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POST COVID-19 NEUROLOGICAL SYNDROME (PCNS) IN AN 11 YEARS OLD BOY, A CASE REPORT

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ABSTRACT

By now more than 92.6[1] persons have been reported to be infected with COVID-19, of which significant part are children. Although children experience milder symptoms compared with adults at the time of the infection, cases of post-covid-19 complications have been reported (2, 3, 4, and 5). Complications might also include the CNS, in our case with cerebellar ataxia-like and polyneuritis-like signs and symptoms.
A 13 year old boy was presented in our clinic with signs of ataxia, occasional vomiting, impaired gait, impaired patellar reflexes on the right leg, incomplete Babinski reflex on the right leg, paresis of the left facial nerve and mild hypertension. Based on the clinical appearance and the parameters that showed past COVID-19 infection, a diagnosis of Post-COVID19 Cerebellar Ataxia-like and Polyneuritis-like was made, meaning a Post Covid-19 Neurological Syndrome (PCNS). Treatment was conducted with antibiotics and immunoglobulins resulting in significant improvement in the following days.
There are few reported cases about neurological complications caused by COVID-19 in children and adolescents, without any other symptoms of the virus. This is one of the first cases of Post-COVID19 Cerebellar Ataxia and Polyneuritis in a child as a result of COVID-19 and the first case in our country.
Keywords: Post-COVID19 complications, Post Covid-19 Neurological Syndrome, cerebellar ataxia, polyneuropathy, children

Introduction: As inflammation is a common reaction to biological insult, many conditions may present with features of neuritis. Common causes include autoimmune diseases, infection, either bacterial or viral, post-infectious immune reaction or a response to physical injury (6, 7).
Coronavirus disease-19 (COVID-19) is firstly a respiratory disease caused by Severe Acute Respiratory Syndrome Corona Virus-2 (SARS-CoV-2). Its pathobiology begins with targeting the angiotensin enzyme two (ACE-2) receptors which are present throughout the body, including neural tissues leading to endothelial dysfunction also at the neuro-vascular units in the brain. On-going hyperinflammation and endotheliitis contribute to the disruption of the blood-brain barrier, allowing entry of innate immune cells into the brain and further pro-inflammatory cytokine cascades (16). COVID-19 seems to be able to promote a hypercoagulable state through unique mechanisms and cross-talks between thrombosis and inflammation (17,18). Recent publications highlight the emerging evidence of a new syndrome- Post Covid-19 Neurological Syndrome (PCNS) with Chang and

colleagues describing patients with prolonged muscle weakness and other forms of myopathy among SARS-CoV survivors in Hongkong [19].
Cerebellar ataxia is a form of ataxia originating in the cerebellum[8], that can occur as a result of many diseases and may present with symptoms of an inability to coordinate balance, gait, extremity and eye movements.[9] Lesions to the cerebellum can cause dyssynergia, dysmetria, dysdiadochokinesia, dysarthria and ataxia of stance and gait.[10]
Polyneuropathy is damage or disease affecting peripheral nerves (peripheral neuropathy) in roughly the same areas on both sides of the body, featuring weakness, numbness, and burning pain.[11]
These two entities may develop as a post-infectious consequence that often presents itself several weeks after the resolution of the acute infection. In our case report they are both result from an asymptomatic COVID-19 infection.

Case report: We present an 11 years old boy who referred to our clinic because of headache, hypertension, muscle weakness and muscle pain, and impaired walk. The present disease started one week before. Medical history showed a dysphonic speech from the age of six, treated with speech occupying therapy.
On admission he was conscious, afebrile and with gait disturbance with slight right-sided hemiparetic gait. During neurological examination verbal and visual contact was established, had dysarthric speech, no dysmetria, tandem gait was impossible to assess, negative Romberg test, Gowers test impossible to execute, cranial nerve examination revealed paresis of the left peripheral facial nerve, muscular tone was normal, muscular strength was normal in the left limbs while it was slightly reduced in the right limbs, tendon reflexes were preserved in the upper limbs with a hypoactivity in the lower limbs more designated on the right limb and positive incomplete Babinski sign on the right, superficial sensibility was preserved while deep sensibility for space was impaired, pathological involuntary movements were not observed and there were no meningeal signs.
Laboratory evaluation and diagnostic procedures were performed. Initial laboratory tests such as CBC, CRP, basic metabolic panel, lipid panel and liver panel revealed normal findings. Additional laboratory tests performed such as AFP level was with normal value, c-ANCA, ANA, Anti dsDNA were not found in serum, IEP serum test revealed normal results (Table 1 and Table 2).

Table 1: Laboratory values in blood

Blood	Value	Reference value
White blood cells (WBC)	5.06	3.5 – 10 x 10^3/uL
Platelets (PLT)	254	150 – 400 x 10^3/uL
Red blood cells (RBC)	5.24	3.5 – 5.2 x 10^6/uL
CRP	< 0.2	0 – 5 mg/L
Glucose	5.97	4.1 – 5.9 mmol/l
Iron	24.1	6.6 – 26 umol/l
Feritin	103	30 – 400 ug/l
Transferin	300.34	130 – 360 mg/dl
AST	22	15-59 U/L
ALT	6	9 – 72 U/L
GGT	15	0 – 36 U/L
LDH	183	0 – 500 U/L
Total Bilirubin	10.7	3 – 22 umol/L

Direct Bilirubin	5.1	0 – 5 umol/L
Amylase	133	25 – 125 U/L
Lipase	23	8 – 78 U/L
Urea	5.2	2.6 – 6.4 mmol/L
Creatinin	63	0 – 104 umol/L
Albumin	46	40- 49 g/L
Total proteins	69	64 – 83 g/L
CK	69	29 – 200 U/L
CKMB	24.66	0 – 24 U/L
IgA	1.12	0.63 – 4.84 g/L
IgM	1.19	0.22 – 2.93 g/L
IgG	8.19	5.40 – 18.22 g/L
Total T3	169	82 – 179 ng/dL
TSH	0.969	0.4 – 4.0 uIU/mL
Total T4	10.7	4.5 – 12.5 ug/dL
Triglycerides	0.59	0 – 2.3 mmol/L
Cholesterol	3.64	0 – 5.2 mmol/L
UHDL	1.4	1.04 – 1.55 mmol/L
DLDL	2.28	2.59 – 4.11 mmol/L
Lactate	2.11	0.5 – 2.2 mmol/L
Sodium	136	135 – 145 mmol/L
Potassium	3.79	3.6 – 5.2 mmol/L
Ionised Calcium	1.21	1.15 – 1.30 mmol/L
Chloride	101	96 – 106 mmol/L
Vitamine B12	294	187 – 883 pg/mL
Uric acid	346	155 – 480 umol/L
D-dimer	1962	0 – 500 ng/mL
Prothrombin time (PT)	14.7	9.8 – 14.2 s
Activated partial thromboplastin time (aPTT)	29.6	27.9 – 37.7 s
Thrombin time	17.9	16.1 – 24.1 s

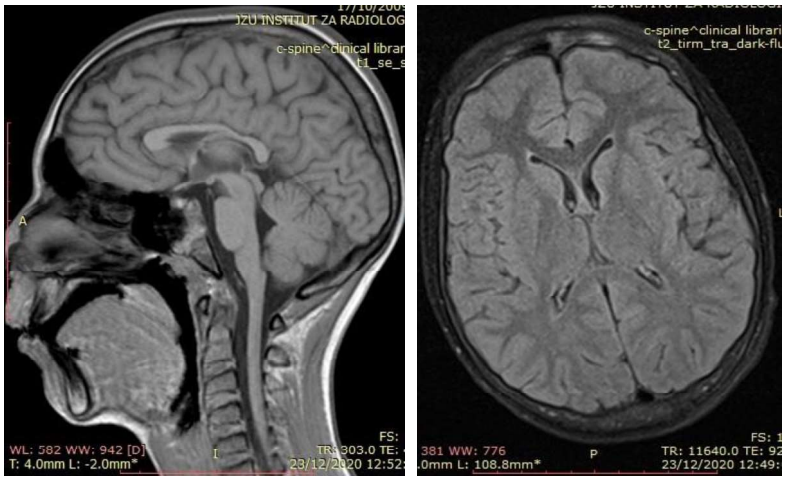
Table 2: Antibodies in blood

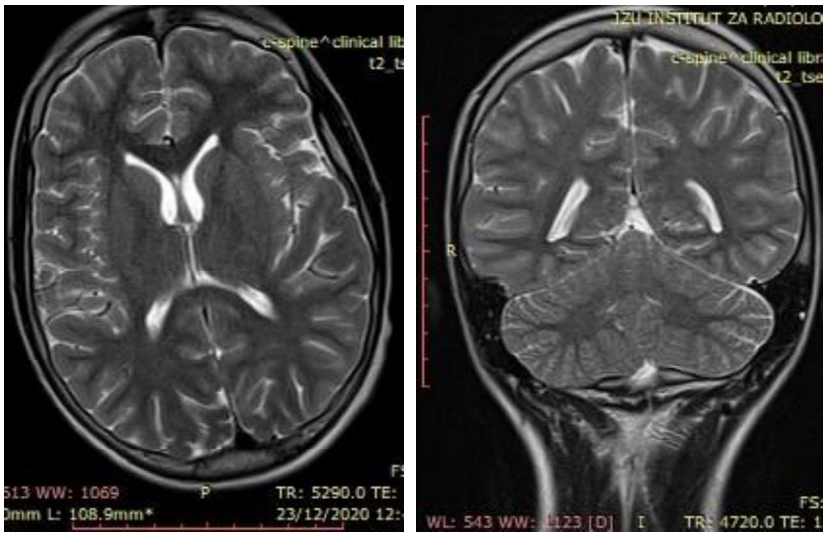
Antibodies (Blood) *	Value	Reference value
antiCCP	**negative**	< 25 IU/ml
ANA-Hep2(IFA)	**negative**	
antidsDNA	**negative**	< 55 IU/ml
Anti-Sm	**negative**	< 25 U/ml
c-ANCA	**negative**	< 5.0 U/ml
ACL-IgG	**negative**	< 10 U/ml
antiSSA	**negative**	< 12.5 U/ml
antiSSB	**negative**	< 12.5 U/ml

antiScl-70	**negative**	< 12.5 U/ml
AFA	**negative**	< 15 U/ml
ACLA IgM	**negative**	

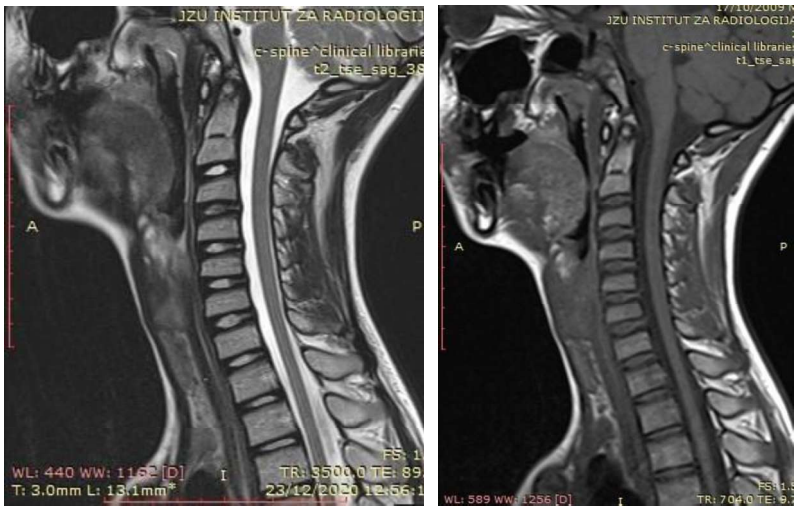
AntiCCP = anti cyclic citrullinated peptide; ANA-Hep2(IFA) = Anti-Nuclear Antibodies HEp-2(indirect fluorescence assay); antidsDNA =_anti-double stranded DNA; Anti-Sm= Anti-Smith antibodies; c-ANCA= antineutrophil cytoplasmic antibodies; ACL-IgG= Anti-cardiolipin autoantibodies- IgG; antiSSA= anti–Sjögren's-syndrome-related antigen A autoantibodies; antiSSB= Anti-Sjögren's syndrome type B (SSB) antibodies; antiScl-70= Autoantibodies against topoisomerase I; AFA= anti-fibrillarin antibodies; ACLA IgM= IgM anticardiolipin antibodies.
Abdominal ultrasound, chest X-ray, fundoscopic examination, brain CT scan and brain and spinal cord MRI revealed normal findings (Picture 1 and Picture 2). Electroencephalography (EEG) activity was normal, no epileptic activity nor cerebral dysfunction was recorded in the tracing (Picture 3). EMNG revealed normal findings.

Picture 1: T1W, T2W and FLAIR Brain MRI sample images

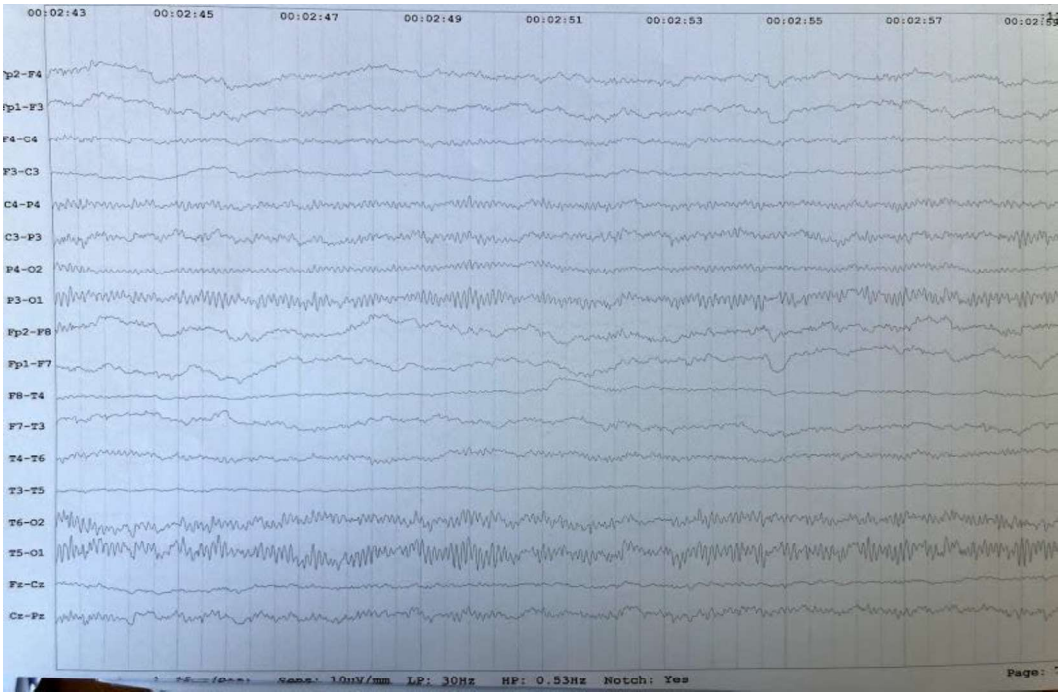




Picture 2: T1W and T2W cervical spinal cord MRI sample images



Picture 3: EEG sample of the patient



Lumbar puncture was done (Table 3) and electrophoretic separation of CSF proteins (Table 4) showed a total proteins content of 3.79 g/l, albumin content of 3260 mg/l and Immunoglobulin: IgG of 237 mg/l with a IgG index of 0,3 x 10^{3} and IgG synthesis in CNS was 0 mg/24 h. According to the characteristics of the electrophoregram there is an immunological activity in the brain that corresponds to dysfunction of the hemathoencephalitic barrier with stressed compressive characteristics.

Table 3: Laboratory values in CSF

CSF	**Value**	Reference value
Appearance	**Clear**	clear
Glucose	**4.4**	2.7 – 4.1 mmol/L
Red blood cells	**0**	0
White blood cells	**0**	0 – 6 x 10^{6}/L
Protein	**3.79**	0.15 – 0.45 g/L
Albumin	**3260**	50 – 250 mg/L
Albumin coefficient	**59.50**	0.8 – 7.4 x 10^{3}
IgG	**237**	3 – 30 mg/L

IgG index	**0.3**	0.1 – 0.7 x 10^{3}
Chloride	**134**	116 – 127 mmol/l
Lactate	**1.9**	1.1 – 2.4 mmol/l

Table 4: Electrophoregram

CSF	Results	Value ranges
Total proteins (g/l)	3.79	0.15-045
Albumins(mg/l)	3260	50-250
IgG(mg/l)	237	3-30
Albumins coefficient (10^{3})	59.5	1.8-7.4
IgG index (10^{3})	0.3	<0.7
IgG synthesis in CNS (mg/24h)	0	<5

Two days after the admission ataxic gait was observed and a positive Romberg test with falling to the right.
Regarding hypertension pediatric cardiologist, nephrologist and endocrinologist were consulted. Renal artery Doppler ultrasound showed normal findings. 24 h Holter monitoring was done, which revealed normal findings. All laboratory findings were in normal range (Table 5). The hypertension was treated with antihypertensive drugs and it was stabilized in a few days.

Table 5: Laboratory values in urine

Urine	Value	Reference value
Metanephrin	1.0	< 5.5 umol/day (U)
Vanilmandelic acid (VMA)	14.6	7.0 – 68 umol/day (U)
Diuresis	1.7 L	0.8 – 1.5 L
Amylase	291	24-400 U/L

The findings from the COVID-19 specific IgG showed an elevated range of 52.59 AU/ml (Table 6).

	Value	Reference value
COVID-19 RBD (Receptor-Binding Domain) IgG	52.59	< 1.00 AU/mL

Treatment was implemented with intravenous immunoglobulins during five days with a dose of 400 mg/kg bw/day. He made a dramatic improvement over the next few days and was able to walk well and was fully recovered at the end of the second week.

Discussion: There are very few cases in the children and adolescents who have experienced neurological post COVID-19 complications. Our report is among the rarest with cerebellar ataxia-like and polyneuritis -like signs symptoms.
The affected child had no history of change or loss of taste and smell, nor the other specific COVD-19 symptoms. The only proof of past infections were the elevated COVID-19 specific IgG.
The results from the foregram with elevated proteins and immunoglobulins were indicating Guillain Barre Syndrome and electromyoneurographic findings were normal, but the clinical signs were indicating polyneuropathy.
Other possible infections which might give these neurological sign and symptoms were excluded with normal findings.

Conclussion: Although common symptoms of COVID-19 in children are cough and fever, it is important to note, however, that these symptoms may not always be present [12, 13, 14] or they may go unnoticed. The vast majority of reported infections in children are mild or asymptomatic, with few recorded childhood fatalities attributed to covid-19 (2, 3, 4, and 5). Additionally, there are few cases in pediatric population where post-COVID-19 complications emerge and need in-patient treatment.
Currently, as we are still experiencing the pandemic and its effects, it is too early to describe the full clinical picture of PCNS. However, we believe published evidence has already made an undeniable case for medicine to recognize the increasing numbers of ex-patients with Post COVID Neurological Syndrome (PCNS) and the need for on-going neurological and cognitive/affective monitoring of all cases of COVID-19 (irrespective of the severity from asymptomatic, mild to severe) for PCNS (15,16).

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