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Case report

Cyclopia, a newborn with a single eye, a rare but lethal congenital anomaly: A case report

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ABSTRACT

Introduction and importance: Cyclopia is a rare congenital disorder characterized by facial abnormalities. In this condition, the orbits of the eye are not properly divided into two cavities so that they can be seen either as a single eye field or two bilateral fields that are very close to each other. This syndrome affects the embryos that are either aborted or stillborn upon delivery or, at best, die shortly after birth.

Case presentation: This case report is of a 37-week- and 5-day-old female fetus with a birth weight of 2300 g, a height of 43 cm, and a head circumference of 31 cm. She was born to a 44-year-old mother through normal vaginal delivery at Mahzad Hospital, Urmia, Iran. In the physical examination, an eye and a 4-cm proboscis were seen in the middle of the forehead. The newborn also had no nose, and his outer ears were normal. No cleft lip or cleft palate was observed. Unfortunately, the newborn expired 13 h after birth.

Clinical discussion: Cyclopia leads to a stillbirth since the brain and other parts of the body do not grow normally in fetuses with this disorder. Moreover, it can be diagnosed using ultrasonography while the fetus is growing inside the uterus.

Conclusion: Early diagnosis during pregnancy using diagnostic methods and proper management of this abnormality should be emphasized to prevent further harm to the newborn and the mother with this syndrome. Moreover, many of these newborns should be offered early neonatal palliative care.

1. Introduction

Cyclopia is a rare genetic disorder occurring as a birth defect [1]. Its incidence rate is reported to be 1 in 13,000 to 20,000 newborns [2]. In this health condition, the eye's orbits are not properly divided into two cavities so that they can be seen either as a single eye field or two bilateral fields that are very close to each other [3]. This congenital disorder affects both animals and humans [4]. Patients with cyclopia syndrome typically have a missing or dysfunctional nose with a long snout. The outer ears are usually curved, broken, or crumpled inwards. Most patients also have a 3- to 5-cm polyp in the middle of the forebrain [3]. This syndrome mostly affects the embryos that are either aborted or stillborn upon delivery or, at best, die shortly after birth [5].

This study reports the clinical condition of a baby born with cyclopia and who died after enduring this anomaly for 13 h. This case report was reported according to the SCARE 2020 Guidelines to ensure the quality of reporting [6].

2. Case presentation

The present case report is of a 37-week- and 5-day-old female fetus born to a 44-year-old Kurdish mother through normal vaginal delivery at Mahzad Obstetrics and Gynecology Hospital, Urmia, Iran. She (his mother) had a history of cesarean delivery at the age of 32, where the newborn was completely healthy. She was from a family with low socioeconomic status and lives in a village far from Urmia city. She had seen a gynecologist only once during this pregnancy and had not performed any pregnancy examinations or diagnostic evaluations such as ultrasonography. She also mentioned a history of taking levothyroxine for her hypothyroidism. She had no history of smoking and denied a

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history of alcohol and drug abuse. Moreover, she did not state any history of exposure to teratogens during pregnancy, especially in the first trimester. During history-taking at admission, the parents did not mention the history of congenital anomalies or close family marriage in their relatives.

After the onset of labor signs, the mother went to the hospital and gave birth to a 37-week- and 5-day-old female fetus with a birth weight of 2300 g, height of 43 cm, and head circumference of 31. In the initial physical examination, an eye and a 4-cm proboscis were seen in the middle of the forehead (Fig. 1). The newborn had no nose, and his outer ears were normal. Although the newborn had micrognathia, no cleft lip or cleft palate was observed [see Additional file]. The newborn's skin was cyanotic, possibly due to hypoxia. His vital signs at birth were as follows: Temperature: 36.3, Heart Rate: 183 bpm, Respiration Rate: 69 bpm, Blood Pressure: 57/25 mmHg, Oxygen Saturation: 86%. The newborn's Apgar score could not be calculated. He was transferred to the Neonatal Intensive Care Unit (NICU) and placed in an incubator. In the chest X-ray conducted at birth, the newborn's right lung was shown to be completely collapsed (Fig. 2). Therefore, to manage this condition, a chest tube was immediately placed in the right chest. We used the ventilator for the newborn continuously until the newborn died. Cyclopia may sometimes also be associated with cardiac defects (e.g., atrial septal defect, hypoplastic left heart, anomalous communication between right ventricle and aorta). However, in this case, the echocardiography report did not show any associated cardiac abnormalities. Moreover, brain MRI demonstrated the fusion of the frontal horns of the lateral ventricles with abnormal genu and rostrum of the corpus callosum and partial fusion of the cingulate gyrus anteriorly. The anterior cerebral artery was azygous and displaced anteriorly. This newborn had features consistent with lobar holoprosencephaly (Fig. 3), including a poorly formed corpus callosum and azygous anterior cerebral artery. Other organs were shown to be normal, and no other congenital malformations were found. Unfortunately, the newborn expired within 13 h after birth. Unfortunately, her parents did not give consent for an autopsy.

3. Discussion

Holoprosencephaly is a common brain defect that often leads to facial anomalies such as close ocular orbits, microcephaly, cleft lip, and cleft palate. Holoprosencephaly is a disorder caused by the failure of the prosencephalon (fetal forebrain) to adequately develop and divide into the left and right hemispheres [7]. This disorder results in the formation of a single-lobed brain structure and severe craniofacial defects. In most cases of holoprosencephaly, the abnormalities are so severe that neonates die before birth [8]. Holoprosencephaly consists of three subtypes, including alobar, semi-lobar, and lobar holoprosencephaly. In the alobar subtype, the brain is not divided, and there are severe facial defects. In the semi-lobar subtype, the brain's hemispheres are partially divided and cause a moderate form of the disorder. There are two separated hemispheres in the lobar subtype with minor structural defects [8,9].

In patients with milder forms of holoprosencephaly, craniofacial defects include microcephaly, orbital hypotelorism, flat nasal bridge, and abnormal anterior teeth. In this regard, the cleft lip is the mildest facial abnormality in holoprosencephaly [9], while the most severe facial abnormality is cyclopia. In patients with cyclopia, a hereditary disease, the face is seen with a single eye field and an incomplete nose above the eye [2]. Parents of neonates with cyclopia should warn their

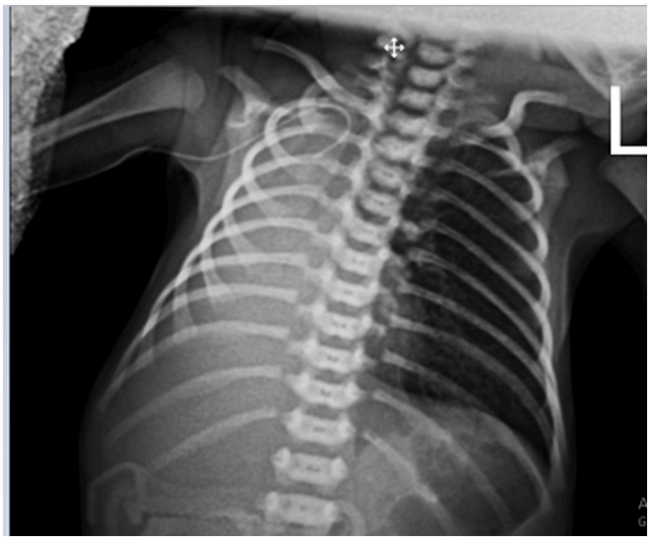

Fig. 2. The chest radiograph of the newborn with cyclopia.

Fig. 1. The newborn with cyclopia syndrome.

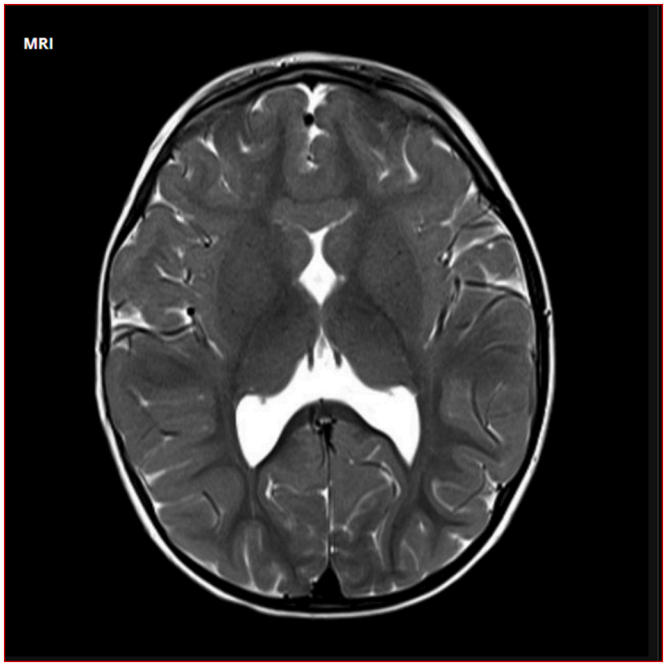

Fig. 3. Infant's brain MRI with lobar holoprosencephaly features.

first-degree relatives who may be forming a family about the increased risk of cyclopia or other milder forms of holoprosencephaly [10].

The present case report is of a 37-week- and 5-day-old female fetus born to a 44-year-old mother. The newborn had no nose, and no cleft lip or cleft palate was observed, although the newborn had micrognathia. The newborn's skin was cyanotic. Chest X-ray revealed that the newborn's right lung was completely collapsed. Therefore, to manage this condition, a chest tube was immediately placed. We ventilated the newborn continuously until she died. Brain MRI demonstrated that the newborn had the characteristics of lobar holoprosencephaly, including a poorly formed corpus callosum and azygous anterior cerebral artery.

As there is no cure for this condition, legal abortion is the solution to prevent further harm to the newborn and the mother. Recognizing potential risk factors and informing parents is another suggested solution. Ingestion of certain plants during pregnancy can increase the risk of cycops and should be avoided.

The Sonic Hedgehog (SHH) gene is located in the long arm of chromosome 7 (7q35.1 band) and regulates the expression and synthesis of proteins in the nervous system to form the correct shape of the brain. SHH gene also regulates the correct formation of the hands and nose. Furthermore, the Paired Box 6 (PAX6) gene regulates the correct synthesis and development of the eyes. In cyclopia, the above genes mutate and lose their normal function. The SHH gene plays a key role in promoting the expression of other genes in the cell, such as PAX6 and PAX2 [11].

Cyclopia can be diagnosed using ultrasonography while the fetus is growing inside the uterus. This congenital disorder occurs between the third and fourth weeks of pregnancy, and conducting medical ultrasound after this time can usually show obvious signs of cyclopia or other forms of holoprosencephaly. In addition to orbital hypotelorism, abnormal formation of the fetus's brain and internal organs may be seen on ultrasound [12]. When the ultrasound shows an abnormality but cannot provide a clear picture, the physician may recommend fetal Magnetic Resonance Imaging (MRI). If cyclopia is not diagnosed during the pregnancy, it can be diagnosed by medically examining the newborn at birth [3].

The exact causes of cyclopia remain unknown [4]. However, researchers believe that several factors can increase the risk of cyclopia. These include genetic factors, multiple pregnancies, especially twinning, female sex, previous unexplained miscarriages, gestational diabetes, infections during pregnancy, exposure to UV light, smoking, using alcohol and certain medications during pregnancy, and cyclopamine - a highly alkaloid toxin. Another risk factor related to this anomaly is *Veratrum californicum*, found in corn lily or false hellebore. It is implicated in causing cyclopia (when ingested believing the plant to be hellebore, which can cure the morning sickness symptoms associated with the first few months of pregnancy) [4,5].

Cyclopia often leads to a stillbirth since the brain and other parts of the body do not grow normally in fetuses with this disorder. The brain of a neonate with cyclopia cannot manage the formation of the other organs that are necessary for survival [13]. In 2015, the live birth of a newborn with cyclopia was reported in Jordan. The newborn died in hospital within 5 h after birth [14]. Most studies have shown that a baby born with cyclopia syndrome has a maximum lifespan of 10–12 h [1,3,13], but despite the anomaly of the respiratory system, our case survived 13 h, which was the longest survival time of a newborn with cyclopia syndrome. A newborn who develops cyclopia often does not survive pregnancy. This is because the brain and other organs do not develop normally. The brain of a newborn with cyclopia cannot sustain all the body's systems needed to survive.

Newborns with this lethal congenital malformation, even if they survive longer than expected, become severely impaired and palliative care should be considered. The goals of palliative care in the neonatal context are to prevent and relieve pain and suffering of neonates and provide support for families. Such care includes planning with the family about the practicalities of the death and continuing family support after the baby dies [15]. Prenatal palliative care emphasizes the importance of planning for the experience of losing an infant. Pre-natal diagnosis of congenital heart defects produces an ethical dilemma for both parents and physician. The right to decide should be left to the parents, while the caregivers have to support them with nondirective counselling, with the information necessary for parental decision [16].

4. Conclusion

Early diagnosis of cyclopia during pregnancy using diagnostic methods such as ultrasonography and the proper management of this abnormality should be strongly emphasized to prevent further harm to the newborn and the mother. However, such cases remain undiagnosed in developing countries where pregnant women do not receive regular prenatal care.

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Ethical approval

All ethical principles were considered in conducting this case report. All patient information kept confidential.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Authors' contributions

NP, AH, AA, NF, SR, and RG contributed in data collection, manuscript drafting and reviewing, and approval of final manuscript. RG and NP has contributed in case management, data collection, manuscript

drafting and reviewing, and approval of final manuscript. NP performed the study supervision.

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Declaration of competing interest

None.

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