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Holoprosencephaly with Cyclopia and Proboscis in a Female Namibian Baby: A Case Report

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Abstract

We present a case of Holoprosencephaly (HPE) with cyclopia and proboscis that was delivered in Katutura Intermediate Hospital, Namibia. The mother was a 24-year-old, G2P1 with no known comorbid conditions and no history of illicit or over-the-counter drug use. Her first pregnancy was uneventful and resulted in delivery of a normal baby. She had not attended antenatal clinic by the time of her presentation with the index pregnancy and the abnormality was picked up from the booking sonar. She went into spontaneous preterm labour and delivery before the planned date for admission for termination of pregnancy and physical examination of the baby confirmed the diagnosis of Holoprosencephaly with cyclopia. The pictures presented in this article were taken after obtaining parental consent.

Keywords

Abnormality, Congenital, Cyclopia, Holoprosencephaly, Proboscis

1. Introduction

Holoprosencephaly refers to a group of disorders arising from failure of normal forebrain development, or incomplete cleavage of the prosencephalon, during embryonic life—at approximately the 18th and the 28th day of gestation (Dubourg C 2007). It is a rare condition with varying degrees of affection. In its worst form, cyclopia, fetuses do not reach full term and those that do, don't survive extra uterine life. There are several risk factors implicated in the causation of these disorders but it is not uncommon to find no single risk factor like in the

case being described in this article. Since cyclopia is incompatible with life, early antenatal attendance and identification of such cases by ultrasonography, and discussion of termination of pregnancy with the parents are of paramount importance.

2. Case Presentation

A 24-year-old G2P1 mother presented to the antenatal clinic unsure of her last normal menstrual period. She had not had any antenatal visit during the current pregnancy. Routine antenatal history taking revealed that the mother did not have any comorbidities, no history of over-the-counter or illicit drug use and no history of febrile illness during pregnancy. She had no recollection of any congenital abnormalities in her family. Her physical examination was unremarkable. Ultrasound examination showed a singleton pregnancy at an estimated gestation age 30 weeks with a single midline ocular structure (Figure 1), hydrocephaly with almost no brain tissue (Figure 2), a 2-chambered heart (Figure 3) and gross polyhydramnios (AFI of 55.3 cm).

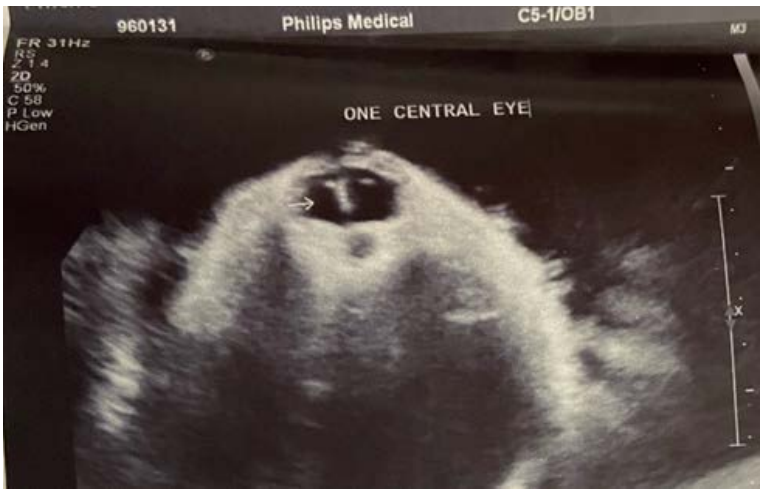

Figure 1. Ultrasound picture showing a single central eye with two pupils.

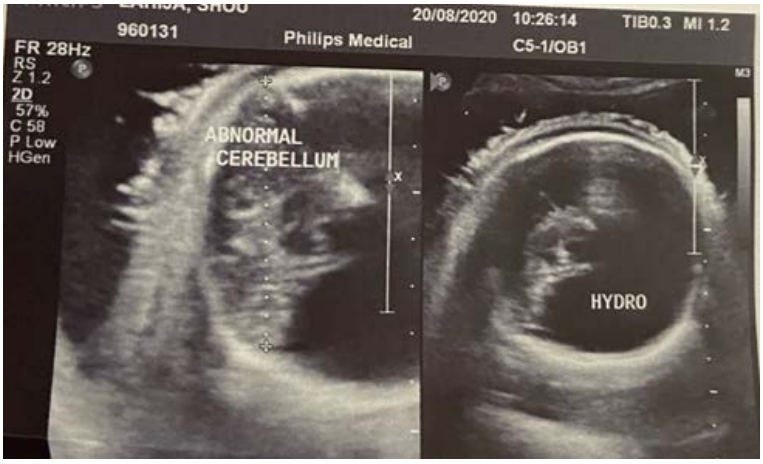

Figure 2. Ultrasound showing abnormal cerebellum and hydrocephalous.

The findings from ultrasound examination and likely outcome from the pregnancy were explained to the mother and her partner and they were counselled about termination of pregnancy, which they accepted. Labour, however, started spontaneously a day later and the mother had a vaginal delivery. The outcome was a still female baby with birth weight of 1.700 g.

At delivery approximately 3000 ml of clear amniotic fluid drained. On examination the baby had microcephaly (head circumference was 27 cm and body length of 58 cm), one diamond-shaped eye with two pupils, and absence of nose. It had a proboscis-like structure above the eye and some degree of micrognathia. See pictures below taken immediately after birth (Figure 4). A diagnosis of Holoprosencephaly with cyclopia was made.

Figure 3. Ultrasound showing a 2-chambered heart.

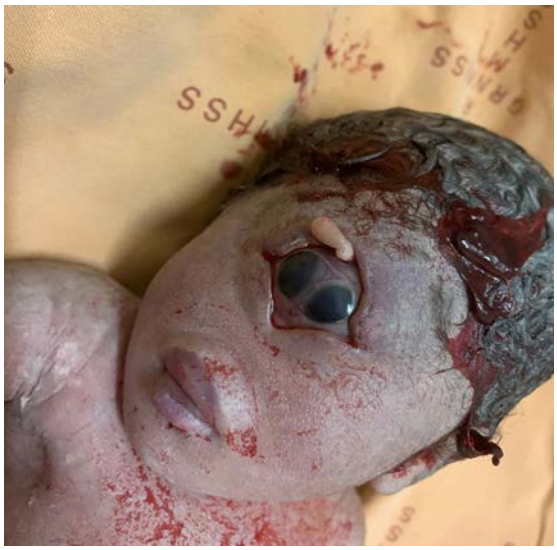

Figure 4. Photographs showing baby with a single midline ocular structure with 2 pupils and a proboscis above the eye. Photographs were taken after getting consent from parents.

Significant findings on postmortem included:

HEAD AND NECK

1) Skull: **holoprosencephaly (brain not separated into two hemispheres)**

2) Intracranial content; **microcephaly** (Brain weight; 49 **g)**

3) Orbital, nasal and aural cavities**: choana atresia**

4) Mouth, tongue and pharynx: **small round oral cavity**

5) Neck structure**: short neck**

6) Thoracic cage and diaphragm**: unremarkable**

7) Mediastinum and esophagus**: unremarkable**

8) Trachea and bronchi: **unremarkable**

9) Pleurae and lungs: unremarkable, thymus 11 g, left lung one lobe, right lung 2 lobes

Right Lung weight**: 14 g**

Left Lung weight: 18 g

10) Heart and pericardium: **one chambered heart, atriums not fully developed**

Heart weight: 12 **g**

3. Discussion

Holoprosencephaly (HPE) refers to a group of disorders arising from failure of normal forebrain development (incomplete cleavage of the prosencephalon) during embryonic life which normally takes place at approximately the 18th and the 28th day of gestation [1].

There are three classic types described in increasing severity—lobar HPE, where the right and left ventricles are separated, but with some continuity across the frontal cortex; semilobar HPE with a partial separation, and the most severe form, alobar HPE, also known as cyclopia, cyclocephaly or synophthalmia. In this condition there is a single brain ventricle and no interhemispheric fissure [2] [3]. Phenotypically the spectrum of HPE ranges from cyclopia or proboscis in the most severe cases, to midline cleft lip, a simple hypotelorism or even no anomalies in the less severe forms [1]. Babies with lobar and semilober HPE may be born alive and may survive extra-uterine life but with developmental delay and low intelligent quotient.

Cyclopia is characterized by the failure of the embryonic prosencephalon to properly divide the orbits of the eye into two cavities. It is the severest facial expression of the holoprosencephaly syndrome. It is a rare condition with sporadic occurrence. It accounts for approximately 1 in 100,000 births [4] [5]. In Namibia this is probably the first case of its kind as there is no documented literature regarding this abnormality. This concretizes the rarity of this condition. This abnormality occurs predominantly in females [6]. The reason for its predominance in the female gender is not clear yet.

There is great dysmorphism in the severely affected foetuses/babies. This index baby was delivered still (without life). The condition is not compatible with

life and usually results in miscarriage/abortion and even if the child is born alive it dies hours after birth (Winter 2015). It is thus a great contributor to perinatal mortality. It had a single central facial diamond-shaped eye with 2 pupils and proboscis, representing the nose, above the eye. The other extracranial features like polydactyl, renal dysplasia, and an omphalocele reported in other literatures (Salama 2015) were absent in the index case. Conspicuously, however, there was a one chambered heart and a very short neck.

The etiology of HPE is still not clearly understood. Heterogenous risk factors, both genetic and environmental, have been implicated. Multiple genes like sonic hedgehog, transforming growth factor beta-induced factor (TGIF), Chromosomal defects like trisomy 13, trisomy 18, and triploid are mentioned in several literatures [1] [4] [7] [8]. Environmental factors like maternal diabetes, drugs (alcohol, retinoic acid, aspirin, lithium), infections during pregnancy have also been implicated. Investigative history from the mother, however, failed to come up with any risk factor in this case.

Diagnosis: Sonography is the most helpful investigation in the antenatal diagnosis of cyclopia. The usual/normal ultrasound however may fail to pick up some features that may be helpful in making a diagnosis [9]. The imaging modality of choice is high-resolution MRI scans. In cases where MRI is not available or unaffordable, physical examination of the baby at birth offers the best diagnosis. In this case, sonar done at approximately 30 weeks, due to late booking, showed a foetus with a single ocular structure in the middle of the face, almost no brain tissue, brain was replaced with fluid and had a two-chambered heart seen. There was gross polyhydramnios with an AFI of 55.3 cm. All these were in keeping with cyclopia. At birth the baby exhibited classic features of alobar holoprosencephaly as described above.

4. Conclusion

Early recognition of these conditions during the antenatal period is of paramount importance as some, like Cyclopia (the alobar form of holoprosencephaly), are not compatible with life and others are associated with developmental delays and/or low intelligent quotient (IQ). It is therefore important to inform parents/families of the abnormality and the possible outcome during the antenatal period so that they, together with the managing medical team, decide on whether termination of pregnancy may be undertaken. All antenatal units, therefore, should incorporate routine antenatal anomaly ultrasound in their program to try to detect abnormalities like these.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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