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Case Report

Agnatia-otocephaly complex in a low-resource setting and its implication for maternal and child health: a case report

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ABSTRACT

Agnatia-otocephaly complex is an extremely rare congenital fatal anomaly. This case is being reported to raise awareness of this condition and the need for sonographers to deliberately evaluate for this anomaly in patients with severe polyhydramnios in pregnancy. This allows for more effective management of this congenital anomaly. We report a 31-year-old gravida 3 para 2 who presented with complaints of difficulty with breathing and ultrasound scan findings of live fetus with severe polyhydramnios at about 34 weeks of gestation. About 2 days on admission, she spontaneously ruptured membranes and had assisted vaginal breech delivery of a live male 1.9 kg neonate who suffered early neonatal death after 20 min of active resuscitation with agnatia-otocephaly complex anomaly noticed. She was counselled on the neonatal outcome and the need for autopsy, but the parents declined. Otocephaly should be suspected in cases of fetal anomaly with polyhydramnios. In this patient, severe polyhydramnios was a presenting feature, deliberate effort could have been made to identify this congenital anomaly. It highlights the need for better training and provision of advanced tools to aid diagnosis. In this case, the neonatal outcome was fatal, and the mother suffered from respiratory distress from polyhydramnios, which could have been avoided by accurate prenatal diagnosis. Otocephaly poses a significant challenge for patients and clinicians globally, especially in low-income countries, due to its rarity, high fatality rate and complexity. This case is being reported to raise clinician awareness for proper sonographic evaluation and better management of this rare congenital disorder.

Keywords: Agnatia-otocephaly complex, Polyhydramnios, Prenatal diagnosis, Congenital anomaly, Foetal sonographic evaluation

INTRODUCTION

Agnatia-otocephaly complex (also known as agnathia-microstomia-synothia or otocephaly) is an extremely rare fatal anomaly. It was first discussed by Theodor Kerckring, a Dutch physician who made anatomical observations of this condition in his historical notes Spicilegium Anatomicum in 1670.[1] Otocephaly is the most severe form of the first-arch anomalies, and it is possibly due to arrest in the development of the first branchial arch as a result of an insult to the neural crest cells.[2,3] Genes, chromosomal mutations, or teratogens could cause this rare familial and non-familial neurocristopathy of the first pharyngeal arch.[2,3] The prevalence is less than 1 in 70,000 births.[4]

The main features are agnathia, melotia and synotia of external ears in the neck region, microstomia and aglossia.[5] This congenital anomaly is considered fatal due to severe respiratory dysfunction after delivery.[5] The prognosis of otocephaly is very poor, and early neonatal death is very common, especially when airway management is not done correctly. Therefore, prenatal diagnosis of otocephaly is very important, considering the high fatality rate of the anomaly, as it helps in better management and appropriate counselling of parents. This fatality is higher in low-income countries due to lack of sophisticated prenatal diagnostic tools and skills.

This case is being reported to raise awareness of this very rare congenital anomaly and the need for sonographers to

deliberately evaluate for this anomaly in patients with polyhydramnios in pregnancy.

CASE REPORT

We report a 31-year-old gravida 3 para 2 at 33 weeks 4 days gestational age. She was referred from a primary health centre (PHC) following an ultrasound scan finding of polyhydramnios for expert care.

She had presented to the referring centre with complaints of lower abdominal pain of 24 hours duration. There was a history of difficulty with breathing from severe abdominal distention. There was no history of fever, no dysuria, no increased urinary symptoms and no nocturia. No liquor drainage, no bleeding per vaginam, she still felt fetal movement. She is not a known hypertensive or diabetic. No family history of diabetes or congenital anomaly. No previous history of a baby with a congenital anomaly. She had ingested an herbal concoction in early pregnancy (first trimester) for the treatment of febrile illness. The exact content of the herbal concoction could not be ascertained by the patient. She does not take alcohol or tobacco products in any form. No exposure to radiation.

Following the abdominal pain, she presented to the primary health care where an obstetrics scan report showed a single, viable, intrauterine fetus with severe polyhydramnios (amniotic fluid volume deepest vertical pocket – 128.87 cm), estimated fetal weight – 2.74 kg. The placenta was not low-lying. No fetal anomaly was noted in this report. Following the obstetrics scan findings, she was referred to our facility for expert care. Her pregnancy was uneventful throughout the antenatal period. She has had 2 previous vaginal deliveries and no history of congenital anomaly in any of the children.

Pregnancy was desired and spontaneously achieved. There was no attempt at termination of pregnancy. Booked at the PHC at 24 weeks GA. Booking parameters were said to be normal, though she was unaware of the parameters. HIV test, hepatitis B and C test, and VDRL were all negative. Her pregnancy was uneventful, and the obstetric scan was normal except for her last scan, which showed severe polyhydramnios.

On presentation, she was morbidly obsessed (body mass index of 41 kg/m^2), in mild respiratory distress, afebrile, not pale, anicteric, acyanosed, not dehydrated and no pedal edema. Her pulse rate was 92 bpm, blood pressure was 120/80 mmHg, and oxygen saturation was 95% in room air. Her abdomen was markedly distended and moved with respiration, symphysio-fundal height of 44 cm. There was a single fetus, breech presenting, no contractions, and the fetal heart rate was 142 bpm. Speculum examination done – cervix was closed. A diagnosis of multipara with severe polyhydramnois ? cause at 34weeks was made..

She was admitted, her random blood sugar was 135mg/dl, the fasting blood glucose was 92 mg/dl, and the glycated haemoglobin (HbA1C) was 4.5%. She was given parenteral analgesia (acetaminophen), for which the abdominal pain subsided. On the second day of admission, she spontaneously ruptured the membrane with associated labour pain, which was increasing in intensity and frequency. On examination, she was having three strong uterine contractions in 10 minutes, with each lasting about 40 seconds, and her fetal heart rate was 145 bpm. Her cervix was 4 cm dilated, and a fetal buttock was felt. The presenting part was at station 0-1, and there was no cord prolapse. She subsequently progressed in labour and had assisted vaginal breech delivery with outcome of a live male 1.9 kg who suffered early neonatal death after 20 min of active resuscitation which Ambu bag and mask with agnatia-otocephaly complex (microstomia, aglossia, agnathia, synotia and melotia) noticed (Figure 1). She was counselled on the baby's condition and the need for an autopsy, but the parents declined. She was discharged to the postnatal clinic, where she was counselled on preconceptional care and discharged to family planning at 6 weeks postpartum.

Figure 1: Baby delivered with features of agnatia-otocephaly complex.

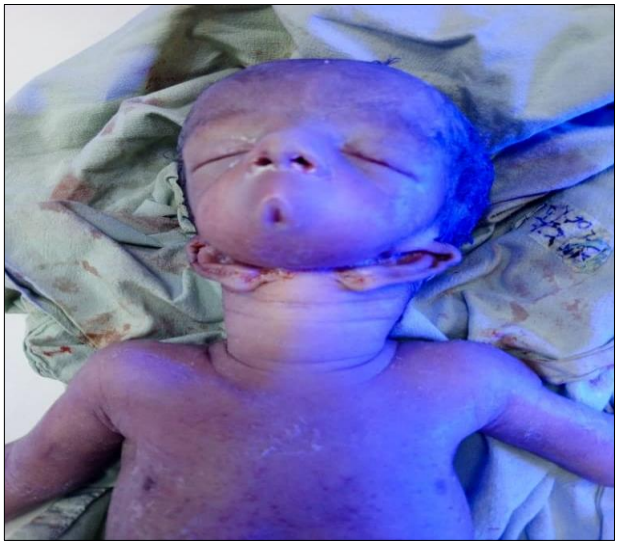

Figure 2: Facial Features of the baby with agnatia-otocephaly complex.

DISCUSSION

The word 'otocephaly" refers to the relationship of the face and the ears. It is a rare, often fatal congenital anomaly characterized by agnatia, microstomia, aglossia, synotia and melotia.[2] It is also often associated with facial, cranial and extracranial malformation. Otocephaly can be an isolated malformation or may be associated with other anomalies.

The severe first and second arch defects are mainly responsible for this congenital malformation. According to Leech, this syndrome complex of otocephaly can be divided into four distinct types: isolated agnathia; agnathia with holoprosencephaly; agnathia with situs inversus and visceral anomalies; agnathia, holoprosencephaly, situs inversus and other visceral anomalies.[4,6] A retrospective study of 26 cases of otocephaly by Sabu et al showed that 42% were isolated and 58% were associated with other anomalies.[7] The most common associations were skeletal, followed by central nervous system anomalies, and genitourinary anomalies. Syndromes noted were Treacher Collins, Al Awadi Raas Rothschild, Nager acrofacial dysostoses, and femoral facies syndrome.[7] In the present case, microstomia, aglossia, agnathia, synotia and melotia malformation were the obvious congenital anomalies (Figure 2). Other associated anomalies could not be ascertained due to the parents' refusal of autopsy due to cultural reasons.

There are a few proposed teratogenic effects as the cause for otocephaly, such as exposure to streptonigrin antibiotics and trypan blue, and theophylline.[2,4] In our case, there was use of herbal medication in early pregnancy, whose content the patient could not identify. The genetic basis of otocephaly is still largely unclear.[8] However, certain genes, including OTX2, PRRX1, and CRKL, have been identified as potential contributors to agnathia.[9,10] The expression of the transcription factor OTX2 in mesenchymal cells of the midbrain, head, and neural crest cells has been shown to cause craniofacial malformations and holoprosencephaly.[10,11] Genetic studies could not be carried out in our case as relatives refused consent.

Otocephaly is usually suspected on radiological antenatal assessment when it is impossible to visualize the mandible, and the ears are in a very low and medial position. Otocephaly should also be suspected in cases of polyhydramnios.[3] A report by Faye-Paterson et al showed that polyhydramnios may be the presenting feature during pregnancy.[12] In this patient, polyhydramnios was a presenting feature, deliberate effort could have been made to identify this congenital anomaly. This limitation was due to a lack of skill, and a sophisticated scanning machine was needed to make the diagnosis, as seen in low-income countries like ours. It highlights the need for better training and provision of advanced tools to aid diagnosis.

Prenatal diagnosis is very pertinent as it does not only help in counselling of patients but also in the choice of delivery. A report by Kajiwara et al showed that a caesarean section was done for a case of undiagnosed otocephaly, and the neonate died a few hours later as the baby was deemed not resuscitable due to airway obstruction. This caesarean section could have been avoided if prenatal diagnosis had rightly done. In our case, although it was a missed diagnosis, caesarean section was not done because patient was managed as a normal labour.

Although otocephaly is a fatal syndrome where most cases have had adverse neonatal outcomes.[8,13-15] There are cases of successful management of otocephalic neonates after birth where enteral feeding was successful in such newborns with isolated agnathia with nasogastric tubes, gastrostomy tube and assisted breathing via tracheostomy.[16-18]

Due to the missed antenatal diagnosis due to poor resource-setting, provisions for emergency airway intervention like tracheostomy and gastrostomy were not made, hence, the patient could not benefit from these interventions, contributing to the early demise of the neonate. This highlights the challenge in maternal and child health, especially in low-income countries.

The long-term survival is almost impossible due to the poor prognosis associated with the agnathia otocephaly complex. Infants born alive typically succumb to respiratory distress resulting from the absence of a supportive mandible, which leads to the underdevelopment of crucial adjacent structures, particularly the naso-mandibular complex, and oropharynx.[8,13-15] This respiratory distress, coupled with feeding difficulties, speech, and hearing impairments, further compounds the challenges faced by affected individuals.[17,18]

In this case, the neonatal outcome was fatal, and the mother suffered from respiratory distress from polyhydramnios. To ensure maternofetal safety, sonographers need to improve their skill and equipment to enable them to identify congenital conditions like otocephaly.

CONCLUSION

Otocephaly poses a significant challenge for patients and clinicians globally, especially in low-income countries, due to its rarity and complexity. Early antenatal scan is vital in identifying this congenital anomaly, which allows for safer early termination of pregnancy or proper management preparation for the complications. This case is being reported to raise clinician awareness for proper sonographic evaluation and better management of this rare congenital disorder.

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