Hemifacial Microsomia; Goldenhar syndrome.

Each letter of the abbreviation O.M.E.N.S. indicates complications systematic and inclusive classification.

Anomalies of the face [1, 2, 4, 5, 6]. Eyes, ears and spine in the clinical atlas of congenital anomalies of the face [1, 2, 4, 5, 6].

Occipitalisatio atlantis, spina bifida occulta and others. Thus pointing to changes in the spine: hemivertebrale, general name "oculo-auriculo-vertebral dysplasia", Pindborg (1963) reported their observations under the general name "oculo-auriculo-vertebral dysplasia" or Goldenhar syndrome.

In 1952, the Swiss ophthalmologist Goldenhar (GS), and if it is not - Hemifacial Microsomia [1-3].

Historically, if a patient is diagnosed with epibulbar dermoid among the 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 of live births and occurs in 1 case per 1000 children with congenital deafness. The ratio of boys to 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, preauricular 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, dextrocardia;
• urogenital anomalies: renal ectopia, renal agenesis, fused kidneys, multicystic kidneys, double ureter, hydrenephrosis;
• central nervous system: diffuse cerebral hypoplasia, hydrocephalus due to Sylvian duct stenosis, dilated lateral ventricles or asymmetrical hydrocephalus, corpus callosum lipoma, asymmetric lateral ventricles, absence of the septum pellucidum, cephalic paralysys, musculoskeletal dysgenesis, vertebral abnormalities, holoprosencephaly, Arnold-Chiari malformation, hypothalamic hamartoma, aplasia/hypoplasia of the temporomandibular joints;
• gastrointestinal tract: rectal atresia, tracheoesophageal 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 dystosis Francesketti, CHARGE, VATER, OEIS and Townes-Brocks syndromes, Wildervank syndrome, Nager dysostosis, MURCS association (Mueller duct aplasia, renal aplasia and cervicothoracic somitic 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
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, mesosphyngoscopy. 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 microsomnia (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 microsomnia 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.
КЛІНИЧНИЙ ВИПАДОК ГЕМІФАЦІАЛЬНОЇ МІКРОСОМІЇ У НОВОНАРОДЖЕННОГО ХЛОПЧИКА ВІД МАТЕРИ С Z-21

И.В. Ластівка1, А.Г. Бабінцева1, В.В. Анцупова2, А.І. Перижняк1, І.В. Кошурба4, Л.І. Бришевац4

Буковинський державний медичний університет 1
(м. Чернівці, Україна)

Національний медичний університет імені О.О. Богомольця 2
(м. Київ, Україна)

КНП «Чернівецький обласний перинатальний центр» 3
(м. Чернівці, Україна)

Національний університет охорони здоров'я 4
(м. Київ, Україна)

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

Захворюваність на ГФМ становить 1:3500-1:7000 живороженних і зустрічається у 1 випадку на 1000 дітей з врождженою глухотою. Соотношення мальчиків і дівчат становить 3:2. Етиологія та тип успадкування вивчені недостатньо. Існує три можливі патогенетичні моделі: судинні аномалії та крововилив в черепно-лицьовій області, пошкодження хряща Меккеля та аномальний розвиток клітин черепно-мозкового венозного 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 новорожденного хлопчика від матері з Z-21 у вигляді деформації лівої вушної раковини з атрезією слухового ходу та "живими" ушками, що поєднано з уродженням аномалії серця (дефект міжінтеркардіалної перетинки) та головного мошка (гіпоплазія мозолистого тіла).

Акцентована увага на необхідності захисту дитини в усьому рівні, включаючи підготовку до хірургічного втручання. Ключові слова: геміфаціальна мікросомія; синдром Гольденхара.

Контактна інформація: Babintseva Anastasiya Gennadiyevna – Doctor of Medicine, Ph.D., Associate Professor, Department of Pediatrics, Neonatology and Perinatal Medicine, Bukovinian State Medical University, Chernivtsi, Ukraine. e-mail: babintseva@bsmu.edu.ua
ORCID: http://orcid.org/0000-0002-3859-6431

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

HFM prevalence is 1:3500-1:7000 among newborns and is encountered in 1 out of 1000 children with congenital deafness. The ratio of boys to girls is 3:2. The etiology and type of inheritance have not been sufficiently studied. There are three possible pathogenetic models: vascular anomalies and hemorrhage in the cranio-facial area, damage to the Mekel’s cartilage and the development of cells in the venous system of the cranio-cerebral groove. Factors from the external environment, maternal internal factors and genetic factors (mutations OTX2, PLCD3 and MYT1) can also cause hemifacial microsomia. In the article a clinical case of hemifacial microsomia in a newborn boy from a mother with Z-21 in the form of deformity of the left auricular canal with atresia of the auditory channel and "false" ears, which is combined with a congenital heart anomaly (defect of interventricular septum) and of the brain (cerebellar hypoplasia). The emphasis was placed on the need to protect the child at all levels, including preparation for surgical intervention. Key words: hemifacial microsomia; Goldenhar syndrome.

Contact Information: Anastasiya Babintseva – Doctor of Medicine, PhD, MD, Associate Professor, Department of Pediatrics, Neonatology and Perinatal Medicine, Bukovinian State Medical University, Chernivtsi, Ukraine. e-mail: babintseva@bsmu.edu.ua
ORCID: http://orcid.org/0000-0002-3859-6431

© I.V. Lastivka, A.G. Babintseva, V.V. Antsupova, A.I. Peryzhniak, I.V. Koshurba, L.I. Brishewsai, 2021