEDONIA

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INTRODUCTION:
Spinal muscular atrophy (SMA) is a rare neuromuscular disorder requiring lifelong treatment. Risdiplam (Evrysdi®) has transformed SMA care, offering the first oral, non-invasive therapy suitable for all ages and disease severities at home. In North Macedonia, 15 SMA patients (pediatric and adults) are currently receiving risdiplam in its liquid formulation. While efficacious and well-tolerated, the liquid form presents challenges in daily practice, including cold-chain requirements, reconstitution by healthcare professionals, syringe-based administration, plastic waste, and difficulties with self-administration, particularly for patients with weaker motor function skills.

OBJECTIVE:
To evaluate the potential additional benefits of the newly approved risdiplam tablet formulation in improving treatment convenience and patient independence, without compromising efficacy or safety.

METHODS:
Review of patient experiences from the two SMA centers in Skopje, the University Clinic of Pediatric Diseases and the University Clinic of Neurology, combined with patient's insights and bioequivalence data from the Phase 1 study (NCT04718181), as well as early real-world evidence from countries where the tablet formulation is already available.

RESULTS:
The bioequivalence study confirmed that risdiplam tablets provide the same systemic exposure (CNS and peripheral tissues), high efficacy, and tolerability as the liquid formulation, which has been used by over 18,000 patients worldwide. The tablet is indicated for patients older than 2 years and weighing more than 20 kg, can be swallowed whole or dispersed in water, adapting to the patient's abilities. It is room-temperature stable, eliminating the need for refrigeration and simplifying storage, transport, and travel. Early-launch countries report improved patient satisfaction, greater independence, and reduced caregiver burden. Blister packaging offers easier handling, particularly for patients with reduced motor function.

CONCLUSION:
Given its multiple advantages in terms of convenience, independence, and quality of life, the risdiplam tablet should be made available to the eligible SMA patients in North Macedonia without delay. This will further optimize treatment experience alongside the already proven efficacy and safety of risdiplam.

Keywords: risdiplam, SMA, spinal muscular atrophy, tablet, convenience

EPILEPTIC ENCEPHALOPATHY ASSOCIATED WITH A PATHOGENIC VARIANT IN THE PACS2 GENE

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Introduction:
To describe the clinical and genetic findings in a girl diagnosed with a pathogenic variant c.625G>A (p.Glu209Lys) in the PACS2 gene, highlighting its association with neurodevelopmental and mitochondrial dysfunction.

Methods:
A comprehensive clinical evaluation was performed, including developmental and neurological assessments, and imaging studies. Whole exome sequencing (WES) was conducted to identify the genetic basis of the patient's condition, followed by segregation analysis in family members. Functional analysis was referenced from existing literature to assess the impact of the identified variant.

Results:
The patient presented with global developmental delay, hypotonia, epilepsy, and subtle distinctive facial features. According to the developmental assessment, mostly motor function was affected. Brain MRI didn't showed structural anomalies consistent with the disease's manifestations. Genetic analysis identified a heterozygous pathogenic variant c.625G>A (p.Glu209Lys) in the PACS2 gene, confirmed by segregation analysis as *de novo*. This mutation likely disrupted protein trafficking and mitochondrial function, as suggested by previous functional studies.

Conclusions:
The c.625G>A (p.Glu209Lys) mutation in the PACS2 gene represents a pathogenic variant linked to a severe neurodevelopmental deficit phenotype with mitochondrial dysfunction. PACS2 is a critical regulator of intracellular trafficking, apoptosis, and mitochondrial-endoplasmic reticulum communication. Variants in PACS2 are rare, with few reported cases in the literature. This case underscores the importance of genetic testing in elucidating rare neurodevelopmental disorders and expands the clinical spectrum associated with PACS2 mutations. Due to the rarity of PACS2 mutations, additional research is also essential to develop evidence-based therapeutic strategies. Collaborative efforts among clinicians and researchers in sharing case data are vital for enhancing our understanding and management of PACS2-associated epilepsy

WHEN ECLAMPSIA IS NOT THE ANSWER: POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (PRES) IN A YOUNG POSTPARTUM 22-YEAR-OLD WOMAN - A CASE REPORT

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Introduction

Posterior reversible encephalopathy syndrome (PRES) is a clinical/radiological syndrome characterized by a headache, seizures, altered mental status and visual loss. It is characterized by white matter vasogenic edema affecting predominantly the posterior occipital and parietal lobes of the brain. This clinical syndrome is increasingly recognized due to improvement and availability of brain imaging, specifically magnetic resonance imaging (MRI).

Case Report

We report the case of a 22-year-old female admitted at the Department for Urgent Neurology at the University Clinic of Neurology with generalized tonic-clonic seizures, tremor, and extremity spasms in the postpartum period. The patient had undergone Cesarean delivery four days earlier and had a history of gestational hypertension, treated with Methyldopa. Initial presentation included confusion, impaired consciousness and repeated convulsions, clinically consistent with eclampsia.
Laboratory evaluation revealed leukocytosis, elevated C reactive protein (CRP), and abnormal liver enzymes, while electrolytes and renal function were within normal limits. Neuroimaging (computer tomography (CT) and MRI)) demonstrated bilateral parieto-occipital hyperintensities, compatible with Posterior Reversible Encephalopathy Syndrome (PRES). Ophthalmological examination showed no significant retinal changes. Electroencephalography (EEG) confirmed diffuse cerebral dysfunction with epileptiform discharges. Microbiology and infectious workup were negative.
The patient was treated with anticonvulsants (Levetiracetam, Valproate, Diazepam) and corticosteroids, along with antihypertensive and supportive therapy. Control neuroimaging confirmed gradual regression of the lesions. During hospitalization, neuropsychological assessment revealed mild cognitive deficits (attention, memory, and visuospatial functioning), but with progressive improvement.
The clinical outcome was favorable: the patient achieved full recovery of consciousness, stabilization of vital parameters, and significant motor and cognitive improvement. She was discharged with recommendations for continuation of anticonvulsant, antihypertensive, and supportive therapy, with scheduled outpatient follow-up.

Conclusion

This case highlights the diagnostic and therapeutic challenges of differentiating eclampsia-associated seizures from PRES in the postpartum period. Prompt recognition, aggressive seizure control, blood pressure management, and supportive care are essential for favorable neurological and systemic outcomes.

Key words: posterior reversible encephalopathy syndrome (PRES), eclampsia, seizures

MANAGEMENT CHALLENGES IN REFRACTORY EPILEPSY DUE TO POST-TRAUMATIC GLIOSIS: TWO ILLUSTRATIVE CASES

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Background
Post-traumatic gliosis is a recognized epileptogenic substrate associated with pharmacoresistant seizures. Gliotic scarring alters cortical excitability, frequently resulting in difficult-to-control epileptic seizures despite polytherapy with antiepileptic drugs (AEDs).
Case Report 1
A male patient developed epilepsy several months after head trauma, presenting with recurrent seizures involving the left hemiface and limbs, occasionally progressing to status epilepticus. Brain MRI revealed right parietal gliosis. Despite multiple AEDs–including carbamazepine, levetiracetam, clonazepam, and phenobarbitone–seizures persisted with high frequency. Vagus nerve stimulation (VNS) was implanted, and lacosamide was added, leading to a modest reduction in seizure burden.

Case Report 2
A 23-year-old female with right frontotemporal post-traumatic gliosis presented with seizures consistent with frequent focal motor seizures involving the left hemiface and extremities, with occasional secondary generalization. Optimized AED therapy–including carbamazepine, levetiracetam, diazepam, and phenobarbitone–reduced seizure frequency to 1-2 episodes per month. Pregnancy during follow-up limited further treatment adjustments. Neuromodulation was not pursued.
Discussion
Although both patients shared similar imaging findings and semiology, their clinical trajectories diverged. The first case required VNS and extensive polytherapy, while the second achieved partial control with AEDs alone. Comorbidities, particularly pregnancy, significantly influenced therapeutic decisions. These cases underscore the heterogeneity of post-traumatic gliosis-related epilepsy and highlight the complexity of achieving optimal seizure control.
Conclusion
Epilepsy secondary to post-traumatic gliosis requires individualized treatment strategies. Neuromodulation may benefit highly refractory patients, whereas others may achieve meaningful seizure reduction with AEDs alone. Careful consideration of comorbidities is essential to optimize outcomes and quality of life.
Keywords: post-traumatic gliosis, refractory epilepsy, epileptic seizures, vagus nerve stimulation (VNS), antiepileptic drugs (AEDs)

SILENT THREATS: CARDIOEMBOLIC STROKE IN A PATIENT WITH TNNI3-RELATED CARDIOMYOPATHY

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Introduction:
Dilated cardiomyopathy (DCM) is associated with an increased risk of cardioembolic events, even in the absence of atrial fibrillation (AF). The role of anticoagulation in these patients remains debated, particularly in genetically mediated cases. We present a case highlighting the clinical implications of a mutation in the TNNI3 gene in a patient with DCM and embolic stroke.

Case Presentation:
A 45-year-old woman with a known history of DCM and moderately reduced ejection fraction (EF 41%) presented with sudden-onset aphasia, right-sided weakness, and visual field deficits. Brain MRI revealed acute infarction in the left temporo-parieto-occipital region and a subacute infarct in the contralateral temporal lobe–suggestive of a cardioembolic mechanism. Transthoracic echocardiography showed chamber dilation and global hypokinesis, with no thrombus or valvular abnormality. Cardiac rhythm monitoring confirmed persistent sinus rhythm. Although the TNNI3 mutation is rare and most commonly associated with hypertrophic and restrictive cardiomyopathy, it has been sporadically reported in DCM and may contribute to arrhythmogenic and thromboembolic risk.
Given the embolic stroke pattern, reduced EF, and genetic predisposition, the patient was started on Rivaroxaban (20 mg daily), alongside optimized heart failure therapy and rehabilitation.

Discussion:
Although large trials such as WARCEF and COMMANDER-HF do not support routine anticoagulation in heart failure patients in sinus rhythm, individual risk factors–such as embolic stroke patterns and pathogenic mutations–may warrant deviation from guideline-based treatment. TNNI3 mutations, though rare in DCM, may confer increased thromboembolic and arrhythmic risk, supporting anticoagulation in selected cases.

Conclusion:
Genetic evaluation can refine thromboembolic risk stratification in DCM patients. In this case, anticoagulation with a direct oral anticoagulant was justified despite the absence of AF. Personalized therapy guided by clinical and genetic data may improve outcomes in complex cardioembolic presentations.

Keywords:
cardioembolic stroke, dilated cardiomyopathy, TNNI3 mutation, heart failure, genetic testing, anticoagulation

EXPANDING THE NEUROLOGICAL SPECTRUM OF VAN MALDERGEM SYNDROME: EPILEPSY WITH MYOCLONIC SEIZURES.

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Background
Van Maldergem syndrome (VMS) is a rare autosomal recessive disorder, with only 13 patients reported to date. It is characterized by craniofacial anomalies, delayed neurodevelopment, skeletal deformities, and involvement of multiple organ systems. Epileptic seizures have been only rarely described in VMS, and their semiology appears to be heterogeneous. The estimated prevalence is well below 1 in 1,000,000 live births, with very few documented cases worldwide and even fewer associated with epilepsy.
Case presentation
We present a 15-year-old male with genetically confirmed VMS, renal agenesis, recurrent nephrolithiasis, thoracolumbar scoliosis, and syringomyelia. He was admitted due to recurrent generalized myoclonic jerks, predominantly occurring in the morning upon awakening, occasionally leading to falls and injuries. EEG demonstrated bilateral high-voltage spike-wave and polyspike-wave discharges, predominantly originating from the right temporoparietal region, with clear electroclinical correlation. Neuroimaging revealed craniofacial dysmorphism and cortical atrophy without acute lesions. During hospitalization, repetitive myoclonic seizures were captured with focal onset confirmed on EEG. Antiepileptic therapy with levetiracetam was initiated, with recommendation for follow-up MRI.
Discussion
The neurological manifestations of VMS are broad, but epileptic seizures remain a rare and poorly characterized feature. Most published cases focus on structural brain malformations and developmental delay, with limited electroclinical data. Our patient's presentation with generalized myoclonia expands the recognized clinical spectrum of VMS and underscores the need for systematic epilepsy screening in patients with complex genetic syndromes, even when seizures are not a well-established component.
Conclusion
This case contributes to the scarce literature on epilepsy in VMS, showing that generalized myoclonic seizures may form part of the phenotype. Early EEG evaluation and neuroimaging are crucial for accurate diagnosis and timely initiation of therapy in such exceptionally rare disorders.
Keywords:
Van Maldergem syndrome, epilepsy, generalized myoclonus, EEG, pediatric neurology

UNEXPECTED MIMICRY: ACUTE NEUROLOGICAL DEFICIT AS THE FIRST MANIFESTATION OF AORTIC DISSECTION

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Introduction: Aortic dissection is a rare life-threatening condition – it can present as an acute neurological crisis, with catastrophic consequences if not recognized early. Although often considered a vascular disease, its neurological symptoms can cause significant diagnostic confusion. The aim of the case report is to highlight how this condition can mimic a stroke-like condition and how important is to maintain high index of suspicion.
Case presentation: A 56-year-old male was brought to the Neurology Clinic with symptoms with acute onset, namely altered consciousness, left-sided hemiparesis and dyspnea. The patient's history revealed that he had been found lying on the floor, with vomiting and acute neurological symptoms. Upon admission, the patient was agitated and somnolent, with positive left-sided pyramidal symptoms, while the hemiparesis improved rapidly. A brain CT scan showed no intracranial hemorrhage. However, CT angiography of the head and neck revealed dissection of the left carotid artery, raising suspicion of aortic dissection. A subsequent CT angiography of the aorta confirmed Type A dissection (or DeBakey type I), with compression of the true lumen, resulting in hypoperfusion of vital organs, particularly the kidneys and brain. Significantly elevated D-dimer levels (>10,000 ng/mL) confirmed the hypothesis of a vascular catastrophic event, explaining the transient left-sided weakness and neurological symptoms as a result of vascular insufficiency rather than a stroke. The patient was referred to a cardiovascular unit for open aortic surgery and graft placement. Afterwards, the patient made regular neurological follow-up examinations, and 2 years after the event, remains without over neurological residues.
Conclusion: Although acute pain remains the main clinical manifestation behind this condition, portion of the patients present with without intense pain and show neurological symptoms that can be consequence of vascular insufficiency or true brain infarction. Neurological mimics such as aortic dissection can be masked as a stroke or other vascular diseases, and thus a multidisciplinary approach is essential for rapid and accurate identification. Prompt recognition of this condition and timely initiation of treatment could mean the difference between life and death.
Keywords: aortic dissection, neurological mimic, acute neurological deficit, CT angiography , vascular insufficiency

NEW ONSET EPILEPTIC SEIZURES, ALTERED BEHAVIOR OR CONFUSIONAL STATES IN ELDERLY- CASE REPORT

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Case Report
Epileptic seizures, altered behavior and periods of confusion are common after the age of 65. Epileptic seizures, originating in the temporal lobes, can present clinically in a variety of ways and can be difficult to diagnose. Loss of consciousness may not be evident. Reported here is a rare case of a 69 year old woman who presented with clinical features of depression, mood changes and periods of confusional states but she was subsequently diagnosed as suffering from complex partial seizures due brain tumor,that was not seen on Computed tomography. She made a partial recovery after neurosurgical surgery of underlaying reason and now is on antiepileptic treatment. In conclusion this case highlights the importance of history taking and clinical evaluation of older patients for causes other than primary psychiatric illness and the need for video EEG monitoring in the psychiatric department. It also highlights the importance of consideration of diagnosis of CPS in older patients.
Keywords: Complex Partial Seizures-Deppresion-Confusion-Brain Tumor-Antiepiletic Drugs

POSTERIOR COTRICAL ATROPHY-OUR CLINICAL EXPERIENCE- CASE REPORT

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Case Report

Posterior cortical atrophy (PCA) is a rare, early onset, neurodegenerative syndrome that is characterized by impaired visuospatial/visual-constructional skills. This case reports a a 65 years old retired nurse, with hypothireoosis and hypertension 10 years ago. who presented with clinical features of anxiety and depression on 60 age. Two years later she started forgetting recent dates, mistakes while cooking and reading, unable to read a wall clock. She was taken on ophtalmological examination, which cant explain her symptoms. On her first neurologic visit was started antidepresant therapy and suggested futher investigations. There were found visuospatial changes and changes in verbal episodic memory and executive functions (CDT ⅕ , mistakes in redrawing 2 and 3D figures, changes in semantic, episodic and procedural memory, reduced spontaneous speech, naming and changes in understanding and performing more complex tasks. The ability to read and writing are severely impaired. Below average is also abstract thinking, simpler arithmetic operations are significantly affected.) NMR of the brain was performed with a posterior parieto-occipital atrophy. The fammily refused futher clinical investigation. We started therapy with s a cholinesterase inhibitor and NMDA antagonist. During following 4 years with minimal changes on pschylogocial tests and she is functional in visuospatial orientation (she never lost in a familiar space, cooks for herself, washes dishes, and gets dressed independently (sometimes she makes mistakes, which additionally disturbs her), she sometimes has difficulties with making the bed. In conclusion this case highlights the importance of differential diagnostic consideration of affective and mood disorders and early forms of dementia.

Keywords: Posterior Cortical Atrophy-Deppresion- Alzheimer Dementia- cholinesterase inhibitors-NMDA antagonists

LEWY BODY DEMENTIA-OUR CLINICAL EXPERIENCE-CASE STUDY

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Case Report:
Lewy body dementia is an umbrella term that includes the clinical diagnoses of both Parkinson disease (PD) dementia and dementia with Lewy bodies (DLB), making it the second most common degenerative dementia. Because of the complexity of clinical presentation, it is often misdiagnosed and mistaken for other dementias, which may result in administering inappropriate therapy. A 72-year-old woman, retired ortophedic surgeon, was admitted with a severe psychomotor agitation and hallucinations that lasted continuously in two weeks time and get worsened two days before. Two years before this presentation, her husband noticed frequent phases of anxiety with severe tachycardia, rare cases of night awakening, occasionally getting lost in a familiar space and she had sometimes visual hallucinatoins Her family reported that occasionally they saw her staring off into space and had to make an effort to get her attention. Neurological exam: She had mild rigidity in both arms and mild bradykinesia bilaterally. She walked slowly with decreased stride length and limited arm swing. Pull test was positive.Due to strong psychomotor agitation, haloperidol was administered parenterally, twice 5 mg for the next 5 days, and the patient's parkinsonism worsened to the point of akinesia. The neuroleptic therapy was discontinued, a biperiden 5mg was given parenterally and the condition improved the next day. In the following period, after the improvement of her condition and the ability to swallow, intensive physical therapy for verticalization and walking was carried out. This case highlights the role of the neurologist in making a clinical diagnosis in the absence of additional investigations.

Key words: Lewy body disease, Hallucinations, Parkinsonian disorders, Dementia

CASPR2 ANTIBODY-ASSOCIATED AUTOIMMUNE ENCEPHALITIS AND EPILEPSY: A RARE CASE REPORT IN A 5-YEAR-OLD CHILD

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Introduction: CASPR2 antibody-associated autoimmune encephalitis (AE) in children is a rare neurological disorder. CASPR2 antibody targets multiple epitopes of CASPR2 protein, which may lead to brain inflammation and peripheral neuropathy. CASPR2 autoantibody disease has a variable clinical phenotype that includes cerebellar syndromes, epilepsy, pain syndromes, movement disorders, sleep disturbances, psychosis, altered consciousness and associations with neoplasms such as thymoma. While tumors are uncommon in children with this form of AE, early diagnosis and immunotherapy are crucial for a favorable outcome.
Methods: We present a case of a 5- year-old boy, admitted in PICU due to altered qualitative change in the state of consciousness including somnolence and abnormal personality behavior. The parents reported a history of seizure, which reoccurred during the hospitalization. Diagnostic workup included complete blood work, extended infectious panels, neuroimaging including brain CT and brain MRI, lumbar puncture with CSF analysis, and electroencephalography (EEG). Based on the clinical course, neurological sign and symptoms, EEG abnormalities of encephalitis and CSF findings, further investigation was directed toward autoimmune encephalitis. A panel of autoantibodies in blood and CSF were performed, with particular emphasis on identifying autoimmune etiology of encephalitis and epilepsy.
Results: Subsequent testing for neuronal autoantibodies revealed positive CASPR2 IgG antibodies in blood presenting a key finding that confirmed the diagnosis of CASPR2 autoantibody-associated neurological disease. Brain MRI revealed normal findings as well as thoracic CT scan. The treatment included implementation of intravenous immunoglobulina as well as oral antiepileptic therapy with Levetiracetam. Gradual clinical improvement was observed in the following days, with seizures cessation and gaining of complete state of consciousness.
Conclusion: This case underlines the importance of including autoimmune encephalitis in the differential diagnosis of pediatric patients with unexplained altered mental status and seizures. While CASPR2 antibodies are more commonly associated with autoimmune encephalitis in adults, they should not be overlooked in the pediatric population, especially when classical infections do not explain the presence of neurological symptoms.
Keywords: autoimmune encephalitis, CASPR2 antibodies, epilepsy

MULTIPLE CAVERNOMA SYNDROME – A CLINICAL CASE REPORT

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Introduction: Multiple Cavernoma Syndrome is a rare genetic disorder marked by many vascular abnormalities in the brain and spinal cord. It can cause seizures, headaches, and intracerebral hemorrhage and is frequently linked to mutations in the CCM1, CCM2, or CCM3 genes. While many lesions are asymptomatic, others might lead to significant neurological consequences. Surgical intervention may be considered for symptomatic or bleeding lesions, but conservative therapy is favored in stable situations.
Case report: Here we report a case of a 12-years-old boy who was hospitalized due to unilateral right sided diplopia and paresis of n.abducens. A variety of laboratory tests, biochemical analyses, were done, all of which revealed normal findings. The brain and orbital MRI with contrast revealed multiple cavernous malformations, the most pronounced change in the pons, as well as some lesions with bleeding in the subacute phase. A lumbar puncture was performed to examine the cerebrospinal fluid, which revealed clear cerebrospinal fluid unescorted by pleocytosis as well as proteinorachia, meanwhile, the electrophoregram showed evidence of an active immune response in the CNS. Electroencephalogram was conducted revealing regular alpha rhythm unaccompanied by spike waves and complexes. In addition genetics support multiple cavernous syndrome. During the hospital admission, the patient received conservative care as well as anti-edematous and anti-inflammatory treatment, with a slight improvement of the general state, neurological signs and the visual sight and perception.
Conclusion: Early diagnosis with advanced MRI methods and genetic screening is crucial for risk assessment, treatment planning, and family counselling and prevents serious brain-related complications.
Keywords: Multiple Cavernoma Syndrome; Diplopia; Genetic mutation

NEUROLOGICAL ASSESSMENT AND SEQUELLAE OF PEDIATRIC CEREBRAL ISCHEMIC STROKE: CASE SERIES IN A TERTIARY CARE HOSPITAL

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Introduction: Ischemic stroke in the children remains a diagnostically grueling condition due to its low prevalence and variable clinical donation. Hemiparesis is a frequent incarnation, yet the underpinning etiology and long- term issues are frequently miscellaneous. Timely neuroimaging, particularly MRI, is essential for evidence and characterization of cerebral infarction. In recent times, the identification of thrombophilic threat factors through inheritable testing has contributed to a deeper understanding of pediatric stroke pathophysiology. Objectives: To estimate the neurological features, neuroimaging findings, and neurological issues of sixteen pediatric cases with MRI- verified cerebral ischemic stroke, presenting with hemiparesis and seizures, and to probe factors contributing to the variability in their neurological sequelae.

Methods: Sixteen children with cerebral ischemic stroke verified with brain magnetic resonance imaging (MRI). Clinical data, including neurological sign and symptoms, and neuroimaging results, were collected. Due to seizures electroencephalography was performed. Inheritable analyses for thrombophilic gene mutations were also performed as well as cardiological examination including echocardiography and electrocardiography.
Results: All sixteen patients had ischemic lesions identified on MRI, with lesion locations varying among individuals. All patients presented with hemiparesis and 13 patients manifested symptomatic epilepsy. All patients were initiated on antiepileptic drugs due to seizures. All of the tested patients had abnormalities detected on thrombophilic gene panel testing, revealing homozygous mutations associated with hypercoagulability. Long-term outcomes varied, with differences in motor, cognitive, and sensory deficits observed.
Conclusions: Pediatric ischemic stroke poses significant diagnostic and therapeutic challenges due to its diverse presentations and multifactorial etiologies. In this series of 16 pediatric ischemic stroke patients**,** diversity in neuroimaging, genetics, and clinical profiles underscores the multifactorial nature of outcomes. Early MRI, genetic evaluation, and cardiological screening are critical for accurate diagnosis and tailored intervention. Despite uniform seizure presentation and hemiparesis, outcomes ranged widely-reinforcing the need for structured, early rehabilitation and multidisciplinary follow-up. These elements are essential for improved motor recovery, seizure control, and long-term quality of life in this vulnerable population.
Keywords: cerebral ischemic stroke, hemiparesis, symptomatic epilepsy

FAMILIAL CASE REPORT
SPINAL MUSCULAR ATROPHY- INTRAFAMILIAL PHENOTYPIC VARIABILITY AND TREATMENT RESPONSE

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Introduction
Spinal muscular atrophy (SMA) is an autosomal recessive neuromuscular disorder caused by homozygous deletions or mutations in the SMN1 gene. Disease severity is modulated by the number of SMN2 gene copies, which influences the production of functional SMN protein. SMA type 3 typically presents after 18 months of age with variable proximal muscle weakness.
We report a familial case of three siblings diagnosed with SMA type 3, all carrying three copies of the SMN2 gene, who demonstrate marked intrafamilial phenotypic variability and individual therapeutic requirements and responses.

Methods
Clinical data were retrospectively collected, including neurological assessments and genetic testing. SMA diagnosis was confirmed by homozygous SMN1 deletions with three SMN2 copies in each sibling. Maternal testing identified a 2+0 silent carrier status, confirmed by g.27134T>G and g.27706-27707delA polymorphisms.

Case Presentations
Patient 1: A 6-year-old boy presented with only mild exertional fatigue. SMA type 3 was confirmed genetically. He was started on risdiplam and remains clinically stable with no disease progression.
Patient 2: A 15-year-old male exhibited progressive proximal weakness, gait difficulty, tongue fasciculations, and polyminimyoclonus. Diagnosed at age 14, he began risdiplam with reported stabilization and slight motor improvement.
Patient 3: A 19-year-old female remains asymptomatic despite genetic confirmation. She has no clinical or neurophysiological evidence of motor neuron involvement to date. She is under routine clinical surveillance for early signs of disease manifestation.

Conclusion
Intrafamilial phenotypic variability in siblings with identical SMN1 mutations and SMN2 copy number is a well-documented and important aspect of SMA. While genetics provide a foundational understanding, additional biological, environmental and stochastic factors modulate the clinical picture. Recognizing and studying this variability is crucial for both clinical management and research into future therapeutic targets.

Keywords: spinal muscular atrophy, intrafamilial phenotypic variability , SMA type 3, Risdiplam.

DOUBLE TROUBLE: DCX MUTATION-ASSOCIATED SUBCORTICAL BAND HETEROTOPIA – A CASE REPORT

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Background: Subcortical band heterotopia (SBH), or "double cortex," is a rare neuronal migration disorder. DCX-related disorders include classic thick lissencephaly–typically more severe anteriorly and usually seen in males–and SBH, which predominantly affects females. Onset of focal seizures with secondary generalization during adolescence is uncommon, making diagnosis more challenging.

Case Report: We present a 14-year-old female with new-onset focal seizures progressing to secondary generalization. EEG revealed focal epileptiform discharges in the right frontal region with contralateral spread. The patient also exhibited behavioral difficulties consistent with mild intellectual disability. Lamotrigine therapy was initiated and successfully achieved seizure control. Brain MRI showed predominantly frontal, symmetric subcortical bands beneath the cortical ribbon–findings consistent with SBH ("double cortex"). Genetic testing identified a **de novo** heterozygous **DCX** mutation, supporting the clinical diagnosis. The patient and her family received cognitive support and genetic counseling. Seizures in DCX-associated SBH typically begin in childhood but may, as in this case, present in adolescence or early adulthood–especially when the heterotopic band is thin. MRI, in particular, reveals the characteristic symmetric subcortical bands (often frontal predominant) and helps determine the extent of cortical involvement, which correlates with cognitive and behavioral outcomes. Our patient demonstrated mild intellectual disability and behavioral issues, consistent with prior reports that link band thickness to neurodevelopmental impairment. Phenotypically, heterozygous females usually exhibit a milder form compared to males with classic lissencephaly. There is significant variability between– and to a lesser extent, within–families, with severity roughly correlating to the thickness and extent of the subcortical band on imaging.

Conclusion: This case highlights the value of MRI in diagnosing DCX-associated "double cortex" in females presenting with adolescent-onset focal epilepsy. Genetic testing is essential for confirming the diagnosis, guiding prognosis, and informing family counseling. Early recognition enables optimized seizure management, cognitive support, and informed family planning.

Keyword: Subcortical band heterotopia, DCX mutation, genetic epilepsy

SINGLE-IMAGE EEG INTERPRETATION: MULTIMODAL LARGE LANGUAGE MODELS RIVAL EXPERT NEUROPHYSIOLOGISTS

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Introduction
Electroencephalography (EEG) is a noninvasive diagnostic technique and it's interpretation requires extensive training, limiting access in underserved regions. This study evaluates multimodal large language models (LLMs), xAI's Grok and OpenAI's ChatGPT, against certified neurophysiologists in interpreting EEG patterns from single image, aiming to provide a cost-effective, accessible tool for preliminary assessments.
Methods
We analyzed 30 anonymized EEG images (10 normal, 10 epileptiform, 5 slow-wave, 5 artifact/mixed) from clinical sources, standardized in 10-20 bipolar montage (50 μV/mm, 30 mm/s). LLMs interpreted images blindly, then with patient details (e.g., age, symptoms) Neurophysiologists provided independent interpretations. Accuracy, sensitivity, and specificity were calculated.
Results
Grok achieved 95% accuracy, ChatGPT 93%, with ~5% misclassifications (e.g., artifacts as spikes), agreeing with experts interpretations. LLMs outperformed in speed (seconds vs minutes). Unlike CNNs (pattern-focused) or RNNs (sequence-focused), LLMs provided reasoned written reports.
Conclusion
This study highlights multimodal LLMs' potential in EEG interpretation from single image, offering high accuracy at negligible cost. By assisting workloads and giving free access, these tools can support education, clinical effectivness and global reach in neurophysiological report interpretations mainly helping, not replacing human expertise. Further studies with larger datasets are warranted for more accurate results. In the future as the AI expansion curve progresses and LLMs become more sophisticated and advanced the gap between professionals and AI will shrink and probably match their human counterparts. However, today the technology is already here in a simple one-click, ready to use solution that holds promise for assisting clinical neurology.
Keywords: EEG interpretation, large language models, artificial intelligence, neurology, diagnostics

ИНТЕРПРЕТАЦИЈА НА ЕЕГ ОД ЕДИНЕЧНА СЛИКА: МУЛТИМОДАЛНИ ГОЛЕМИ ЈАЗИЧНИ МОДЕЛИ НАСПРОТИ ЕКСПЕРТИ НЕВРОФИЗИОЛОЗИ

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Вовед
Електроенцефалографијата(ЕЕГ) е неинвазивна дијагностичка метода чија интерпретација бара обемен тренинг и искуство, што го ограничува нејзиниот пристап во недоволно развиени региони. Оваа студија ја оценува примената на мултимодални големи јазични модели (LLMs), Grok на xAI и ChatGPT на OpenAI, во споредба со сертифицирани неврофизиолози при интерпретација на ЕЕГ од единечна слика, со цел обезбедување ефтина и достапна алатка за прелиминарни проценки.
Методи
Анализирани беа 30 анонимизирани ЕЕГ снимки (10 нормални, 10 со епилептиформни промени, 5 со бавни бранови и 5 со артефакти/мешани). Сите беа стандардизирани со 10-20 биполарна монтажа (50 μV/mm, 30 mm/s). LLM моделите прво интерпретираа „слепо“ (само од слика), а потоа со дополнителни клинички податоци (возраст, симптоми). Независно ЕЕГ ги анализираа и неврофизиолозите. Пресметани беа точност, сензитивност и специфичност.
Резултати
Grok постигна 95% точност, а ChatGPT 93%, со приближно 5% погрешни класификации (на пример, артефакти интерпретирани како шилец-бранови). Резултатите беа во согласност со експертските интерпретации. LLM моделите беа значително побрзи (секунди наспроти минути). За разлика од CNN или RNN модели, LLM обезбедија логично структурирани пишани извештаи.
Заклучок
Оваа студија ја потенцира примената на LLM во интерпретација на ЕЕГ од слика со висока точност и минимални трошоци. Со олеснување на работата и бесплатен пристап, овие алатки можат да ја поддржат едукацијата, клиничката ефикасност и глобална достапност, асистирајќи, а не да ја заменат човечката експертиза. Потребни се поголеми студии за дополнителна валидизација. Денес технологијата е веќе достапна како едноставно „one-click“ решение што ветува значајна помош во клиничката неврологија.
Клучни зборови: ЕЕГ интерпретација, големи јазични модели, вештачка интелигенција, неврологија, дијагностика

CHOREA AS NEUROLOGICAL MANIFESTATION OF SYSTEMIC LUPUS ERYTHEMATOSUS – A CASE REPORT

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ABSTRACT
Introduction. Neuropsychiatric lupus (NPSLE) is the least understood yet perhaps the most prevalent manifestations of lupus. It affects 22% to 95% of the pediatric patients with SLE. Chorea is rare manifestation and often other etiologies are more common in pediatric population. **Case report.** In this case we present a 14 years old female with involuntary movements of the left side extremities. She had been diagnosed with SLE two years earlier, characterized by a rash, joint pain and positive antinuclear antibodies (ANA). She had been receiving treatment with hydroxychloroquine, immunosuppressant and corticosteroids for disease control. Also with this case we present the steps of making the diagnose, the clinical manifestation and the therapeutic pathway that we chose with high pulse dose of corticosteroids. **Conclusion.** Chorea as a neurological manifestation of SLE is rare but important, particularly in adolescent patients. While it can be part of the neuropsychiatric lupus spectrum, it is often misdiagnosed or underrecognized. The pathophysiology of chorea in SLE is not entirely understood but is thought to involve a combination of vascular changes, direct autoimmunity against brain tissue, and perhaps inflammatory cytokines affecting the basal ganglia, which are involved in the control of movements.

Key words: Systemic lupus erythematosus, neuropsychiatric lupus, pediatric NPSLE

GAPS AND OPPORTUNITIES IN ADULT SMA CARE IN NORTH MACEDONIA: INSIGHTS FROM THE SMA ADULT CARE BENCHMARKING INITIATIVE

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BACKGROUND
Adults living with spinal muscular atrophy (SMA) in North Macedonia face a complex care landscape shaped by limited resources, centralized treatment access, and systemic challenges. A national report, developed as part of the European SMA adult care benchmarking and OdySMA initiatives, provides a comprehensive overview of the current state of adult SMA care in North Macedonia and identifies areas for improvement.

OBJECTIVE
To assess the accessibility, quality, and structure of care for adults living with SMA, and to inform policy and clinical practice changes by benchmarking national data against European standards.

METHODS
Data was collected via structured surveys and interviews involving healthcare professionals (HCPs) and the patient organization STOP-SMA. The analysis focused on transition pathways, care continuity, multidisciplinary team availability, treatment access, social support, and national policy frameworks.

RESULTS
Key strengths include access to disease-modifying therapies (notably risdiplam), government funding for rare disease treatments, and active patient advocacy. However, critical gaps persist. Transition from pediatric to adult care is unstructured and unsupported by formal protocols. Multidisciplinary care is lacking, with most adults seeing a neurologist only once yearly. Centralization of treatment poses significant logistical challenges for patients. Standards of care exist but are not fully aligned with patient needs, and adult patients have limited access to assistive devices, trained caregivers, and social or educational support. The absence of a dedicated SMA registry further limits data-driven policy development. While training for HCPs exists, there is no structured education for caregivers or personal assistants.

CONCLUSION
Adult SMA care in North Macedonia remains fragmented and underdeveloped. Coordinated national action is urgently needed to improve the transition process, expand multidisciplinary care, decentralize treatment access, and strengthen social and caregiver support systems. The findings underscore the importance of integrating patient voices and empowering national stakeholders to align care delivery with real-world needs, ensuring sustainable improvements in quality of life for adults living with SMA.

Keywords: SMA, spinal muscular atrophy, care, adult

ФАБРИЕВА БОЛЕСТ ПРИКАЗ НА СЛУЧАЈ

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Вовед: Fabry болеста е ретко X-хромозомско наследно лизозомално заболување предизвикано од мутација во GLA генот, со дефицит на ензимот α-галактозидаза А и акумулација на гликосфинголипиди. Болеста е мултисистемска, со зафатеност на бубрезите, срцето и нервниот систем.
Материјал и методи: Прикажуваме случај на 46-годишен пациент со генетски потврден Fabry синдром, следен и третиран од страна на нефролог со специфична терапија. Направени беа магнетна резонанца на мозок, електромиографија (ЕМГ) и невропсихолошко тестирање.
Резултати: Пациентот презентираше невролошки манифестации на централниот и периферниот нервен систем. MRI покажа мултипли промени во белата маса на ЦНС карактеристични за Fabry болест, ЕМГ потврди тешка периферна невропатија, а невропсихолошкото тестирање укажа на когнитивни дефицити.
Заклучок: Овој случај ја нагласува важноста на мултидисциплинарниот пристап и редовниот мониторинг кај Fabry болест. Раното препознавање и навремената терапија можат да ја забават прогресијата и да ги намалат невролошките компликации.
Клучни зборови: Fabry болест, GLA мутација, MRI, EMG, когнитивни нарушувања

FABRY DISEASE CASE REPORT

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Introduction: Fabry disease is a rare X-linked lysosomal storage disorder caused by mutations in the GLA gene, leading to deficiency of the enzyme α-galactosidase A and accumulation of glycosphingolipids. The disease is multisystemic, affecting kidneys, heart, and the nervous system.
Material and Methods: We present a case of a 46-year-old patient with genetically confirmed Fabry disease, followed and treated by a nephrologist with specific therapy. Brain MRI, electromyography (EMG), and neuropsychological testing were performed.
Results: The patient presented with neurological manifestations involving both the central and peripheral nervous systems. MRI revealed white matter changes consistent with Fabry disease, EMG confirmed peripheral neuropathy, and neuropsychological testing demonstrated cognitive deficits.
Conclusion: This case highlights the importance of a multidisciplinary approach and regular monitoring in Fabry disease. Early recognition and timely therapy may slow disease progression and reduce neurological complications.
Keywords: Fabry disease, GLA mutation, MRI, EMG, cognitive impairment

CURRENT LANDSCAPE OF NEUROMYELITIS OPTICA SPECTRUM DISORDER (NMOSD) MANAGEMENT IN NORTH MACEDONIA: A REAL-WORLD OVERVIEW

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Introduction
Neuromyelitis Optica Spectrum Disorder (NMOSD) is a rare, relapsing autoimmune disorder of the central nervous system, primarily affecting the optic nerves and spinal cord. Most commonly associated with anti-AQP4 antibodies, NMOSD can lead to severe neurological disability and blindness if left untreated. . Recent advances in targeted immunotherapies, including monoclonal antibodies, have transformed the treatment paradigm, significantly reducing relapse rates and improving long-term functional outcomes

Objective
To provide an overview of the current epidemiological data, clinical characteristics, and treatment outcomes of NMOSD in North Macedonia.

Methodology
A retrospective analysis was conducted using patient history files from the University Clinic of Neurology in Skopje, reviewing all confirmed NMOSD cases based on clinical, serological, and imaging criteria. Diagnosis was based on the 2015 International Panel for NMO Diagnosis (IPND) criteria. Demographics, disease phenotype, AQP4-IgG serostatus, treatment regimens, adverse events, relapse rates, and Expanded Disability Status Scale (EDSS) outcomes were recorded.

Results
To date, 24 patients have been diagnosed with NMOSD in North Macedonia, with an incidence of 1-2 new cases annually. The majority of patients (86%) are female, with a mean age of 39 years. Among them, 59% (n=14) are AQP4-IgG seropositive. All 14 patients eligible for treatment with satralizumab are currently receiving it. Satralizumab (Enspryng®) is the only registered and available treatment for AQP4-positive NMOSD in the country. No adverse events or treatment discontinuations have been reported to date. Importantly, all treated patients have remained relapse-free, with a trend toward EDSS stabilization or improvement.

Conclusion
Although NMOSD remains a rare condition in North Macedonia, current management–centered around early diagnosis and treatment with satralizumab-shows promising clinical outcomes, including stable or improving disability scores and complete relapse prevention in treated individuals. Continued monitoring and awareness, as well as earlier diagnostics, remain critical for optimizing care for this vulnerable patient population.

Keywords: NMOSD, satralizumab, AQP4, disability, treatment

СИНДРОМ НА ГОРЕЊЕ ВО УСТАТА И ДИЈАБЕТИЧНА ПОЛИНЕВРОПАТИЈА – КОИНЦИДЕНЦИЈА ИЛИ КОРЕЛАЦИЈА?

Приказ на случај

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Синдромот на горење во устата (СГУ) претставува ретко клиничко нарушување, карактеризирано со хронична болка и чувство на печење во клинички непроменета орална слузница, кое трае најмалку четири до шест месеци.
Во овој труд се презентира случај на 56-годишна пациентка со хронична, дифузна орална болка со карактер на печење. Дијагнозата на СГУ беше поставена по темелно исклучување на низа диференцијални дијагнози, меѓу кои орална кандидијаза, влакнеста леукоплакија, орален лихен планус, локални инфективни процеси, вирусни етиологии, гастроезофагеална рефлуксна болест, автоимуни состојби како реуматоиден артритис и системски лупус еритематодес, како и нутритивни дефицити.
Дополнителните испитувања опфатија лабораториски анализи, вклучувајќи комплетна крвна слика, биохемиски панел и одредување на HbA1c, кој укажа на лошо регулиран дијабетес мелитус. Магнетна резонанца на мозок (со TOF серија) не покажа патолошки наоди, додека електромионеврографијата (ЕМНГ) даде резултати во насока на дијабетична полиневропатија. Физикалниот преглед не откри специфични орални промени, но беа евидентирани клинички знаци на периферна полиневропатија.
Со оглед на клиничката слика, резултатите од испитувањата и исклучувањето на други можни етиологии, поставена е веројатна дијагноза на СГУ. Пациентката беше третирана амбулантски, со акцент на едукација и симптоматска терапија.
Овој случај претставува редок клинички пример, со оглед дека СГУ најчесто се јавува кај жени во постменопауза, а патофизиолошките теории најчесто ја вклучуваат улогата на естрогенската модулација во преносот на болка. Дијагностичките критериуми и терапевтските стратегии за СГУ сè уште еволуираат, а овој приказ дава дополнителен увид во можните клинички пристапи и потенцијалната поврзаност помеѓу СГУ и дијабетична полиневропатија.
Клучни зборови: Синдром на горење во устата, дијабетична полиневропатија, хронична орална болка, невропатија

BURNING MOUTH SYNDROME AND DIABETIC POLYNEUROPATHY – COINCIDENCE OR CORRELATION?

Case Report

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Burning Mouth Syndrome (BMS) is a rare clinical disorder characterized by chronic pain and a burning sensation in clinically normal oral mucosa, persisting for at least four to six months.
This paper presents the case of a 56-year-old female patient with chronic, diffuse oral pain of a burning nature. The diagnosis of BMS was established after a thorough exclusion of numerous differential diagnoses, including oral candidiasis, hairy leukoplakia, oral lichen planus, local infectious processes, viral etiologies, gastroesophageal reflux disease, autoimmune conditions such as rheumatoid arthritis and systemic lupus erythematosus, as well as nutritional deficiencies.
Additional investigations included laboratory tests, comprising a complete blood count, biochemical panel, and HbA1c measurement, which indicated poorly controlled diabetes mellitus. Brain MRI (with TOF sequence) revealed no pathological findings, while electromyoneurography (EMNG) results were suggestive of diabetic polyneuropathy. Physical examination did not reveal specific oral changes, but clinical signs of peripheral polyneuropathy were evident.
Considering the clinical presentation, diagnostic findings, and exclusion of other potential etiologies, a probable diagnosis of BMS was established. The patient was treated on an outpatient basis, with an emphasis on patient education and symptomatic therapy.
This case represents a rare clinical scenario, given that BMS most commonly occurs in postmenopausal women, with pathophysiological theories often implicating estrogen-mediated modulation of pain receptors. Diagnostic criteria and therapeutic strategies for BMS are still evolving, and this case provides additional insight into potential clinical approaches and the possible association between BMS and diabetic polyneuropathy.

Keywords: Burning Mouth Syndrome, diabetic polyneuropathy, chronic oral pain, neuropathy

REAL-WORLD OUTCOMES OF A COMPLETE TRANSITION TO SUBCUTANEOUS OCRELIZUMAB IN MULTIPLE SCLEROSIS: A SINGLE-CENTER STUDY ON EFFICACY, SAFETY, AND PATIENT EXPERIENCE

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INTRODUCTION:
Ocrelizumab (OCREVUS®) is a high-efficacy therapy for both relapsing and primary progressive multiple sclerosis (MS). The recent introduction of a subcutaneous (SC) formulation offers potential advantages over the intravenous (IV) infusion in administration efficiency, patient satisfaction, and healthcare resource optimization. This study presents the first real-world data from the Balkan region following its implementation.

OBJECTIVE:
To assess real-world outcomes, patient satisfaction, and healthcare professional (HCP) experience following a transition from IV to SC ocrelizumab, alongside its use for initiating therapy in ocrelizumab-naïve MS patients.

METHODS:
Between March and September 2025, all MS patients (n=95) on maintenance ocrelizumab at our clinic were transitioned to the SC formulation. Additionally, 60 ocrelizumab-naïve patients initiated therapy directly with SC formulation. Efficacy, safety events, patient-reported satisfaction, and HCP feedback on administration time and workflow were collected prospectively.

RESULTS:
A 100% conversion rate from IV to SC was achieved without treatment interruption, and all 60 ocrelizumab-naïve patients successfully commenced therapy. Efficacy was maintained, with no relapses or new MRI activity observed during follow-up. The safety profile was favorable, with no serious injection-related reactions. Patient satisfaction was exceptionally high, with over 90% reporting a "significantly better" experience. For HCPs, the total administration and observation time per patient was reduced from approximately 5-6 hours to under one hour, substantially increasing the clinic capacity and decreasing the burden of work.

CONCLUSION:
The complete transition to SC ocrelizumab is feasible, safe, and maintains treatment efficacy. The SC formulation significantly enhances the treatment experience for both patients and HCPs, optimizes healthcare resources, and facilitates timely initiation of high-efficacy therapy. These real-world findings support SC ocrelizumab as a new standard of care in MS management.

Keywords: Multiple sclerosis, Ocrelizumab, Subcutaneous, Patient satisfaction, Real-world data, SC

A SINGLE-CENTER REAL-WORLD EXPERIENCE WITH SUBCUTANEOUS OCRELIZUMAB: TRANSITION OUTCOMES AND HEALTHCARE BENEFITS

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INTRODUCTION:
Ocrelizumab (OCREVUS®) is a high-efficacy therapy for both relapsing and primary progressive multiple sclerosis (MS). The recent introduction of a subcutaneous (SC) formulation offers potential advantages over the intravenous (IV) route of administration, including improved administration efficiency, greater patient satisfaction, and optimized healthcare resource utilization.

OBJECTIVE:
To present the first preliminary real-world experience with ocrelizumab SC in the Balkan region, evaluating patient outcomes, satisfaction, and healthcare professional (HCP) experience following the transition from IV to SC administration in MS at the University Clinic of Neurology, Skopje.

METHODS:
Between February and August 2025, all MS patients (n=95) receiving maintenance ocrelizumab were transitioned to the SC. In parallel, 55 ocrelizumab-naïve patients initiated treatment directly with ocrelizumab SC. Data on efficacy, safety, patient's preference, and HCP feedback regarding administration time and workflow were retrospectively collected during routine clinical practice.

RESULTS:
A complete conversion from IV to SC ocrelizumab was achieved; 55 ocrelizumab-naïve patients successfully initiated SC therapy. Efficacy was preserved, no clinical relapse(s) reported during the follow-up period. The safety profile was favorable, no serious injection-related reactions. Two-thirds of patients reported high satisfaction with the SC comfort and convenience, and 85.7% expressed a preference to continue with SC administration. HCPs's administration and observation time decreased from approximately 5-6 hours with IV infusion to under 1 hour with SC dosing, markedly improving workflow and clinical capacity.

CONCLUSION:
Transition from IV to SC ocrelizumab in routine practice is feasible, safe, and effective. The SC formulation reduces treatment burden, enhances HCP's efficiency, and optimizes healthcare resources while maintaining clinical efficacy. These preliminary real-world findings support ocrelizumab SC as a new, patient- and system-friendly standard of care in MS management.

Keywords: multiple sclerosis, Ocrelizumab, Subcutaneous, Real-world data, SC, MS

CENTRAL PONTINE MYELINOLYSIS IN A 30-YEAR-OLD MALE WITH CHRONIC ALCOHOL USE AND HYPONATREMIA

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Introduction:
Central Pontine Myelinolysis (CPM) is a severe demyelinating disorder within the spectrum of Osmotic Demyelination Syndrome (ODS), most often related to correction of chronic hyponatremia in predisposed patients, such as those with alcohol use disorder. Manifestations include dysarthria, dysphagia, quadriparesis, pseudobulbar affect, and altered consciousness. Diagnosis relies on magnetic resonance imaging (MRI). No specific therapy has been established, and treatment is usually supportive.
Case Report:
A 30-year-old male with chronic alcohol and methamphetamine use was initially admitted to the Infectious Diseases Clinic due to profuse vomiting. Laboratory tests revealed hyponatremia, which was corrected according to standard guidelines. Shortly after correction, his neurological status worsened with somnolence, spasticity, anarthria, and pseudobulbar affect. Upon transfer to the University Clinic of Neurology, serum sodium and other laboratory parameters were within normal range. Neurological examination revealed a Glasgow Coma Scale score of 12, limb rigidity, and a positive glabellar tap sign. Cerebrospinal fluid analysis showed nonspecific intrathecal IgG synthesis. MRI demonstrated symmetric T2/FLAIR hyperintensities in the pons and bilateral thalami, confirming CPM.
Treatment and Results:
Supportive care was initiated, including vitamin supplementation (thiamine, folate, B12). High-dose corticosteroid therapy with gradual tapering was administered, after which the patient showed marked improvement: recovery of motor function, restoration of speech, and resolution of somnolence. He was discharged ambulatory with assistance and returned one month later fully independent.
Conclusion:
CPM may occur even after seemingly appropriate correction of hyponatremia, particularly in patients with chronic alcoholism. Although corticosteroids are not standard treatment, this case demonstrates unexpected recovery following high-dose therapy, suggesting a potential role warranting further investigation. Early recognition with MRI and supportive management remain key to improving outcomes.
Keywords: **Central Pontine Myelinolysis, Hyponatriemia, Osmotic Demyelination**

ТЕШКОТИИ ВО ВНИМАНИЕ И КОНЦЕНТРАЦИЈА КАЈ ПАЦИЕНТИ СО ВАСКУЛАРНА И ДЕГЕНЕРАТИВНА ДЕМЕНЦИЈА

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АПСТРАКТ
ВОВЕД: Вниманието и концентрацијата претставуваат едни од најчесто нарушените когнитивни функции кај пациенти со деменција, а нивната точна проценка е од суштинско значење за планирање на соодветни интервенции. Целта на ова истражување беше да се споредат перформансите поврзани со вниманието и концентрацијата кај пациенти со дегенеративна деменција (ДД) и васкуларна деменција (ВаД).
МЕТОДИ: Во истражувањето беа вклучени 62 испитаници, распределени во две групи според клиничката дијагноза. Когнитивната проценка беше спроведена со **Trail Making Test (TMT-A и TMT-B)**, **Verbal Span** (напред и назад) и **Stroop тестовите** (1, 2 и 3). Анализата ги опфати постигнувањата според видот на деменција, како и според демографските фактори: возраст, пол и ниво на образование.

РЕЗУЛТАТИ: Не беа забележани значајни разлики меѓу групите во однос на вниманието и концентрацијата. Сепак, кај пациенти со ДД, постарите од 65 години покажаа значајно полоши резултати на TMT-A и TMT-B ($p < 0,05$), додека кај ВаД возраста не влијаеше врз изведбата. Повисокото образование кај пациенти со ВаД беше поврзано со подобри резултати на Stroop 1 и 2 ($p < 0,05$). Полот не покажа значајно влијание во ниту една од групите.

ЗАКЛУЧОК: Иако двата типа на деменција предизвикуваат слични нарушувања во вниманието и концентрацијата, одредени демографски фактори – пред сè возраста и образованието – можат да играат модифицирачка улога во изведбата на специфични когнитивни задачи. Овие наоди ја потенцираат потребата од индивидуализиран пристап во когнитивната проценка и во планирањето на интервенции, со цел подобрување на квалитетот на живот кај пациентите со деменција.
Клучни зборови: дегенеративна деменција, васкуларна деменција, внимание, концентрација, когнитивна проценка

ATTENTION AND CONCENTRATION DIFFICULTIES IN PATIENTS WITH VASCULAR AND DEGENERATIVE DEMENTIA

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ABSTRACT

Introduction: Attention and concentration are among the most frequently impaired cognitive functions in patients with dementia, and their accurate assessment is essential for planning appropriate interventions. The aim of this study was to compare attentional and concentration-related performance in patients with degenerative dementia (DD) and vascular dementia (VaD).
Methods: The study included 62 participants, divided into two groups based on clinical diagnosis. Cognitive assessment was conducted using the Trail Making Test (TMT-A and TMT-B), Verbal Span (forward and backward), and Stroop tests (1, 2, and 3). The analysis examined performance according to dementia type, as well as demographic factors: age, gender, and level of education.

Results: No statistically significant differences were observed between the groups in terms of attention and concentration. However, among DD patients, those over the age of 65 showed significantly poorer results on TMT-A and TMT-B ($p < 0.05$), while age did not affect performance in the VaD group. Higher education among VaD patients was associated with better results on Stroop 1 and 2 ($p < 0.05$). Gender did not show a significant influence in either group.
Conclusion: Although both types of dementia lead to similar impairments in attention and concentration, certain demographic factors - primarily age and education may play a moderating role in the execution of specific cognitive tasks. These findings highlight the need for an individualized approach in cognitive assessment and intervention planning, aimed at improving the quality of life in patients with dementia.

Keywords: degenerative dementia, vascular dementia, attention, concentration, cognitive assessment

CEREBRAL VENOUS SINUS THROMBOSIS WITH INTRACEREBRAL HEMORRHAGE IN A 47-YEAR-OLD WOMAN – A CASE REPORT

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Introduction:
Cerebral venous sinus thrombosis (CVST) is a rare but potentially life-threatening condition, more commonly affecting women with hormonal or thrombophilic risk factors. Early diagnosis is key to a favorable outcome.

Case Report:

We present a 47-year-old woman with a history of two spontaneous miscarriages, multiple failed IVF attempts, and one successful pregnancy. She was receiving progesterone therapy for irregular menstruation and endometrial hyperplasia. A uterine myoma was diagnosed, and surgery was planned.

Days before admission, she experienced headache and toothache and was treated for dental caries. The headache was misattributed to dental causes, delaying diagnosis. After a sudden decrease in consciousness and a generalized seizure, she was urgently admitted to the Neurology Clinic.

CT imaging revealed left transverse sinus thrombosis, venous infarction, and an intracerebral hematoma in the left temporal region. D-dimer was elevated (976.7 ng/ml), while other coagulation markers were normal. EEG showed low-voltage theta activity over the left hemisphere. In the absence of other risk factors, hormone therapy was considered the likely cause and was discontinued.

Treatment and Outcome:

She was treated with low-molecular-weight heparin, antiepileptic and antiedema therapy. Follow-up CT showed infarct reduction and hematoma resolution. Repeat EEG was normal. Upon stabilization, she was discharged with apixaban (5 mg twice daily) for anticoagulation.

Conclusion:
This case underscores the importance of timely recognition of CVST and the potential for diagnostic delays due to overlapping or misleading symptoms. The patient's history of pregnancy loss and venous thrombosis supports the need for further rheumatologic assessment and illustrates the broader relevance of individualized risk evaluation and early intervention in achieving favorable outcomes.

ANTI-YO ANTIBODY-ASSOCIATED SYNDROMES: CLASSIC AND ATYPICAL PRESENTATIONS

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Introduction:
Paraneoplastic syndromes (PNS) are rare immune-mediated disorders triggered by underlying malignancies and often precede tumor detection. They result from cross-reactive immune responses rather than direct tumor invasion, leading to diverse systemic and neurological manifestations. Anti-Yo antibodies are most commonly associated with cerebellar degeneration, typically linked to ovarian and breast cancers. We present two cases of anti-Yo-associated syndromes – one classic and one atypical – highlighting the clinical spectrum and diagnostic challenges.

Case 1:
A 54-year-old woman presented with several months of vertiginous symptoms, progressing to severe gait instability, diplopia, dysarthria, and multidirectional nystagmus. Previous investigations, including brain CT, CT angiography, and neurophysiological studies, were unremarkable. On admission, she exhibited pronounced truncal and locomotor ataxia with a full constellation of cerebellar signs. Tumor markers were markedly elevated, and anti-Yo antibodies tested positive. Brain MRI revealed cerebellar hypotrophy with hypersignal changes. She was diagnosed with subacute cerebellar degeneration secondary to an undiagnosed ovarian carcinoma. High-dose corticosteroids resulted in partial neurological improvement.

Case 2:
A 45-year-old woman presented with acute behavioral changes and memory impairment, followed by focal seizures evolving into status epilepticus. Brain MRI demonstrated hypersignal changes in the insular and cerebellar regions, while CSF analysis was unremarkable. Anti-Yo antibodies were positive, and tumor markers CA-125 and S100 protein were mildly elevated; however, extensive evaluation revealed no malignancy, although a few functional ovarian cysts were identified. Seizures and cognitive symptoms resolved with high-dose corticosteroids.

Conclusion:
Although some paraneoplastic syndromes are linked to specific onconeural antibodies, neither the antibodies nor the clinical presentations are entirely tumor-specific. Anti-Yo antibodies, typically associated with ovarian and breast cancers, have also been reported in colon, lung, and Hodgkin's disease. Importantly, PNS can present atypically, and since they often precede tumor detection, recognizing unusual manifestations and investigating occult malignancies are essential for timely diagnosis and management.

IMPORTANCE OF MEDICATION THERAPY MANAGEMENT FOR NEUROLOGICAL PATIENTS WITH POLYTHERAPY

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Introduction
To achieve optimal symptom control or disease modification, many neurological patients require polytherapy. Polytherapy is associated with an increased risk of adverse drug reactions, pharmacokinetic and pharmacodynamic interactions, poor adherence, and reduced quality of life. Medication Therapy Management (MTM) has emerged as a structured, patient-centered approach designed to optimize therapeutic regimens and minimize drug-related problems. The relevance of MTM is especially pronounced in neurology, where neuropharmacological therapies are often defined by narrow therapeutic indices, complex titration regimens, and a high probability of interactions with concomitant medications. The objective of this article is to highlight the importance and necessity of incorporating MTM for neurological patients receiving polytherapy.

Materials and Methods
A retrospective observational study was conducted using data obtained from the database “Moj termin”. The study focused on patients with a confirmed diagnosis of G40 from January 2023 - June 2025. A subgroup of 50 patients was identified based on polytherapy, defined as the use of more than five distinct medications. The prescribed medications were systematically analyzed using a drug-drug interaction (DDI) screening tool, with potential interactions identified and categorized by severity (minor, moderate, major) and clinical significance. In addition, narrative medical records from the “Findings and Anamnesis” section were systematically reviewed.

Results
The interactions varied in both number and severity, with the majority of patients predicted to experience at least one moderate or major interaction. Clinical data from the “Findings and Anamnesis” section indicated that 43 patients (86%) exhibited documented outcomes attributable to these interactions.

Conclusion
Obtained results emphasize the need for structured Medication Therapy Management (MTM) in patients with neurological disorders undergoing polytherapy as an instrument that can support healthcare providers in the early identification and prevention of drug-related problems.

Keywords: polytherapy, medication therapy management, drug interaction

ASSOCIATION OF HLA ALLELES WITH OLIGOCLONAL BAND STATUS IN MULTIPLE SCLEROSIS PATIENTS

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Background: The presence of cerebrospinal fluid (CSF) oligoclonal bands (OCB) is a key diagnostic marker in multiple sclerosis (MS), with prevalence varying among populations. Genetic factors, particularly HLA class I and II alleles, may influence OCB status and contribute to heterogeneity in MS clinical expression. Previous studies have reported associations between HLA-DRB115 and OCB-positive MS, whereas alleles such as HLA-DRB104, *03, or *13 have been linked to OCB-negative MS. However, findings remain inconsistent across different populations.

Objective: To compare the distribution of HLA-A, HLA-B, HLA-C, HLA-DRB1, and HLA-DQB1 alleles between OCB-positive and OCB-negative MS patients, and to explore potential genetic associations with intrathecal IgG synthesis.

Methods: This retrospective-prospective observational study included MS patients stratified according to OCB status. HLA allele frequencies were analyzed using the χ^2 test, and Fisher's exact test was applied when expected values were <5. Statistical significance was set at $p<0.05$, and odds ratios (OR) were calculated for significant associations.

Results: Analysis of the entire cohort showed no significant differences in allele distribution for HLA-A, HLA-B, HLA-C, HLA-DRB1, or HLA-DQB1 ($p>0.05$). Subgroup analysis revealed significantly higher frequencies of HLA-A11 ($p=0.028$, OR=0.37), HLA-B40 ($p=0.0038$, OR=0.32), and HLA-B*57 ($p=0.0227$, OR=0.09) in OCB-negative patients compared to OCB-positive patients. No significant associations were observed for other allelic groups. Compared to European cohorts, the proportion of OCB-negative patients in our sample was higher, similar to recent data reported from Spanish populations.

Conclusion: Our findings indicate associations of HLA-A11, HLA-B40, and HLA-B57 with OCB-negative status in MS patients, whereas HLA-DRB115 showed no association, contrary to most previous studies. These results suggest potential population-specific differences in the genetic background influencing OCB expression. Larger, multicenter studies are needed to clarify the role of HLA alleles in determining OCB status and their implications for MS prognosis.

Keywords: multiple sclerosis, oligoclonal bands, HLA alleles, immunogenetics, CSF

ASSOCIATION OF VITAMIN D LEVELS WITH OLIGOCLONAL BAND STATUS IN MULTIPLE SCLEROSIS PATIENTS

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Background: Vitamin D deficiency is recognized as one of the most important environmental risk factors for multiple sclerosis (MS). In addition to its neuroprotective effects, vitamin D plays a central role in maintaining immune homeostasis by regulating T lymphocyte activity, modulating antigen-presenting cells, and shifting the balance between pro-inflammatory and anti-inflammatory cytokines. Genetic studies have demonstrated vitamin D response elements within HLA gene promoters, supporting the hypothesis that insufficient vitamin D may lead to impaired antigen presentation and contribute to MS susceptibility and disease progression.

Objective: To investigate the association between serum vitamin D levels, cerebrospinal fluid oligoclonal band (OCB) status, and the clinical course of MS in different patient populations.

Methods: This clinical, retrospective-prospective, observational study included patients with relapsing-remitting MS (RRMS), secondary progressive MS (SPMS), and primary progressive MS (PPMS), treated and followed at the University Clinic of Neurology. Serum vitamin D levels were compared according to OCB status. Additional variables included EDSS score, IgG index, and intrathecal IgG/IgM synthesis. Statistical analyses were performed using Mann-Whitney U test, Kruskal-Wallis test, and Spearman rank correlation.

Results: Across all MS phenotypes, vitamin D levels were consistently higher in OCB-positive than in OCB-negative patients. Statistical significance was reached only in the overall cohort ($p<0.05$), while no significant differences were observed between phenotypes among OCB-positive patients. Correlation analysis revealed a nonsignificant positive association between vitamin D levels and OCB status.

Conclusion: Our findings suggest that vitamin D levels may be influenced by OCB status, although not significantly across individual MS subtypes. These results differ partially from previous literature, reflecting the complexity of interactions between vitamin D metabolism, immunogenetics, and disease course. Given the known role of vitamin D in modulating relapse activity, disability progression, and neuroprotection, further large-scale studies are strongly warranted to clarify its clinical and therapeutic implications in MS management.

Keywords: multiple sclerosis, vitamin D, oligoclonal bands, HLA, EDSS

IN-HOSPITAL GUIDANCE FOR PATIENT SELECTION FOR SUBCUTANEOUS OCRELIZUMAB IN MULTIPLE SCLEROSIS

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INTRODUCTION
The introduction of ocrelizumab (OCREVUS®), a high-efficacy disease-modifying therapy (DMT), offers significant therapeutic benefits for patients with multiple sclerosis (MS). However, its administration is often centralized in tertiary hospitals, creating significant travel, time, and financial burdens. The upcoming availability of a subcutaneous (SC) formulation presents a transformative opportunity, therefore, a clear, evidence-based guidance for identifying eligible patients is required before the product initiation.

OBJECTIVES
To present our recently created in-hospital guidance for the selection of eligible MS patients to prescribe and start ocrelizumab SC. This guidance has been developed in anticipation of the SC formulation becoming available and will be implemented in our neurology department to ensure the right patient is prescribed ocrelizumab based on evidence-based criteria.

METHODS
The methodology involved creating a clear decision-making guidance by a multidisciplinary team of neurologists and pharmacists, synthesizing data from the OPERA, ORATORIO, and OCARINA clinical trials with international, regional treatment guidelines and ocrelizumab Summary of Medicinal Product Characteristics.

RESULTS
The primary result is clear, decision-making guidance that defines the criteria for prescribing ocrelizumab therapy. The guidance defines: 1) inclusion criteria based on general criteria such as age, EDSS score, and a confirmed MS diagnosis; 2) absolute and relative exclusion criteria; 3) specific considerations for patients switching from other DMT due to relapse(s), MRI activity, or adverse reaction; and 4) a mandatory baseline screening checklist to be completed for every patient.

CONCLUSIONS
Developing a clear patient selection guidance prior to initiation of ocrelizumab SC is a crucial step for clinical governance and responsible prescribing. This proactive approach ensures that from day one, treatment decisions are standardized, evidence-based, and aligned with safety recommendations. Our guidance provides a practical tool for neurologists to confidently and efficiently identify the appropriate MS patients for this new SC therapeutic option, streamlining the decision-making process in a hospital setting.

Keywords: MS, multiple sclerosis, ocrelizumab, SC, subcutaneous, administration, protocol, guidance