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Case Report

Otocephaly: a case report

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ABSTRACT

A case of otocephaly was reported in 26±4 week's female fetus during routine fetal autopsy at GMCH, Chandigarh, India. Mother was 25 years old, second gravid. The first child is one year old normal male baby. Present pregnancy resulted in spontaneous abortion. Antenatal history, past history, family history and medical history of mother was not suggestive of any ethiological factor responsible for the defect. The external examination showed 2 vessels in umbilical cord. There was anteroposterior lengthening of skull, mouth was in the form of a proboscis with a small opening in the centre, the right ear was absent. The left pinna was low placed and had small tags. On internal examination oral cavity was found small with hypoplastic mandible, tongue was absent (aglossia), thoracic cavity was small, left lung was absent, right lung had only single lobe, heart dilated with normal position of major vessels, In abdominal cavity gut was opening in a dilated cloaca like chamber. X-ray examination revealed small hypoplastic mandible and maxilla. Otocephaly is a rare lethal syndrome of microstomia, agnatia and ear anomalies. Other anomalies associated are holoprosenxcephaly, skeletal, genitourinary, cardiovascular system, endocrine gland hypoplasia etc. The differential diagnosis includes Treacher Collins syndrome, Goldenhar syndrome and Mobius syndrome. The etiology, incidence, causative factors of this case will be discussed in light of available literature.

Keywords: Otocephaly, Agnathia, Aglossia

INTRODUCTION

Otocephaly is a rare, often lethal anomaly characterized by microstomia, aglossia, agnathia and synothia.[1] Agnathia-otocephaly is considered to be the most severe form of first branchial arch malformation.[2] The estimated prevalence of otocephaly is less than 1 in 70,000 new-born infants.[3] The most affected part is the upper face, even without any severe brain malformation. Abnormalities include cyclopsia**,** synopthalmia, proboscis, hypertelorism, or uni/bilateral microphtalmia/anopthalmia and nasal malformation.[4,5] Studies had mentioned that infants with otocephaly do not survive long after birth. Only a very few with milder forms of malformation survive.[6] Various reports suggest the prenatal diagnosis of otocephaly mostly in the third trimester of pregnancy.[7-9]

CASE REPORT

A case of otocephaly was reported in 26±4 week's female fetus during routine foetal autopsy at department of anatomy GMCH, Chandigarh, India. The fetus was obtained as a result of spontaneous abortion from department of Obstretics and Gynecology, GMCH, Chandigarh. The family history, medical, occupational history of parents was noted. Obstretics and antenatal history of each mother were noted. Fetus was examined externally. Photographs and radiology of fetus was also done. Autopsy was performed following routine procedure. The internal examination was done and other organs /system with any anomaly were also noted and correlated with the history. The external examination showed 2 vessels in umbilical cord. There was antero-posterior lengthening of skull. Mouth was in the form of a proboscis with an opening in the centre, right ear was

absent, left pinna was low placed and had small tags, anal opening was absent. On internal examination showed gut opening in a dilated cloaca like blind chamber, absent left lung, dilated heart with normal position of major vessels. X-ray examination revealed small hypoplastic mandible and maxilla. Otocephaly is a rare lethal syndrome of microstomia, agnathia and ear anomalies.

DISCUSSION

Otocephaly also called as agnatia-otocephaly or agnatia-microstomia–synothia is an extremely rare lethal anomaly, characterized by hypoplastic mandible, microstomia, midfacial location of the ears in the form of auricular malposition called melotia and synothia.[2] The term "OTO" refers to relationship of the ears to the face. It was first described by Kerking in 1717. The estimated prevalence of Otocephaly is less than 1 in 70,000 newborn infants.[3]

Studies had mentioned that the cause of otocephaly could be due to exposure to teratogenic effects of several agents such as strepnigrin antibiotics and trypan blue, theophylline. In our case there was no history of exposure to drugs as mentioned above.[10]

Eventhough the genetic basis of otocephaly is still largely unclear, small number of ODC cases had identified that mutations occurring in 2 genes OTX2 and PRRX could be a reason.[11] Another study by tan et al mentioned that the craniofacial malformations such as long tubular nose, micrognatia, cleft palate as well as congenital heart disease because of deletion of human chromosome 22q11.2.[12]

In addition to craniofacial abnormalities the CNS is the most common organ system involved.[8] Whereas, situ inversus, renal ectopia, absence of pituitary gland, absence of adrenal glands, single umbilical artery etc. are the other associated anomalies.[13] In present case also we came across single umbilical artery (Figure 1).

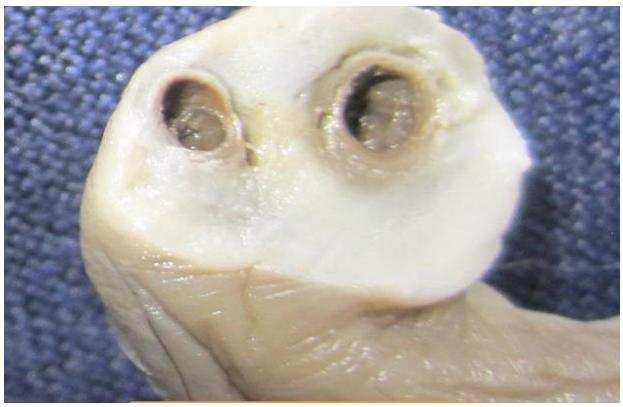

Figure 1: Umbilical cord with two vessels.

According to Leech**,** syndrome complex of otocephaly can be divided into 4 types:

1. Isolated agnathia
2. Agnathia with holoprosencephaly
3. Agnathia with situs inversus and visceral anomalies
4. Agnathia, holoprosencephaly, situs inversus, other visceral anomalies.[14] The case we describe belongs to type 3.

Wagner JH reported a case of otocephaly (25 weeks gestation) with facial malformations such as, proboscis, cardiac anomalies without any disruption in brain morphology. In our present case the (patient, second gravid) 26 weeks gestation, female fetus showed otocephaly with facial malformation - mouth was in the form of proboscis with small opening in the center, right external ear was absent, heart was dilated with normal position of major vessels, there was no brain malformation[15] (Figure 2).

Figure 2: Mouth in the form of proboscis with an opening in the centre.

A case of otocephaly in a male fetus with multiple anomalies was described by Kwei shuai, anomalies included midline proboscis, absence of mandible, small protruding mouth without an opening, absence of tongue, and simple soft extremely low-set ears. Findings in our case had many resemblances with the above mentioned case, which included aglossia, low set left ear and formation of proboscis below the nose at the place of mouth with a narrow opening in the centre.[16]

Ozden et al reported a premature male infant with otocephaly, which showed synophthalmia with frontal proboscis, agnatia, aglossia, low set ears.[17] Authors had reported cases of otocephaly with absence of mandible, small mouth, cleft palate, low set ears & pulmonary hypoplasia. In our present study along with other features of otocephaly there was absence of left lung and right lung was with a single lobe.[18]

Embryologically, formation of the face, neck, nasal cavities, mouth, larynx, and pharynx are contributed by branchial arches. The facial framework is formed by first arch. Each branchial arch consists of four components: (1) an aortic arch, (2) a cartilaginous rod, (3) a muscular component, and (4) a nerve portion innervating muscles

and mucosa. It is the derivative of each branchial arch cartilage component that is of particular relevance to the otocephaly syndromes.[1] Mandibular aplasia occur due to a defect of migration of neural crest cells to the ventral portion of the first branchial arch during gastrulation, which then results in a range of associated findings such as ventromedial displacement of the external ear structures (synotia), absence of the tongue (aglossia) and small oral aperture (microstomia**).**[5,1] Downward displacement of the ears with or without fusion and microstomia are secondary to lack of spatial separation by the mandible. Although not well understood, otocephaly is thought to be the result of an arrest in the development of the first branchial arch.[1]

Wright on his study on guinea pigs described a spectrum of severity in the phenotype seen within the same sibships, ranging from small mandible to agenesis of mandible with severe defect of eye, nose and brain. This implicated a common genetic cause for nonsyndromic dysgnatia and agnatia-prosencephaly.[19]

Evidences from human experiences and various animal models suggest that otocephaly is the result of heterogeneous developmental defects. Both genetic and environment factors have an impact on the formation of otocephaly.[20]

Prenatal diagnosis of otocephaly is extremely rare however it had been reported on several occasions. Prenatal diagnosis of otocephaly depends mostly on 2 dimensional and 3 dimensional ultrasound.[21,22] Key to diagnosis are low set or midline position of ears but visualisation of this feature is difficult using 2D ultrasound.[5] Several authors had reported that diagnosis can only be achieved in third trimester,[1,4] Agnatia-otocephaly is probably one of the diagnosis where 3D ultrasound helps in demonstrating the position and shape of ears in addition to facial features.[17,23] Prenatal sonographic detection of fetal polyhydramnios is frequent in association with otocephaly but only detected in third trimester of pregnancy.[24]

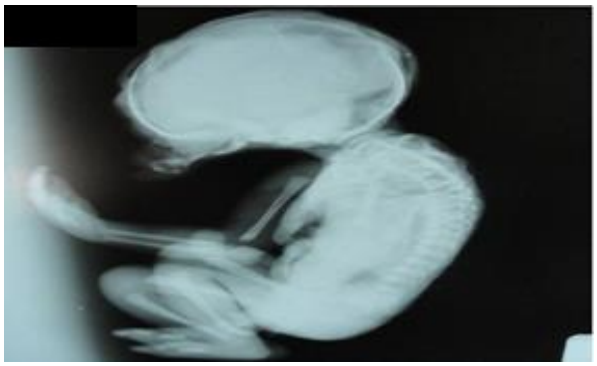

Figure 3: Radiograph showing small mandible and maxilla.

Otocephaly is usually suspected radiological antenatal check-up when it is impossible to visualize the mandible and ears are in very low and medial position.[4,25] In our present case radiograph examination suggested very small mandible and maxilla (Figure 3).

Even though otocephaly is a lethal syndrome there are cases on successful management of otocephalic babies after birth.[26,27] Nasogastric tubes were installed in surviving fetus with isolated agnatia for enternal nutrition.

Table 1: Clinical synopsis related to otocephaly.

Category	Subcategory	Features
Inheritance		Autosomal dominant
Head and neck	Head	Holoprosencephaly [6]
	Face	Mandibular hypoplasia[28] Mandibular agenesis[19]
	Ears	Ear anomalies[6] Conductive hearing loss[6]
	Eyes	Synophthalmia[17]
	Nose	Frontal proboscis[17]
	Mouth	Microstomia[6] Microglossia[6] Aglossia[17] Cleft palate[6]
Neurologic	Central nervous system	Holoprosencephaly [17] Agenesis of corpus callosum[17]
Molecular basis		Caused by mutation in the paired related homeobox gene (prrx1,167420.0001)[28]

Our case does not show any obvious cause for malformation. The case we described belongs to type 3 (according to leech).

CONCLUSION

Otocephaly is usually incompatible with life, so it is important to diagnose on routine antenatal radiological check-up when mandible cannot be visualized. Prenatal diagnosis should be depend 2D or 3D ultrasound. When early diagnosis is made the poor diagnosis should be discussed with parents and termination of pregnancy should be offered.[13] It can be helpful for parental counselling by plastic surgery in less severe cases.[23] The reported case was not given any cause for the malformation and the case belonged to type 3 classification.

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