Cyclopia (Synophthalmia): First Reported Case in Iraq

*Abdulhameed Abdulmajeed Hassan, **Ghazwan Hameed Rasheed

*Department of surgery, College of Medicine, Kirkuk University.

** Azadi Teaching Hospital, Kirkuk.

Abstract:

A full-term newborn male with cyclopia (synophthalmia); with central single eye, and without apparent nasal opening was borned in Azadi teaching hospital. This anomaly was expected to be associated with holoprosencephaly and other visceral anomalies; but this could not be confermed. Observations from clinical examination are presented here, and literature review done. Because of its rare occurrence and tentative evidence for both genetic and environmental etiologies, reporting of this case of cyclopia is encouraged.

Key words: Cyclopia , Synophthalmia , congenital anomalies

Introduction:

Cyclopia is a lethal condition in which a single ocular structure is present in the upper median portion of the face. The cyclopean eye consists of a single eyelid opening, beneath which there may be two small eyeballs that show partial fusion at the posterior portion within a single orbit. The eyes may be reasonably well formed, or they may consist of various rudimentary dysplastic ocular tissues. The single optic nerve, composed predominantly of glial cells, emerges from the midline of the posterior region of the fused globes. Synophthalmia is a less severe condition, but it is also lethal. In this condition, portions of two incomplete, usually symmetrical globes are joined in the midline as a single median ocular structure [(1)]. Figure 1

Cyclopia is associated with dramatic, symmetric deformities of the nose, skull, orbits, and brain. These include cyclopia with absent nasal structures (Fig. 2-A and Fig. 2-B). A proboscis, a cylindrical protuberance, may also be present (Fig. 2-C). In ethmocephaly, the eyes are separate but closely placed (hypotelorism); a proboscis is present (Fig. 2-D). In cebocephaly, ocular hypotelorism is present along with a nasal structure that has a single nostril (Fig. 2-E). The milder form of facial deformities includes ocular hypotelorism, flat nose, and a median cleft lip occur (Fig. 2-F). Subtle, often missed forms include mild hypotelorism, eye abnormalities (iris or retinal colobomas), mild midface hypoplasia, bifid uvula, and single central maxillary incisor tooth (Fig. 2-G)[(2)].

The most common brain deformity associated with cyclopia is holoprosencephaly. The term holoprosencephaly describes a spectrum of cerebral malformations that result from absent or incomplete division of the embryonic forebrain, the prosencephalon. A subclassification of holoprosencephaly can be done based on the extent of sagittal division of the cerebral cortex, thalamus, and hypothalamus. In the most severe form, alobar holoprosencephaly, midline structures are absent and there is no

division of the hemispheres. A single common ventricle is present and the thalami are fused. In semilobar holoprosencephaly, incomplete division of the forebrain results in partial separation of the hemispheres. In lobar holoprosencephaly, there is normal cortical division and two thalami, but abnormalities exist in the corpus callosum, septum pellucidum, or olfactory tract or bulbs.

Recent evidence indicates that failure to develop midline structures of the neural tube results from either genetics or environmental mutations in the homeobox genic sonic hedgehog [(2)].

Clinical Report:

This neoborn was delivered to 40 years old women, gravida 7, para 3, abortion 3. She was pregnant for 39 weeks and developed hypertension, during third trimester. No history of drug intake during pregnancy apart from vitamin supplements. She was admitted into hospital to control her blood pressure and to prepare her for elective C/S. On admission, investigations and abdominal U/S was done. Maternal investigations showed Hb level was 11, 6 gm/dl, PCV 35 l/l, RBS was 65 mg/dl. Maternal blood group was O negative. Abdominal U/S revealed cephalic presentation, BPD was 36 wk, FL 40 wk; placenta was anterior in position, adequate liquor, and suspected microcephaly. At the same day of admission, she delivered by NVD. The neonate was male, with a birth weight of 3100 gm, birth length 48 cm, and occipitofrontal circumference (OFC) of 35 cm. He had a central orbital cavity, with a single eye. There was no apparent nasal opening (fig 3). Oral cavity was normal, no cleft lip or palate. The ears were intact and normal in position. There was bluish discoloration over the face, mostly due to manipulation during vaginal delivery. The limbs were normal, without gross deformities. He had normal urethral and rectal openings, with bilateral descended testes. The placenta was delivered completely.

The baby was admitted into the neonatal care unit, and put in the incubator, with oxygen, intravenous fluid and antibiotics. On blood sampling, blood group was O negative. During the first 24 hour, he developed tachypnea, intercostals recession, and showed signs of respiratory distress. Then, he died on the next day.

Although further congenital anomalies in the brain and other internal body structures were suspected, but this could not be confirmed as autopsy was refused by the family.

The parents and their living children are phenotypically normal.

Discussion:

A neonate male, with cyclopia (synophthalmia), and it is to our knowledge, the first reported case in Iraq. Review of literatures is done, and our case is compared with seven other reported cases. Prioia AD. (Pathology department, Duke University, USA) had reported a case with unilateral synophthalmia, extra cerebral hemisphere, and minor structural abnormalities in the base of skull. He thought, it is a result of failure in separating a monozygous twin [(3)]. Weaver DD et al. (genetics department, Indiana University, USA) reported a 24 weak fetus with Smith_ Lemli_ Optiz syndrome (SLOS), a lobar holoprosencephaly (HPE) and cyclopia (synophthalmia) (fig.4). The fetus had ambiguous genitalia and bilateral 2_3 toe syndactyly. The diagnosis of SLOS was confirmed by genetic study. The author had postulated that the HPE in

this case resulted from severe impairment of Sonic Hedgehog signaling, secondary to abnormal cholesterol metabolism[4].

Koregol MC et al. (obgyn department, Rajir University, Bangalore, India) reported a stillborn male baby of 3, 5 kg, with shoulder dystocia during delivery. He had features of cyclopia which was later confirmed by autopsy [5].

Siebert JR. (children hospital, Seattle, Washington, USA) had reported a case of monochorionic diamniotic twining, and observed one twin with acardia, cyclopia and aprosencephaly. He suggested that hypoxia_ ischemia due to twin reversed arterial perfusion (TRAP) may play a role in the pathogenesis of this case [6].

Worku B. (paediatric department, Tikur Anbessa hospital, Addis Ababa, Ethiopia) had reported a 1200 gm neonate female with a single orbital fossa, absent globes and proboscis like structure on the forehead and she died immediately after birth[7].

Chen CP et al. (obgyn department, Machay memorial hospital, china) described the prenatal use of three_ dimensional/ four_ dimensional (3D/4D) sonographic demonstration of facial dysmorphisms associated with holoprosencephaly in 6 fetuses (2 with cyclopia, 1 with cebocephaly, and 3 with holoprosencephaly_ premaxillary agenesis) [8].

Dane B et al. (obgyn, Haseki hospital, Istanbul, Turkey) had reported a case with semilobar HPE, cyclopia, and radial aplasia. It was detected at 12 weeks of gestation by a means of transvaginal 2D ultrasound. Three dimension (3D) ultrasound provided a better visualization. The necropsy confirmed the sonographic findings [9].

Conclusions:

In this case of synophthalmia, the risk factors that may play a role in its incidence are three previous miscarriages, and the age of the mother. Iraq stills a polluted war area, which may be an additional risk factor. Cyclopia is an abnormality that occurs during the first trimester (MÜller and O'Rahilly 1989), so hypertension in the third trimester is not expected to play a role in its incidence. The underlaying mechanism in this case has been underestimated and requires additional investigation.

Good antenatal care, including early pregnancy U/S, is essential for early diagnosis. Prenatal or postnatal karyotype is recommended. Autopsy should be done. In this case, there was poor ANC and the abdominal U/S failed to diagnose cyclopia.

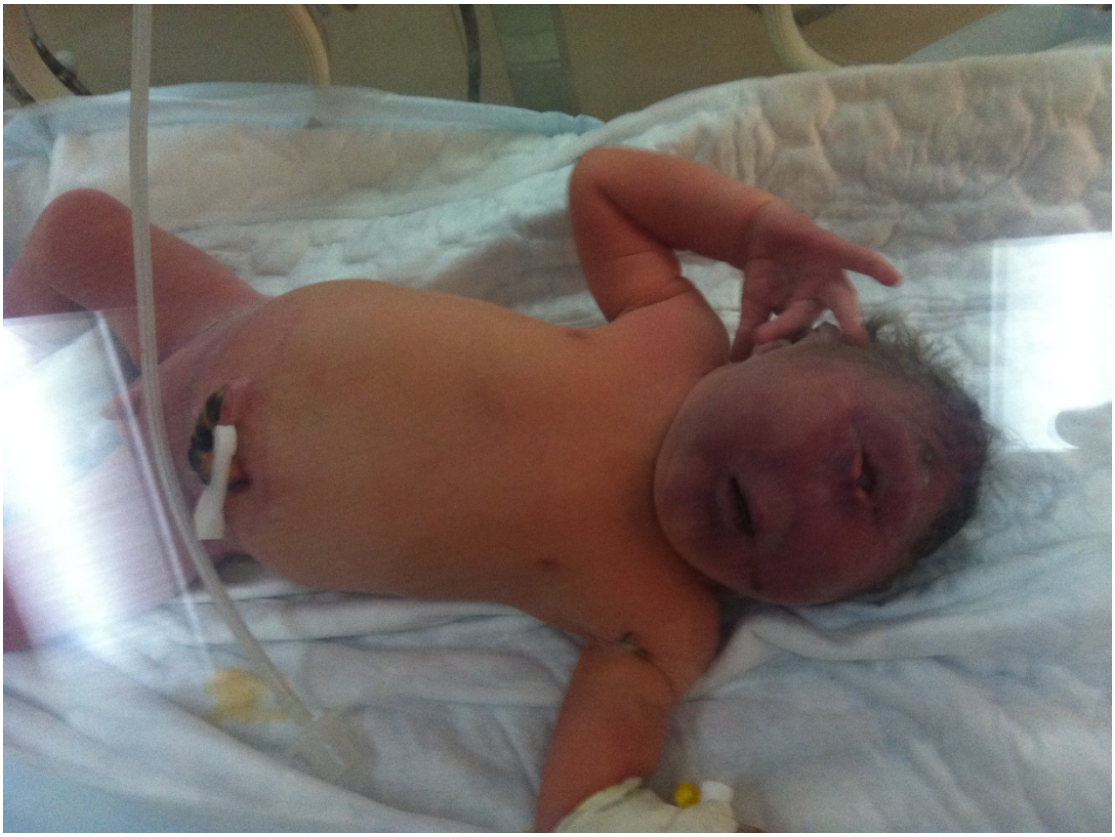

Fig.1: cyclopia

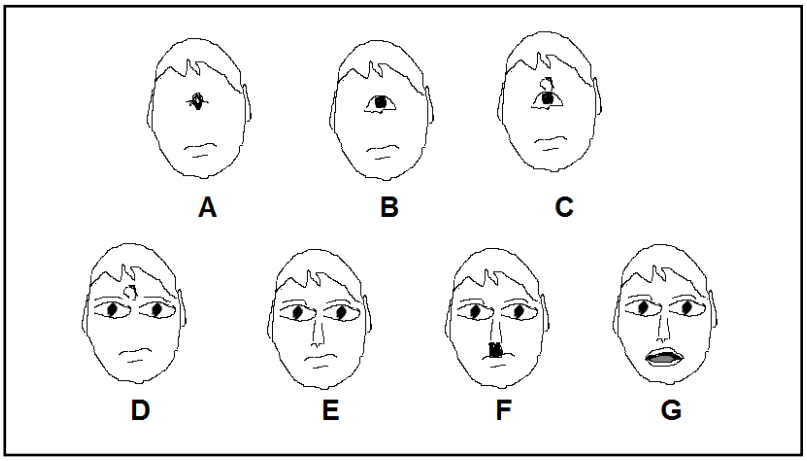

Fig.2: Types of cyclopia [2]

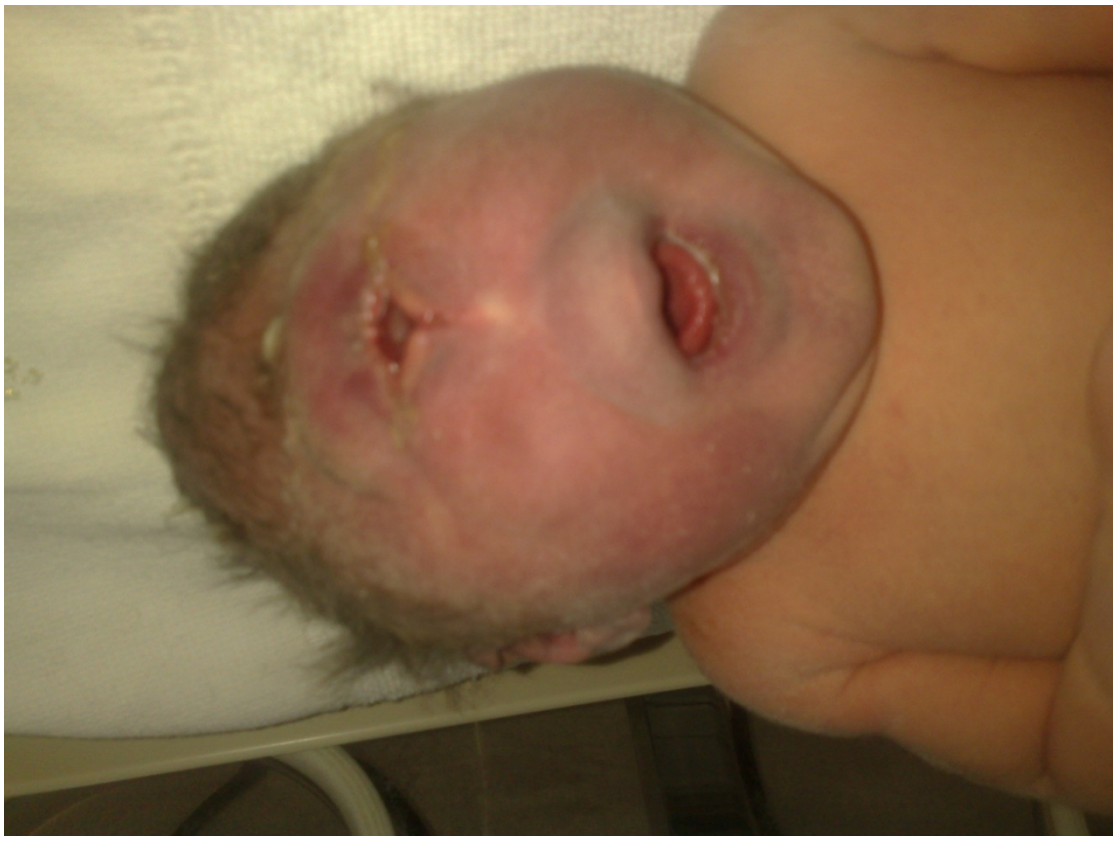

Fig.3: cyclopia

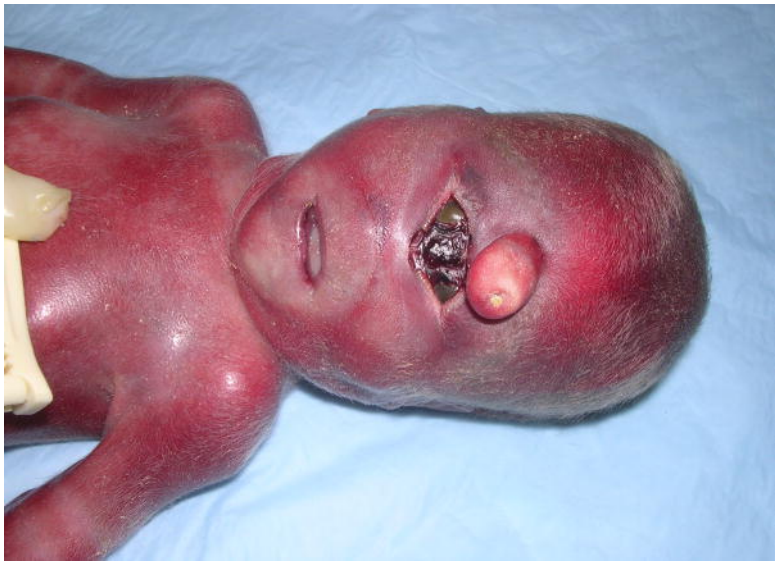

Fig.4: a 24 weak fetus with Smith_ Lemli_ Optiz syndrome (SLOS), a lobar holoprosencephaly (HPE) and cyclopia [4]

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