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The cyclopia. A case report.

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ABSTRACT: A case of cyclopia is described, and an analysis of the literature data is carried out. The material of the study was the corpse of a newborn with cyclopia, stored in the anomalies section of the museum of the Department of Human Anatomy and Medical Terminology of the Azerbaijan Medical University. The face, location of the eye, and proboscis were examined. The proboscis is located below the eye. An anomaly in the topography of the auricles is also noticeable, which indicates a combination of this anomaly with anomalies in other facial structures. The photographs were taken in frontal and lateral projections, with an emphasis on the eye and adjacent anatomical structures.

KEY WORDS: cyclopia, proboscis, holoprosencephaly.

I. INTRODUCTION

Incomplete brain development (holoprosencephaly) greatly affects face shaping. The extreme defect that occurs in holoprosencephaly is median eye (cyclopia). Violation of the normal telencephalic splitting of the forebrain into bilateral hemispheres of the brain leads to holoprosencephaly. This, in turn, reflects a disruption in the work of the prosencephalic organizing center. This results in a number of abnormalities of the upper face, eyes, nose, and ears, the most severe of which is cyclopia (synophthalmia) [1–2]. This is the most severe form of alobar holoprosencephaly, resulting from incomplete splitting of the prosencephalon into the right and left hemispheres. It occurs between 18 and 28 days of pregnancy. Usually the nose is either missing or replaced by a non-functioning proboscis. This proboscis usually appears above the central eye or on the back and is characteristic of a form of cyclopia called rhinencephaly or rhinocephaly [3]. According to [4], the proboscis was present in four of the seven cases. Six out of seven children have additional congenital malformations.

Microscopic examination of the proboscis revealed respiratory epithelium as well as mucous glands in the submucosa, cartilage fragments, and compact bone plates [5]. Although this rare congenital anomaly is incompatible with life, knowledge of the spectrum of sonographic features and appropriate genetic counseling can help in determining the outcome of the current and upcoming pregnancy. Antenatal ultrasound should be performed to lead to early detection of such rare cases, which are incompatible with life, and termination of pregnancy should follow. The early ultrasound diagnosis of this anomaly should be emphasized, which leads to the conclusion that patients with suspected fetal facial defects should be referred to medical centers qualified for prenatal examination. [6–8]. The logical continuation of this statement is the study [9], in which the sonographic diagnosis was based on the intracranial finding of fused thalami without visible midline structures and facial abnormalities, including cyclopia and proboscis. In the investigation, the authors assessed the fetal face using three-dimensional (3D) transabdominal ultrasound and were able to identify cyclopia under the proboscis. These findings are characteristic of alobar holoprosencephaly.

Cyclopamine (a steroidal alkaloid) enables the teratogenic mechanism, resulting in the inhibition of the Sonic Hedgehog (Shh) signal transduction pathway [10].

[11] indicates that cyclopia can take several forms, which are generally grouped as follows: (1) the two orbits may be different but closely spaced. Between them, there may be a median vestigial nose with one nostril (cebocephaly), or the nose may be a tubular structure of skin and soft tissues continuing into the forehead. (2) The two orbits may merge into a single diamond-shaped cavity containing two eyes showing varying degrees of fusion. This is the most common anomaly, and many cases reported in the literature belong to this group. The two eyes may

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be adjacent. There may be a single eyeball that is greatly enlarged and contains a double lens or adjacent double cornea. There may be one vestigial eye, and in some cases, the eyeball is wrinkled. The nose is absent or represented by a nasal proboscis, which may contain a cavity lined with ciliated epithelium. The cavity has an external opening and is internally intimately connected with the ethmoid and its cribriform plate.

[12] after analyzing the literature data, the authors came to the conclusion that 1) the brain equivalent of cyclopia can be not only alobar holoprosencephaly but also more severe anomalies of the forebrain; 2) aprosencephaly can be considered the earliest known variant of the prosencephalic series; and 3) the association "agnathia-holoprosencephaly" is etiologically heterogeneous.

Judging by the literature data, interest in the study of cyclopia is steadily growing [13–14]. Caring for motherhood and childhood and improving the methods of studying the fetus during pregnancy, of course, leads to a decrease in the birth rate of children with this anomaly through premature termination of pregnancy. However, various harmful factors have an impact on the development of the fetus, among which it is necessary to highlight the use of various drugs by pregnant women. Particular attention should be paid to early diagnosis during pregnancy using diagnostic methods and proper treatment of this disorder in order to prevent further harm to the newborn and mother with this syndrome. Moreover, many of these newborns should be offered early neonatal palliative care [15].

According to [16], the presentation of cyclopia has not been fully identified, and new cyclopean syndromes may still occur. A prenatal diagnosis of cyclopia can be made at an early stage using ultrasound, and knowledge of the sonographic spectrum of cyclopia can improve the accuracy of the prenatal diagnosis. The legitimacy of abortion in reported cases in many parts of the world needs to be reviewed.

Holoprosencephaly is the partial or complete inability of the forebrain to divide into hemispheres and may be an isolated finding or associated with a syndrome. Most cases of holoprosencephaly are associated with a syndrome, and approximately 40–60% of fetuses with HPE have trisomy 13, which is the most common etiology of holoprosencephaly [17].

According to [11], one feature of the mothers who gave birth to the Cyclopes was that they gave birth many times. So, of the six cases studied in two mothers, these were the eleventh births, and in two, the tenth births. One childbirth was the fifth, and only one gave birth for the first time. In one case, the girl Cyclops was the first of the twins; the second in this pair was a boy and was apparently normal.

Without SHH signaling, cells cannot determine the direction of stress and move erratically, resulting in insufficient elongation of the optic vesicles and hence the cyclopia phenotype. Because polarized tissue and cell dynamics are common in organogenesis, cell disorientation caused by a loss of mechanosensing may be a pathogenic mechanism for other malformations [18].

A detailed analysis of all the bones of the skull showed that the most affected areas in Cyclopean fetuses were the upper two-thirds of the viscerocranium and the anterior part of the basicranium. The ethmoid, nasal, inferior concha, and lacrimal bones were absent in all cases of cyclopia. The main anomalies were found in the premaxillary region, which affected the development of the anterior dentition. The study supports the notion that malformations of the visceral bones are secondary to defective development of the presphenoidal and mesethmoid cartilages. The ethmoid bones are important midline supports in normal development, and their absence in cyclopia results in non-lateralization of facial features [19]. Anatomical and histological observations suggest that the integrity of the trigeminal nerve is of great importance for the normal development of the embryological structures of the face. Merging of the facial processes along the midline occurs even in the absence of central proencephalic structures. For this reason, the face of cyclopia, both in its positive and negative aspects, is a model for studying the normal development of this area [20].

Thus, the question of studying cyclopia remains open and relevant. Based on the foregoing, we conducted a study of cyclopia in one case in order to compare it with the available literature data and, possibly, supplement it. The aim of the study was to study cyclopia in the corpse of a newborn boy.

II. MATERIALS AND RESEARCH METHODS.

The material of the study was the corpse of a newborn with cyclopia, stored in the anomalies section of the museum of the Department of Human Anatomy and Medical Terminology of the Azerbaijan Medical University. The face, location of the eye, and proboscis were examined. The photographs were taken in frontal and lateral

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projections, with an emphasis on the eye and adjacent anatomical structures.

III. RESEARCH RESULTS.

The studied case of cyclopia is shown in Figures 1 and 2.

Figure 1. The anterior view.

Figure 2. The lateral view.

The eye, as follows from the above figures, is one. It should be noted that the proboscis is located below the eye. An anomaly in the topography of the auricles is also noticeable, which indicates a combination of this anomaly with anomalies in other facial structures.

IV. DISCUSSION.

Much of the mythology of holoprosencephaly centers on cyclopia. Ideas about one-eyed people have been found in many countries for centuries [21].

Literature data show that cyclopia is expressed, although by a common set of anomalous qualities, but in all studies individual features are revealed. For example, in the study [13], the authors point to the absence of the mouth, nose, and proboscis. As in our study, the ears were present at a lower level, in the ventral aspect.

In the study [14], the authors describe two cases of cyclopia. In the first case, the authors point to the presence of the proboscis. In the second case, the presence of "probosciform frontal soft mass" is emphasized and localized, as in the case we studied, "below the eyes".

Also, [4] indicates the presence of the proboscis in four cases out of seven. The authors emphasize the high degree of variation of other anomalies associated with cyclopia.

According to [6], in a medically terminated pregnancy, the study showed cyclopia, synophalmia, fussed eyelids with a small proboscis on the midline of the face, and a malpositioned left ear.

Pointing to an unknown etiology, [7] describes a case of cyclopia with a partially divided eye in a single orbit, an absent nose, and a proboscis above the eye. Other anomalies identified in this case were the polydactyly of the hand.

[15] describes a case of a 37-week- and 5-day-old female fetus in which an eye and a 4-cm proboscis were found in the middle of the forehead. The newborn had no nose, and his outer ears were normal.

[5] In a macroscopic examination of a 34-week-old fetus, an umbilical cord with two vessels, fetal proboscis measuring 4.2 cm, cyclopia, low implanted ears, bilateral polydactyly of the upper limbs with six fingers, and spina bifida occulta in the sacral region were noted.

V. CONCLUSION.

Thus, our study and review of the literature show a wide variety of manifestations of cyclopia. This serves as a kind of incentive for further research involving the latest medical techniques in this area. Also, a wide variety of morphological and clinical manifestations of cyclopia explain a sufficient number of studies on this issue. Also important is the growth of care for motherhood and childhood and the promotion of a healthy lifestyle, which, of course, can significantly reduce the level of such severe anomalies as cyclopia.

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