ISSN 2226-1230 (PRINT) ISSN 2413-4260 (ONLINE)
KEY TITLE: NEONATOLOGIÂ, HÌRURGIÂ TA PERINATAL'NA MEDICINA (ONLINE)
ABBREVIATED KEY TITLE: NEONATOL. HÌR. PERINAT. MED. (ONLINE)

УДК: 617.52:616.716.6]-007.2-008.6-07-053.31
DOI: 10.24061/2413-4260.XI.2.40.2021.10

THE CLINICAL CASE OF HEMIFACIAL MICROSOMIA IN THE NEWBORN BOY FROM MOTHER WITH Z-21

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Summary

Hemifacial Microsomia (HFM) is a term used to identify facial deformities associated with the development of the first and second pairs of branchial arches, characterized by underdevelopment of one half of the face. One type of hemifacial microsomia is oculo-auriculo-vertebral dysplasia or Goldenhar syndrome.

The incidence of HFM is 1:3500-1:7000 of live births and occurs in 1 case per 1000 children with congenital deafness. The ratio of boys to girls is 3:2. The etiology and type of inheritance is studied insufficiently. There are three possible pathogenetic models: vascular abnormalities and hemorrhages in the craniofacial region, damage of Meckel's cartilage, and abnormal cell development of the cranial nerve crest. Environmental factors, maternal internal factors, and genetic factors (OTX2, PLCD3, and MYT1 mutations) may also cause the development of hemifacial microsomia.

The article demonstrates a clinical case of hemifacial microsomia in a newborn boy from a mother with Z-21 in the form of deformation of the left auricle with atresia of the auditory canal and "false" ears on the right, combined with congenital anomaly of heart (atrial septal defect) and brain (hypoplasia of the corpus callosum).

Emphasis is placed on the need of involving a multidisciplinary team of specialists in the management of this patient both in the neonatal period and in the system of subsequent follow-up.

Key words: *Hemifacial Microsomia; Goldenhar syndrome.*

Introduction

Hemifacial Microsomia (HFM) is a term used to identify facial deformities associated with impaired development of the first and second pairs of branchial arches, characterized by underdevelopment of one half of the face. Alternative names: otocraniostenosis, craniofacial microsomia, lateral facial dysplasia, syndrome of the first and second pair of branchial arches, Goldenhar syndrome or oculo-auriculo-vertebral dysplasia. Historically, if a patient is diagnosed with epibulbar dermoid among the symptoms, the disease is called Goldenhar syndrome (GS), and if it is not – Hemifacial Microsomia [1-3].

Firstly HFM was described by Cant (1861) and later by Von Arlt (1881), but this went unnoticed. In 1952, the Swiss ophthalmologist Goldenhar described three cases of eye and ear dysplasia with two characteristic abnormalities: epibulbar dermoid and preauricular growths. These abnormalities were accompanied by coloboma in the middle of the eyelid, microphthalmia, aplasia or hypoplasia of the auditory canal, preauricular fistula and macrostomy. Gorlin and Pindborg (1963) reported their observations under the general name "oculo-auriculo-vertebral dysplasia", thus pointing to changes in the spine: hemivertebrale, occipitalisatio atlantis, spina bifida occulta and others. Since then, GS has been defined as dysplasia of the eyes, ears and spine in the clinical atlas of congenital anomalies of the face [1, 2, 4, 5, 6].

The wide range of anomalies associated with HFM complicates systematic and inclusive classification. In 1991, Vento et al., proposed a system in which each letter of the abbreviation O.M.E.N.S. indicates one of the five main manifestations of HFM: O – orbital distortion; M – mandibular hypoplasia; E – ear anomaly; N – nerve involvement; S – soft tissue deficiency. O.M.E.N.S. the system is easily adapted for data storage, retrieval and statistical analysis. The retrospective study of 154 patients with HFM classified according to O.M.E.N.S. confirmed the concept that mandibular deformity is the "cornerstone" of this anomaly [3, 7].

According to statistics, the incidence of HFM is 1:3500-1:7000 live births and occurs in 1 case per 1000 children with congenital deafness. The ratio of boys and girls is 3:2. The probability of giving birth to the next child with this disease is about 2%, the probability of transmitting the disease to children – less than 3 % [2, 5].

The etiology and type of inheritance are insufficiently studied. Currently, 8 genes have been identified in which mutations can cause HFM. The orthodontic homeobox 2 gene (OTX2) is identified more often than the other seven genes. It also determines the genetic code of the transcription factor. The GSC gene, which determines the clinical manifestations of HFM, is mapped on the long arm of chromosome 14, at locus 14q32 [3, 8, 9].

Most cases of HFM are sporadic due to reduced penetrance, somatic mosaicism and epigenetic changes. There are reports of familial inheritance, which thus requires consideration of autosomal dominant (AD), autosomal recessive (AR) or multifactorial inheritance.

The etiology of the disease does not exclude the role of adverse obstetric and gynecological history of the mother: previous abortions, diabetes, overweight, malnutrition, smoking and alcohol use; and the influence of teratogenic factors in early pregnancy,

such as drugs cocaine, thalidomide, retinoic acid, herbicides [2, 6, 9, 10, 11].

Posvillo (1976), using an animal model, suggested that fetal hypoxia, maternal hypertension, anticoagulants can lead to hematoma in the ear or jaw of the fetus. Hematomas can cause impaired tissue differentiation, which, in turn, can lead to dysplasia of the branching arch in the process of early ontogenesis. Gomes et al. (1984) hypothesized the role of radiological intervention in the 4th or 6th week of pregnancy as a causative factor of the syndrome. Now it is believed that when the source of blood supply changes in the area 1 and 2 of the branchial arches of the embryo, hemorrhage occurs. Rupture of a blood vessel in this place leads to mitotic cell division and incorrect formation of the basic anatomical structures of the human body. Callen et al. (2004) believe that HFM and CHARGE syndrome combine a single pathogenetic mechanism, namely the violation of the tab of the nerve roller [1, 9].

Frequent signs of GS include the following [1, 8]:

• ocular symptoms: epibulbar dermoid, microphthalmia, exophthalmia, anophthalmia, strabismus, eye asymmetry/ dysmorphia, lipodermoids, coloboma, atresia/stenosis of the lacrimal duct;

• auricular symptoms: atresia of the external auditory canal, preuricular appendages, ear dysplasia with or without hearing loss, middle and inner ear abnormalities, asymmetry of the ears, microtia;

• craniofacial deformities: anomalies of the 1st and 2nd pharyngeal arches, facial asymmetry, hypoplasia of the facial skeleton, mandible and/or upper jaw, hemifacial macrosomia, malocclusion, cleft teeth, agenesis of cleft palate , macrostomy, defects in the development of enamel and dentin, deposited in the development of the tooth;

• skeletal abnormalities: spinal cleft, limb abnormalities, microcephaly, ileal foot, dolichocephaly, radiation hemimelia, plagiocephaly, thumb abnormalities, vertebral defects;

• abnormalities of internal organs, heart: atrial and ventricular septal defects (the most common), tetrology of Fallot, aortic coarctation, transposition of the great vessels, dextracardia;

• urogenital anomalies: renal ectopia, renal agenesis, fused kidneys, multicystic kidneys, double ureter, hydronephrosis;

• central nervous system: diffuse cerebral hypoplasia, hydrocephalus due to Sylvian duct stenosis, dilated lateral ventricles or asymptomatic hydrocephalus, corpus callosum lipoma, asymmetric lateral ventricles, absence of the septum pellucidum, celestial paralysis, musculoskeletal dysgenesis, vertebral abnormalities, holoprosencephaly, Arnold-Chiari malformation, hypothalamic hamartoma, aplasia/hypoplasia of the temporomandibular joints;

• gastrointestinal tract: rectal atresia, tracheo-esophageal fistula, esophageal atresia;

• respiratory system: abnormal anatomy of the larynx and pharynx, disorders of the lobular anatomy of the lungs.

Unilateral lesions were observed in 85% of HFM abnormality cases, the bilateral lesions were observed in 10-33% of cases; and right side is affected more often. Combined conductive and sensorineural hearing loss occurs in 50% of cases.

Differential diagnosis is performed with mandibulofacial dysostosis Francesketti, CHARGE, VATER, OEIS and Townes Brocks syndromes, Wildervank syndrome, Nager dysostosis, MURCS association (Mueller duct aplasia, renal aplasia and cervicothoracic schomitic somitic dysplasia). The prognosis for this disease is usually favorable. However, psychosocial problems and autistic behavior have been described [8].

Clinical case

We present our own clinical case of HFM in a newborn boy. The study was approved by the BSMU Research Ethics Committee.

The child was born from the second pregnancy and the second birth at 37 weeks of gestation. This pregnancy took place against the background of the mother's underlying disease Z-21. Childbirth took place by elective caesarean section, without complications from the mother. Mother's heredity is complicated by diabetes and cardiovascular disease in close relatives, and thyroid disease from her father.

The boy's body weight at birth was 2550 g, body length – 49 cm, head circumference – 35 cm, chest circumference – 35 cm. Apgar score at the end of the first minute of life was 8 points, the fifth minute – 8 points; resuscitation measures were not performed.

The condition at birth is regarded as vitally compensated. Somatic and neurological status – without pathological manifestations. But at external inspection of the child the asymmetrical face due to underdevelopment of the left lower third has been noted; underdeveloped auricle on the left; on palpation – displacement of the height of the branch of the lower jaw on the left and the absence of the masticatory muscle on the left (Fig.).

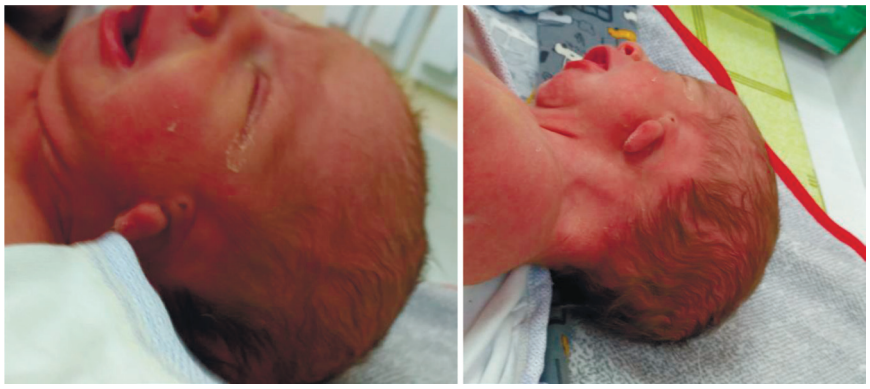

Fig. Phenotypic signs of HFM in the newborn boy

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In accordance with national clinical guidelines and protocols, as well as routes of patients of the medical institution, the child was in a joint stay with the mother under the supervision of medical staff, started enteral feeding with an adapted mixture in physiological volumes. Given the mother's diagnosis of Z-21, the child was prescribed appropriate antiretroviral therapy with a combination of three drugs in enteral administration.

During the second day of life, negative dynamics of the child's condition was noted in the form of manifestations of the syndrome of oppression and vegetative-visceral disorders, as well as a decrease in tolerance to enteral nutrition, in connection with which the child was transferred to the intensive care unit of newborns. The conditions of thermal comfort were provided, non-pharmacological and pharmacological anesthesia was carried out, infusion was established to ensure the physiological needs for fluid and its pathological losses. From the third day of life, the boy showed an increase in jaundice, with the level of total bilirubin, which required phototherapy.

On the fifth day of life, the child was transferred to the ward with the mother in the post-intensive care unit, where he was continued enteral feeding with an adapted mixture through a tube with a gradual expansion of daily to physiological needs, treatment of jaundice, implementation of "early intervention", mother training features of care and feeding of the baby. In total, the boy spent 28 days in the hospital.

The child was consulted by a pediatric dental surgeon, who provided recommendations for further examination: X-ray of the head in a direct view and lateral left projection; child care (teaching a child to suck and feed from a bottle. It was also recommended to consult a pediatric maxillofacial surgeon at the Department of National Medical Bogomolets University, when the child reaches the age of three months.

Examination by a pediatric otolaryngologist included external examination, anterior rhinoscopy, otoscopy, mesopharyngoscopy. It was found that the nasal passages are clear, breathing is free, the turbinates and mucous membranes are pink; the right auditory meatus is normal, clean, the eardrum is gray, the shell has an additional rudiment; left - agenesis of the auricle, absence of the cutaneous part of the ear canal; there is a reaction to auditory stimuli; the mucous membrane of the pharynx is clean, pink; deformation of the lower jaw. It was recommended to carry out a planned surgical correction of the external hearing aid on the left.

The children's ophthalmologist established the absence of pathological signs from the patient's visual analyzer.

Echocardiography examination revealed signs of hemodynamically insignificant open ductus arteriosus, atrial septal defect. Neurosonography revealed hypoplasia of the corpus callosum.

After a consular examination of the child with the participation of narrow specialists, including a geneticist, taking into account the results of clinical and instrumental examination, the child was diagnosed with the main clinical: cerebral depression in a newborn (P91.4) concomitant: congenital malformations that affect the appearance of the face: hemifacial microsomia (Q87.0), contact with a patient or the possibility of infection with human immunodeficiency virus (Z03.71), jaundice in a newborn (P59.8).

A multidisciplinary team of specialists has defined a plan for follow-up of the patient, including continuing the practice of "early intervention", accompanying the child in the family, consulting a pediatric cardiologist, magnetic resonance imaging to confirm or rule out spinal abnormalities, determining the timing of hearing prosthetics, classes with a deaf educator, psychological support of the child's parents, as well as long-term support of the child and family by an infectious disease specialist to monitor the effectiveness of antiretroviral therapy, etc.

Conclusion

The article demonstrates a clinical case of hemifacial microsomia in a newborn boy from a mother with Z-21 in the form of deformation of the left auricle with atresia of the auditory canal and "false" ears on the right; combined with congenital anomaly of the heart (atrial septal defect) and of the brain (hypoplasia of the corpus callosum). Emphasis is placed on the need to involve a multidisciplinary team of specialists in the management of this patient both in the neonatal period and in the system of subsequent follow-up.

Conflict of interest: absent.

Sources of funding: self-financing.

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КЛІНІЧНИЙ ВИПАДОК ГЕМІФАЦІАЛЬНОЇ МІКРОСОМІЇ У НОВОНАРОДЖЕНОГО ХЛОПЧИКА ВІД МАТЕРІ З Z-21

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Резюме. Геміфаціальна мікросомія (ГФМ) – термін, який використовується для ідентифікації деформацій обличчя, пов'язаних з порушенням розвитку перших і других пар зябрових дуг, що характеризуються недорозвиненням однієї половини обличчя. Одним із типів геміфаціальної мікросомії є окуло-аурікуло-вертебральна дисплазія або синдром Гольденхара.

Захворюваність на ГФМ становить 1:3500-1:7000 живонароджених та зустрічається у 1 випадку на 1000 дітей із вродженою глухотою. Співвідношення хлопчиків та дівчат становить 3:2. Етіологія та тип успадкування вивчені недостатньо. Існує три можливі патогенетичні моделі: судинні аномалії та крововиливи в черепно-лицьовій області, пошкодження хряща Меккеля та аномальний розвиток клітин черепно-мозкового нервового гребеня. Фактори зовнішнього середовища, внутрішні материнські фактори матері та генетичні фактори (мутації OTX2, PLCD3 та MYT1) можуть також зумовити розвиток геміфаціальної мікросомії.

У статті продемонстровано клінічний випадок геміфаціальної мікросомії у новонародженого хлопчика від матері з Z-21 у вигляді деформації лівої вушної раковини з атрезією слухового ходу та «хибними» вушками справа, що поєднано з уродженою аномалією серця (дефект міжпередсердної перетинки) та головного мозку (гіпоплазія мозолистого тіла).

Акцентована увага на необхідності залучення мультидисциплінарної команди спеціалістів у веденні даного пацієнта як у неонатальному періоді, так і у системі подальшого катамнестичного спостереження.

Ключові слова: геміфаціальна мікросомія; синдром Гольденхара.

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КЛИНИЧЕСКИЙ СЛУЧАЙ ГЕМИФАЦИАЛЬНЫЙ МИКРОСОМИИ У НОВОРОЖДЁННОГО МАЛЬЧИКА ОТ МАТЕРИ С Z-21

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Summary. Гемифациальная микросомия (ГФМ) – термин, который используется для идентификации деформаций лица, связанных с нарушением развития первых и вторых пар жаберных дуг, характеризующихся недоразвитием одной половины лица. Одним из типов гемифациальной микросомии является окуло-аурикуло-вертебральная дисплазия или синдром Гольденхара. Заболеваемость ГФМ составляет 1:3500 - 1:7000 живорожденных и встречается в 1 случае на 1000 детей с врожденной глухотой. Соотношение мальчиков и девочек составляет 3:2. Этиология и тип наследования изучены недостаточно. Существует три возможных патогенетические модели: сосудистые аномалии и кровоизлияния в черепно-лицевой области, повреждение хряща Меккеля и аномальное развитие клеток черепно-мозгового нервного гребня. Факторы внешней среды, внутренние материнские факторы и генетические факторы (мутации OTX2, PLCD3 и MYT1) могут также вызвать развитие гемифациальный микросомии. В статье продемонстрирован клинический случай гемифациальный микросомии у новорожденного мальчика от матери с Z-21 в виде деформации левой ушной раковины с атрезией слухового прохода и «ложными» ушками, что сопряжено с врожденной аномалией сердца (дефект межпредсердной перегородки) и головного мозга (гипоплазия мозолистого тела). Акцентировано внимание на необходимости привлечения мультидисциплинарной команды специалистов в ведении данного пациента как в неонатальном периоде, так и в системе дальнейшего катамнестического наблюдения.

Ключевые слова: гемифациальная микросомия; синдром Гольденхара.

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Надійшло до редакції 12.04.2021 р.
Підписано до друку 10.06.2021 р.