Morphological, Clinical and Radiological Features of Congenital Cyclopia

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ABSTRACT

Cyclopia is a rare congenital facial abnormality apparently characterized by the fusion of the orbits and the presence of a proboscis below the eye. This abnormality is often associated to severe forebrain malformation incompatible with life, specially a holoprosencephaly. The etiology of cyclopia is unclear and heterogeneous which may be mainly genetic and environmental. Antenatal diagnosis is actually possible thanks to the prenatal ultrasonography. Early prenatal diagnosis is important to decide legal termination of pregnancy at a young age with less psychological impact. We report a case of 33-year old primipara who gave birth to a female fetus at 34 weeks of gestation who died 15 minutes after birth. The mother had no past history of a similar condition. Foetopathology examination and autopsy of the newborn showed a case of synophtal rhinocephale cyclope associated to holoprosencephaly. We discuss risk factors, diagnosis, prognosis, and pregnancy management of cyclopia referring to literature.
INTRODUCTION

Cyclopia is a rare congenital facial-development defect of unknown etiology. The global frequency is estimated at 1/100,000 newborns, including stillbirth. This condition is characterized by a failure of the embryonic prosencephalon to properly divide the orbits of the eye in two cavities. It is presenting as a single midline orbit with absence of the nose and presence of a rudimentary proboscis above the orbit. A wide variation of eyes structure can be distinguished including a single large median eye, a single rudimentary eye, and an absent eye. Most commonly, the two eyeballs are fused into a single structure. Nevertheless, fusion structure may be partial. The nasal proboscis constituted a characteristic feature of cyclopia.

Cyclopia is often associated with serious malformation of the forebrain that is incompatible with postnatal life. In fact, this abnormality constitutes the most severe craniofacial malformation which is typically associated with alobar or rarely with semilobar holoprosencephaly (HPE). The advent of prenatal ultrasonography and ultrasound scan permitted detection of cyclopia during the first trimester, allowing early termination of pregnancy and thus avoiding maternal psychological trauma of giving birth to a deformed infant. We present a case of cyclopia associated to alobar holoprosencephal (HPE). Risk factors, diagnosis, prognosis, and pregnancy management are discussed referring to literature.

CASE REPORT

A 33-year-old primipara was referred to our obstetric department at 34 weeks gestation for preterm labor and hydramnios. She had previously borne two normal children and her family and personal medical and genetic history were negative. There was no history of consanguinity between her and her partner, no maternal diabetes mellitus and no exposure to known teratogens during pregnancy. Examinations for toxoplasmosis, rubella, cytomegalovirus, herpes (TORCH) were negative. Obstetrical ultrasound demonstrated excessive hydramnios and foetal hypotrophy without good visualisation of cephalic extremity. Nine hours later, she delivered vaginally, a leaving female fetus of 2300 gr, a height of 46 cm and an Apgar 3/1/0. The evolution was rapidly fatal and the newborn is decaled died after 15 minutes of life. Autopsy was performed three days later. Foetopathology examination revealed facial malformative abnormalities including single orbit with a cyclopian eye, proboscis with a small blind canaliculus at its free end, and absence of the nose.
There was a microstomia, short neck, dense, low-set hair, and flattened skull in the anteroposterior axis. X-Rays of the skull showed the absence of an orbital cavity and the presence of two fossils extending forward the temporal fossae with a hypoplastic maxillary (Fig 2).

Skull opening showed a normal sized brain with rudimentary and fused cerebral hemispheres without convolutions revealing an alobar HPE (Fig 3).
Examination of the cardiovascular, respiratory, alimentary, and genitourinary systems showed no abnormalities. The fetal annexes’ examination has revealed umbilical cord with two vessels. Genetic consulting was done. Nevertheless, karyotype analysis and histopathological examination were not performed.

DISCUSSION

Cyclopia is a rare congenital facial-development defect characterized by medial monophtalmia with arrhinia and nasal proboscis [1]. Facial dysmorphism associate usually proboscis and may associate short eyelids, with or without eyelashes. Often, there is only one optic nerve with sometimes the presence of a sclerous tissue separating two contiguous optic nerves at the microscopic study. Sometimes the maxillary is hypoplastic or even absent. The hair is very dense and low implanted. The ears are normal, or curved and atrophied, or contiguous on the midline in case of associated otocephaly [3]. Our case displayed most of the features described in literature as occurring in cyclopia.

Cyclopia is always an external manifestation of deep brain abnormalities. In fact, it is most commonly associated to severe malformation forebrain. Indeed, given the common neural origin (prechordal mesoderm), craniofacial anomalies are present in 80% of individuals with holoprosencephaly (HPE). In addition, cyclopia is the most extreme facial defect accompanying alobar HPE [3]. HPE is a rare abnormality resulting from incomplete cleavage of the primitive prosencephalon, or forebrain. According to the importance of prosencephalic cleavage defect, three anatomical forms of variable severity can be distinguished: alobar, semilobar, and lobar varieties [2]. HPE is often associated with other fetal abnormalities and chromosomal aberrations, in particular trisomy 13 (70%), trisomy 18 and triploidy [6].

Prenatal diagnosis of cyclopia is based on sonographic technique. In fact, standard 2D ultrasound (US) is useful to screen facial abnormalities. This sonography examination allows to suspect prenatal diagnosis of alobar HPE by showing a monoventricle brain, fused thalami and absence of corpus callosum. 3D US may be used to obtain additional information such as the nature of the defect [9]. Fetal magnetic resonance can be an important supplement in suspect fetal HPE [10]. In our case, because of the lack of performance, ultrasonography showed fetal hypotrophy and excessive hydramnios without facial details and cerebral features [9].

The etiology of cyclopia remains unclear. Nevertheless, several risk factors may be involved. In fact, the disease has been produced experimentally by the action of magnesium, lithium, sulfonamides, and activator substances like atropine [11,12]. Other environmental factors are incriminated such as alcohol consumption during the first three weeks of pregnancy [2,11]. TORCH infections contracted during pregnancy have been implicated, but not proven to be causative [4,12]. In our case, no risk factor has been identified.

Cyclopia is often associated to chromosomal abnormalities including most frequently trisomy 13 [2,4]. Trisomy 18, deletion of 7p and monosomy 7 may rarely be detected. Nevertheless, the role of inducing factor of these chromosomal alterations in the appearance of cyclopia remains to be proved [13]. Finally, a Mendelian transmission has also been discussed. It is an autosomal dominant inheritance with a partial penetrance and expressiveness, or an autosomal recessive inheritance [14]. In our case, despite adequate medical and genetic counseling, the patient and her partner refused genetic testing and histopathological examination.

The prognosis for cyclopia is very reserved and most children die in utero or in the first hours of life. Medical abortion is currently proposed by the majority of authors. In addition, early prenatal diagnosis is essential to allow early termination of pregnancy. In fact, medical termination of pregnancy will be technically easier with less psychological impact if it is carried out in the first trimester of pregnancy [8].
Genetic counseling is required in case of chromosomal abnormality. If such a balanced abnormality is present in either parent, the risk of recurrence is high and prenatal diagnosis should be offered to the family in the event of a new pregnancy \cite{13}. If the parents have a normal karyotype and the child has a trisomy 13 or 18, the risk of another child affected by this abnormality in the siblings will increase with the age of the mother \cite{13}.

**CONCLUSION**

Cyclopia is a very rare cranio-facial malformation often incompatible with life because of associated with severe cerebral abnormalities. The most striking feature is the central diamond-shaped palpebral fissure apparently containing a single eye and associated to nasal proboscis. Antenatal diagnosis is feasible thanks to obstetrical ultrasonography. Early diagnosis is essential allowing optimal pregnancy termination.

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**REFERENCES**


