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Case report

КАРПЕНТЕРОВ СИНДРОМ - ПРИКАЗ НА СЛУЧАЈ И ТРЕТМАН

CARPENTER SYNDROME – CASE REPORT AND TREATMENT

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Abstract

Introduction. Carpenter syndrome is a polymorphic disorder transmitted by autosomal recessive inheritance, caused by mutations in the RAB23 gene [1]. These genetic disorders are reflected on the biogenesis of intracranial structures. This syndrome was described for the first time in 1900 by the British doctor George Carpenter. It may include congenital heart diseases, mental retardation, hypogonadism, obesity, umbilical hernia, developmental disorder, bone anomalies and frequent respiratory infections. Carpenter syndrome has two main features: craniosynostosis and more than five fingers or toes [2-4].
Aim. To present our experience in treatment of an infant with Carpenter syndrome including trigonocephaly and polydactyly.
Case report. In May 2003, an eleven-month-old male infant with Carpenter syndrome was hospitalized in the Pediatric Department of the University Clinic of Neurosurgery in Skopje, Republic of Macedonia. The infant was referred to our Department from the University Pediatric Clinic because of trigonocephaly and polydactyly with two thumbs on his right hand. The infant had already been twice hospitalized at the University Pediatric Clinic for two recurrent lung infections suggestive of Carpenter syndrome. The diagnosis of trigonocephaly and polydactyly with two thumbs on the right hand was made by physical examination, X-ray of the right infant's hand and computed tomography of the head. According to Oi and Matsumoto classification from 1986 [5], the infant had a severe form of trigonocephaly.
Surgical procedure. Under general endotracheal anesthesia, the infant was placed supine on the operating table, a bifrontal skin incision was made and the scalp flap was created. The bifrontal craniotomy was realized into one bony piece succeeded by a modified Di Rocco's "shell" procedure including frontal translation and transposition rotating the flap for 180 degrees without /touching the orbital rims.
Results. The postoperative period was uneventful except for the expected forehead swelling. The infant was discharged from the hospital on the 7th postoperative day, neurologically intact. Three months after surgery, the head had excellent esthetic appearance, with regular psychomotor development in line with the age of the patient. Six months after the first surgery the patient underwent a second plastic and reconstructive surgery in order to reduce the number of fingers.
Conclusion. The early recognition and multidisciplinary approach could prevent new disabled individuals in the society. Our technique shortens the entire surgical procedure, diminishes the time under anesthesia and its complications, especially in departments where blood saving devices are not available.

Keywords: trigonocephaly, Carpenter syndrome, surgical treatment

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Апстракт

Вовед. Карпентеровиот синдром е полиморфно пореметување пренесено со автосомно рецесивен тип на наследување, предизвикано поради мутација на генот RAB23. Овие генетски пореметувања, меѓу останатото, се рефлектираат и на биогенезата на кранијалните сутури. Опишана за првпат во 1900 година од британскиот доктор Џорџ Карпентер (George Carpenter), овој синдром може да вклучи конгенитални срцеви аномалии, ментална ретардација, хипогонадизам, дебелина, умбиликална хернија, развојни аномалии, аномалии на коските и чести респираторни инфекции. Овој синдром има две главни манифестации: краниосиностоза и зголемен број на прстите на раката или на ногата.
Приказ на случај. На детскиот оддел на Клиниката за неврохирургија во Скопје, Република Македонија, во мај 2003 година било хоспитализира-

но 11 месечно машко бебе со каптентеровиот синдром. Бебето било упатено од Клиниката за детски болести поради тригоноцефалија и полидактилија со две палчиња на десната рака. Претходно бебето елекувано на Детската клиника поради две епизоди на респираторна инфекција, при што е дијагностициран карпентеров синдром. Дијагнозата на тригоноцефалијата и на полидактилијата беше поставена со физикален преглед, нативна рендгенграфија на десната дланка и компјутеризирана томографија на главата. Според класификацијата на Oi и Matsumoto од 1986 се работеше за тешка тригоноцефалија.

Хируршки третман. Бебето беше воведено во општа ендотрахеална анестезија, ставено во дорзална легната положба на оперативната маса, реализирана бифронтална коронарна инцизија на кожата и челен скалпен резен. Краниотомијата беше реализирана во едно парче и проследена со модифицирана Di Rocco процедура, вклучувајќи фронтална транслација и транспозиција, ротирајќи го коскениот флеп за 180 степени без ремоделирање на орбиталните лакови.

Резултати. Постоперативниот период помина без компликации, освен лесен оток на челото. Бебето е пуштено дома по седум дена невролошки интактно. Три месеци по операцијата, главата имаше одличен естетски изглед, со нормален психомоторен развој за возраста. Шест месеци по првата операција, пациентот беше подвргнат на втора реконструктивна операција за намалување на бројот на палците.

Заклучок. Раното препознавање и мултидисциплинарниот приод може да спречи појава на нови хендикепирани лица во општеството. Нашата техника дозволува скратување на целата хируршка процедура намалувајќи го времето во анестезија и нејзините компликации, посебно во институции кои не располагаат со апарати за заштеда на крв.

Клучни зборови: Тригоноцефалија, карпентеров синдром, оперативно лекување

Abstract

Introduction. Craniosynostoses represent developmental anomalies of the craniofacial growth in humans, that is, premature adhesion of the sutures of the calvaria, which leads to craniostenosis, obstructing the normal psychomotor development of infants. The consequences of untreated craniosynostosis can be simple esthetic disfigurations of the normal shape of the head, but can also lead to mental disruptions, difficulties in gaining new skills, disturbed behavior, epilepsy, hydrocephalus, headaches, damaging of the cranial nerves (V, VI, VII), and endocrinopathies [6].

The causes for the craniosynostoses are gener... known; there are many theories and possibili... teratogenic effect of the valproic acid, aminopterin, ... toin, retinoic acid, oxymethazoline, diseases such a... perthyroidism, rickettsiosis, thalassemia, sickle cell ... mia, thyroid diseases in pregnant woman, shunt-ind... after treatment of hydrocephalus, amniotic bands, mu... polysaccharidoses, genetic damages, especially of the g... nes FGFR1-3, NELL1, MSX2, TWIST and GLI3 [1-6].

The principle of formation of the craniosynostoses has been modified in dependence of the thoughts and observations of the authorities. Virchow (1851) suspected that the craniosynostosis was a primary malformation while the deformity of the cranial base is secondary; Moss (1959) concluded that the malformation of the cranial base is the essence for appearance of premature fusion of the cranial sutures on the calvaria; and Park & Powers (1920) suggested much more acceptable theory that the primary defect was located in the mesenchymal blast tissue that led to anomalies in the cranial vault and the cranial base [4].

The incidence of craniosynostoses estimates approximately 0.1-1 (0.6) from 1000 live babies [1,4].The classification of craniosynostoses distinguishes two group s: non-syndromic (primary, simple) craniosynostoses and syndromic craniosynostoses (conjoined with other developmental anomalies, usually on the extremities) [1-6]. The non-syndromic craniosynostoses are divided depending on the suture that is prematurely closed, respectively, as dolychocephaly (scaphocephaly-head with shape of a boat, the most common-56%), brachicephaly (anterior unilateral-anterior plagiocephaly-24%), turricephaly (head in a shape of tower), trigonocephaly (wedge-shaped head-4%), anterior and posterior plagiocephaly and oxycephaly [1-6]. A total of 150 syndromes have been described accompanied by craniostenosis. The most common syndromic craniosynostoses include the following syndromes: Crouzon, Apert, Pfeiffer, Saethre-Chotzen and Carpenter syndromes [1-7].

Carpenter syndrome is a polymorphic disorder transmitted by autosomal recessive inheritance, caused by mutations in the RAB23 gene [1]. These genetic disorders are reflected on the biogenesis of intracranial structures. This syndrome was described for the first time in 1900 by the British doctor George Carpenter. It may include congenital heart diseases, mental retardation, hypogonadism, obesity, umbilical hernia, developmental disorder, bone anomalies and frequent respiratory infections. Carpenter syndrome has two main features: craniosynostoses and more than five fingers or toes [3-6].

The diagnosis of the craniosynostoses is made with physical examination of the child (inspection-characteristic shape of the cranial vault, palpation-a prominent thicken prematurely fused suture, volumetric measurements, cranial index, cranial perimeter), x-ray, EEG,

computed tomograph... resonance of the b... of the brain) [4-8... surgical reconst... tomies going ... constructions ... mal develop... of the shar... pediatries... reconstr... may b... achie... betw... do... re...

computed tomography with 3D reconstructions, magnetic resonance of the brain (for possible associated anomalies of the brain) [4-8]. Treatment of the craniosynostoses is surgical reconstruction, starting with the simple suturectomies going further to the complex cranial vault reconstructions with aim to create enough space for normal development of the brain and the esthetic correction of the shape of the head as well. Others specialists like pediatrics, pediatric psychiatrist, pedagogue, plastic and reconstructive surgeon, orthopedic surgeon, sociologist may be included in the treatment. The best result is achieved if the surgical procedure is realized at the age between 3-7 months of the infant. If the intervention is done before the age of 3 months, there is a high rate of recurrence of the craniosynostosis with a need for additional intervention [5,7].

The **aim** of this paper was to present our experience with this rare form of syndromic craniosynostosis and treatment in order to obtain acceptable results.

Clinical material

In May 2003, an eleven-month-old male infant was hospitalized at the Pediatric Department of the University Clinic of Neurosurgery of the Clinical Center "Mother Theresa" in Skopje, Republic of Macedonia. The infant had been referred to our Department by the University Pediatric Clinic because of trigonocephaly and polydactyly, with two thumbs on his right hand. The infant had already been twice hospitalized at the University Pediatric Clinic disease for two recurrent lung infections suggestive of Carpenter syndrome (Figure 1). The diagnosis of trigonocephaly and polydactyly with two thumbs on the right hand was made by physical examination, X-ray of the right infant's hand and computed tomography scan of the head. According to Oi and Matsumoto classification from 1986 [5], the frontal angle of the axial CT slices showed 89 degrees or severe trigonocephaly.

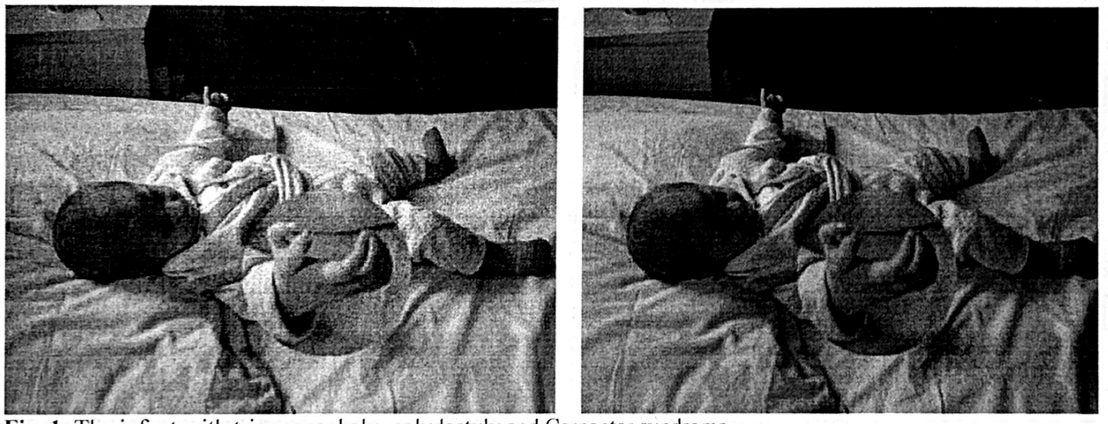

Fig. 1. The infant with trigonocephaly, polydactyly and Carpenter syndrome

Surgical treatment

The procedure was done under general endotracheal anesthesia with the infant placed in supine position (Figure 2). The procedure was started with bifrontal skin incision and creation of the frontal scalp flap.

After elevation of the periosteum, epidural dissection of the free edge of the frontal bone at the great fontanel was performed, followed by bifrontal craniotomy with one-piece free bony flap. The upper edge of the bony flap contained the coronal suture, spreading laterally downward to the both temporal fosses. The lower edge

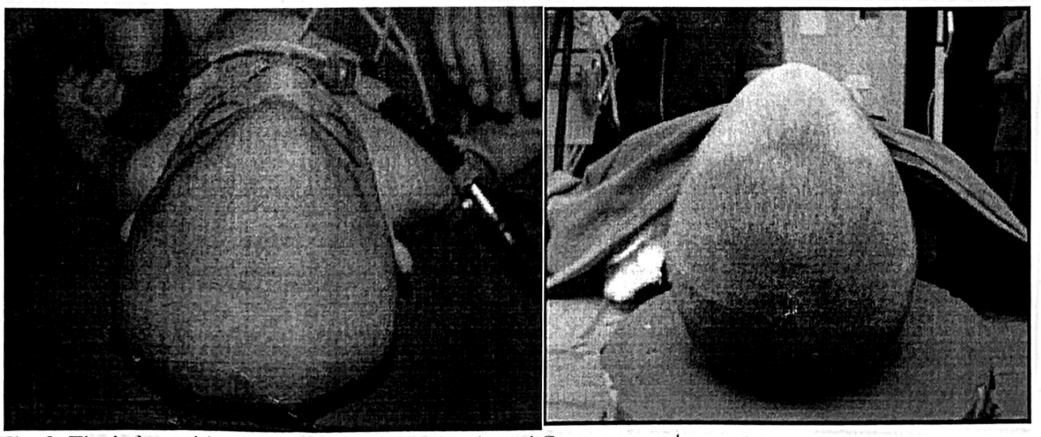

Fig. 2. The infant with trigonocephaly, polydactyly and Carpenter syndrome at surgery

of the bony flap was made just over the supraorbital rims, after creating a "burr-hole" using diamond drill over the frontonasal suture where the biggest thickening of the metopic suture was observed. The bony flap was diminished for 1 cm and rotated for 180 degrees.
The most prominent and thick part of the bone was excised, the midline of the bony flap was fractured in fashion of "green-stick" fracture and radial osteotomies were done for complete remodeling of the forehead. The bony flap was fixed forward and distal to the most frontal part of the cranial base through small bone holes on the free edge of the base with interrupted 2-0 silk sutures. Scalp flap closure was done with interrupted Blair-Donatti 4-0 polypropilene sutures, without using epicranial drainage.

Results

The postoperative period was uneventful except for the expected forehead swelling. The baby was discharged from the hospital one week after surgery. Three months after surgery, the head had excellent esthetic appearance, with regular psychomotor development in line with the age of the patient (Figure 3). Muscular tonus was better after reconstruction and correction of the craniostenosis, no further resistant respiratory infection and no opisthotonus were observed. Six month after the first surgery, the patient underwent a second plastic and reconstructive surgery in order to reduce the number of fingers. The child has been followed for 13 years and the "long term" results showed an excellent esthetic effect and normal psychomotor development, normal IQ, scolarity and socialization.

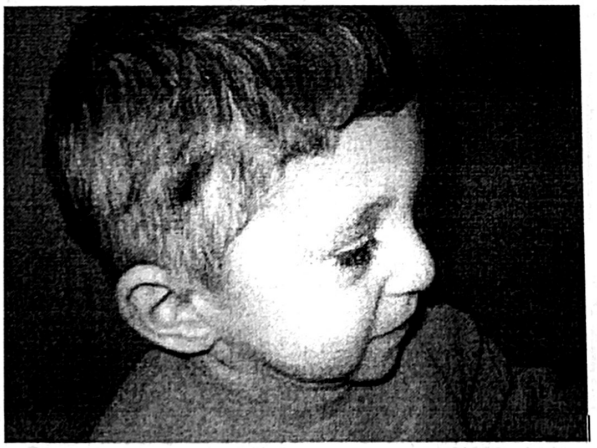

Fig. 3. The infant with syndrome 18 months after surgery

Discussion

The trigonocephaly (premature fusion of the metopic suture) takes 4% of all simple non-syndromic craniosynostosis [8]. The clinical appearance is typical, with wedge-shape, triangular forehead, flattened supraorbital rims, thickened metopic suture and cranial index with normal value. The computed tomography of the brain is also typical, with flattened bilateral frontal lobes, small anterior cranial fossa and small frontal angle [5]. The only treatment for trigonocephaly is surgical correction of the deformity. There are various number of operative interventions in which the common principle is reconstruction of the whole frontal bone, even including complex reconstructions with corrective osteotomies of the roof of the orbits and the lateral ends of the supraorbital rims for advancement and enlargement of the anterior cranial fossa.
Braid and Proctor [7] suggest that the operative correction is done between 6 and 12 months of age of the infant for open reconstruction of the anterior part of the vault because of the associated bigger blood lost, the durability of the intervention and high rate of recurrence if the intervention is done before the age of 6 months of the infant.
Raimondi's [9] opinion is to undertake surgical intervention at the age of 7 months with follow-up period until 13 months of age, presenting his excellent esthetic effect and no signs of recurrence of the deformity, with normal psychomotor development. Our patient was 11-month-old.
All open surgical procedures include bifrontal craniotomy, creation of free bony flap in one or two pieces, excision of the nasal extensions of the frontal bone and frontal extensions of the nasal bones, lateral advancement of the superior orbital ridges by pivoting on their sectioned or green-stick fractured medial edges, replacement of the frontal bony flaps after modified their edges, curvature and orientation. The variations include creation of a free orbital bar and its replacement after opportune remodeling, the insertion of a bone graft in the midline gap resulting from the removal of the upper part of the nasal bones to correct hypotelorisme [3].
Di Rocco's personal surgical technique [3] accomplishes all mentioned goals through a procedure named "shell" surgery because of the characteristic form of the frontal bony flap. In fact, the procedure consists of a frontal craniotomy in order to remove the deformed frontal bone and part of the parietal bones from a line 2 cm above the orbital ridges to the anterior fontanel. The flap is remodeled with the drilling of the thick ridge of the metopic suture and anterior displacement of its lateral aspects. Radial osteotomies converging downwards and towards the midline (so mimicking the lines of the shell) diminish the resistance of the bone and allow modifying its curvature. The nasal processes of the frontal bone and the upper part of the nasal bones are removed. The roof and the lateral walls of the orbits are sectioned and the lateral borders of the superior orbital ridges pushed forward in order to compensate for the hypoplastic orbital cavity. The pushing maneuver is made using the medial borders of the superior orbital ridges, cracked only partially, as pivots. The advance-

ment is maintained by replacing the remodeled frontal bone between the advanced superior orbital rims and the anterior border of the parietal bones [3].

In our case, the lung problems required a shorter surgical procedure and therefore we modified it by translation and transposition of the bone flap without advancement of the orbital rims. The created free frontal bone flap in one piece is osteotomized anterior and distal just above the superior orbital ridges with drilling of the most prominent part of the metopic suture and after that it is rotated for 180 degrees with excision of the most prominent wedge part of the bone flaps. Radial converging linear osteotomies are made on the bone flap with separate green-stick fractures for further enlargement of the intracranial space. The frontal bone flap is repositioned and fixed over the superior orbital ridges with one interrupted 2-0 silk suture on both sides of the forehead. The created reconstruction makes an excellent esthetic and functional effect at 3 months after surgery, especially with the enlargement of the anterior and lateral aspects of the frontal lobes of the cerebrum. Six months after the first surgical cranial procedure, the infant was rehospitalized at the University Clinic for Plastic, Esthetic and Reconstructive Surgery in Skopje in order to reduce the number of thumbs of his right hand.

The possible side effects of the intervention are: bleeding, infection of the wound, with overall incidence under 1%, possible recurrence with further need of additional surgical correction depending on the age of the patient and the type of craniosynostosis. Our long-term results show no complications, no recurrences, and normal development of the child.

Conclusion

The early recognition of these anomalies allows the most adequate treatment according to the conditions of the health system in order to treat deformities of the newborn and infant's head and to prevent abnormal psychomotor development during children's growth.

The multidisciplinary approach could prevent new disabled individuals in the society. Our technique shortens the entire surgical procedure, especially in departments where blood saving devices are not available.

Conflict of interest statement. None declared.

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