Case Report

A rare occurrence: A case report on alobar holoprosencephaly with cyclopia

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ABSTRACT

Alobar holoprosencephaly with cyclopia is a rare lethal congenital anomaly frequently accompanied by other malformations and characterized by large variations in incidence. Alobar holoprosencephaly presents as a congenital brain malformation characterized by the incomplete separation of the brain hemispheres during fetal development, typically occurring between the 4th and 6th gestational weeks, affecting about 1 in 250 conceptuses and 1 in 16,000 live births. This anomaly involves the failure of transverse cleavage into the diencephalon and telencephalon and is often accompanied by various midline facial abnormalities. In this report, we detail a case of a patient diagnosed prenatally with alobar holoprosencephaly with cyclopia, which is a rare, severe craniofacial abnormality encountered in approximately 1 in 100,000 births. Due to the severity of the condition, the decision was made to induce labor, resulting in the delivery of a stillborn baby. Despite the grim prognosis associated with this condition, we emphasize the importance of comprehensive prenatal counseling and support for families navigating such complex medical circumstances. Through this report, we aim to contribute to the understanding and compassionate care of individuals affected by alobar holoprosencephaly with cyclopia.

Key words: Alobar holoprosencephaly, Congenital anomaly, Cyclopia, Fetus, Rare

Alobar holoprosencephaly is a severe form of a developmental disorder of the brain. It occurs during early fetal development when the forebrain, which normally divides into two hemispheres, fails to separate properly. As a result, the brain remains in a single, undivided mass [1]. This condition often presents alongside severe facial abnormalities and intellectual disabilities [2], affecting about 1 in 250 conceptuses and 1 in 16,000 live births [1,3]. In this particular case, alobar holoprosencephaly is accompanied by cyclopia, another rare congenital condition, encountered in approximately 1 in 100,000 births, characterized by the presence of a single, centrally located eye, resembling the mythical cyclops of Greek mythology. It occurs due to abnormal development of the embryo's forebrain during early gestation, resulting in the fusion of the eye sockets and the formation of a single eye structure [1]. Alobar holoprosencephaly, frequently incompatible with life, typically results in the demise of affected individuals before or shortly after birth. This case report explores the intricate intersection of alobar holoprosencephaly and cyclopia, both exceedingly rare congenital anomalies. Alobar holoprosencephaly with cyclopia is visible on all modalities but in general, is identified on antenatal ultrasound, and is best characterized by magnetic resonance imaging (MRI) [2,4,5]. Through detailed clinical observations, diagnostic methodologies, and therapeutic interventions, we unravel the intricacies of managing such complex cases. Furthermore, we underscore the significance of early detection and multidisciplinary collaboration in navigating the challenges posed by this unique neurological anomaly.

This report serves to illuminate the clinical landscape and stimulate further research into these enigmatic conditions.

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CASE REPORT

A 30-year-old woman, gravida 4 and para 3 at 22 weeks of gestation, with a history of normal vaginal delivery, presented to the Department of Obstetrics and Gynecology for routine obstetric examination. Her past medical and family histories were unremarkable, with her previous children being born without congenital anomalies at term. This newborn, born to a non-consanguineous family, had no history of maternal drug use, radiation exposure, or febrile illnesses during pregnancy.

On examination, she was conscious with a blood pressure of 128/84 mmHg, respiratory rate of 18/min, and heart rate of 102/min, along with other stable vitals. On abdominal examination, the uterus was around 22 weeks in size, and external ballottement was present. On vaginal examination, the cervical os was multiparous.

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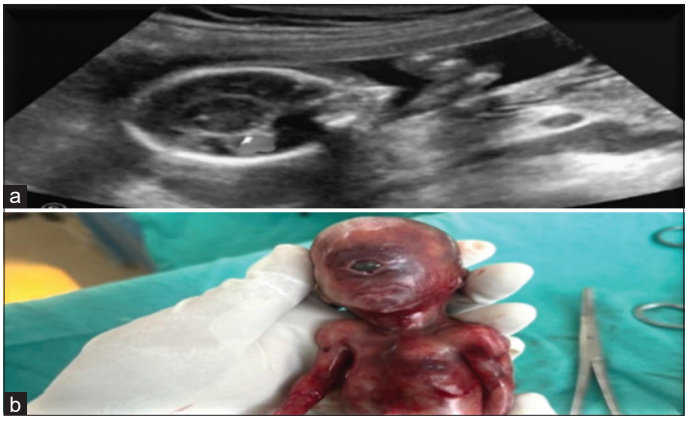

Figure 1: (a) Antenatal sonogram of the fetal head (coronal view) with alobar holoprosencephaly showing monoventricular cavity with surrounding thinned cerebral tissue, fused thalami, and absence of midline structures; (b) Gross showing the presence of a single eye structure and lips on the fetus, whereas the nose was absent

The patient underwent routine antenatal ultrasonography, revealing increased intracranial fluid in the fetus. A follow-up ultrasound showed cystic structures replacing brain parenchyma, along with the absence of orbits, nose, lips, and face (Fig. 1a). The cerebral cortex appeared as a thinned-out mantle, while the midbrain and posterior fossa appeared normal. No apparent cystic mass or subcutaneous edema was observed over the neck. Polyhydramnios was present. Antenatal testing revealed severe hydrocephalus detected early by intrauterine ultrasound, and preterm induction of vaginal delivery led to the birth of a stillborn fetus, weighing 200 g. On examination, the newborn displayed a dysmorphic facial appearance, characterized by a single median eye, absence of a nose, micrognathia, and suggesting a potential diagnosis of alobar holoprosencephaly with cyclopia (Fig. 1b). Brain morphology assessment was challenging due to autolysis. Chromosomal analysis revealed a trisomy 13 karyotype.

DISCUSSION

In alobar holoprosencephaly, the most severe variant, there is a complete failure of division within the prosencephalon. This results in the two lateral ventricles appearing as a single ventricle and fusion of the thalami. Notably, there is an absence of an interhemispheric fissure, optic tracts, and olfactory processes, along with the non-existence of the corpus callosum [1]. Facial development may be significantly impacted due to the shared origin of the embryonic forebrain and mid-face from the prechordal mesoderm, potentially leading to cyclopia, proboscis, ethmocephaly, cebocephaly, and median cleft lip and palate. However, the midbrain, brain stem, and cerebellum typically develop normally. On ultrasound examination, the skull may present as water-filled, necessitating differentiation from conditions such as hydrocephaly and hydranencephaly [2].

In addition, small indicators such as polydactyly, ventricular septal defects, and myelomeningocele require meticulous attention to detail [2]. Holoprosencephaly occurs in 1/16,000 live births [3], and 1/250 during embryogenesis [3]. Approximately, 1.05 in 100,000 births are identified as infants with cyclopia, including stillbirths [3]. Even though approximately 17% of fetuses with alobar holoprosencephaly, as reported by DeMyer [6], and 29%, as reported by Nyberg [7], present with a non-diagnostic face at delivery, careful intrauterine scanning of the face when holoprosencephaly is suspected by sonography can lead to a more definitive diagnosis of cyclopia. In our case, hydrocephalus was diagnosed early in the second trimester (Fig. 1b), along with the absence of orbits, nose, lips, and face, but no fetal MRI to confirm the diagnosis was done.

The etiology of alobar holoprosencephaly is believed to involve both environmental factors and genetics. Holoprosencephaly may be inherited as an autosomal dominant trait, with mutations in the sonic hedgehog gene being the most common cause of familial cases [8]. Trisomy 13 and trisomy 18 are frequently encountered chromosomal anomalies associated with holoprosencephaly [9]. Approximately, 30% of cases are linked to chromosomal defects, notably trisomy 13 and 18, whereas the majority of cases have a normal karyotype [10]. In our case, trisomy of chromosome 13 was present. Among environmental factors, there are maternal diabetes mellitus, alcoholism, cytomegalovirus, rubella or toxoplasma infections, and some drugs (retinoic acid, cholesterol synthesis inhibitors, phenytoin, and salicylates) [11]. Our patient did not have any of the previously mentioned environmental or teratogenic factors present. Furthermore, her family history showed no significant findings. The alobar subtype of holoprosencephaly is not compatible with life, leading to fetal demise. However, children with semilobar, lobar, and middle hemispheric variants demonstrate varying survival rates. Among survivors, seizures are frequently observed as one of the primary manifestations [12]. According to Poenaru *et al*., 2012, diagnosing holoprosencephaly is feasible during the prenatal stage through abdominal ultrasound examination and MRI [13]. In our case, the diagnosis was initially established through prenatal abdominal 4D ultrasound but not verified by MRI. The prognosis for individuals with holoprosencephaly hinges on the severity of the condition and the presence of any accompanying anomalies.

Alobar holoprosencephaly represents a spectrum of severity, with profound implications for neurodevelopment and survival. In our case, prenatal diagnosis allowed for informed decision-making and appropriate planning for the anticipated challenges ahead. The role of multidisciplinary care, including genetic counseling, perinatology, and pediatric neurology, is paramount in providing comprehensive support to affected families.

CONCLUSION

Alobar holoprosencephaly, while rare, stands as the predominant structural congenital brain anomaly, characterized by a multifaceted pathogenesis. Early detection and assessment of severity are crucial for providing parents with insights into potential future outcomes. Although termination of pregnancy is a consideration, it presents formidable challenges for patients, families, and health-care providers alike. By sharing insights from this case report, we aim to foster greater awareness, empathy, and

collaborative care in managing this rare neurological anomaly. Through ongoing research and compassionate support, we can strive to improve outcomes and quality of life for individuals affected by alobar holoprosencephaly.

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