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Left-Sided Facial Defects in a Child with Goldenhar Syndrome at a Tertiary Facility in Nigeria

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Abstract

We describe a female Nigerian infant of otherwise healthy parents with no prior history of congenital anomalies who was born with left-sided cleft lip and palate, left anophthalmia, malformed left auricle, an atrial septal defect, and abnormal fusion of the medial ends of her ribs prior to their insertion into the sternum. She presented on account of respiratory difficulty following bouts of feed aspiration. Cautious feeding and the need for respiratory support are important aspects of care in patients with Goldenhar syndrome.

Keywords

Cleft Lip/Palate, Goldenhar Syndrome, Anophthalmia, Treacher Collins, Microphthalmia, Microtia

1. Case Report

Our patient was a 12-week-old female infant who was referred to the Paediatric Respiratory Unit of the University of Benin Teaching Hospital, Benin City, Edo state from the maxillofacial surgical unit of the hospital in October 2020 on account of recurrent episodes of cough, difficulty with breathing and facial abnormalities.

She was being followed up by the maxilla-facial surgical unit on account of facial abnormalities from birth. These included an absent left eye, left-sided cleft lip and palate and malformed left pinna which was represented by thickened skin folds just above the left mandibular ramus.

The child had a history of recurrent cough and difficulty with breathing and was also noted to choke on feeds (expressed breast milk). She was typically fed

by dropping milk into her mouth using a syringe and at other times, a cup and spoon were used.

At the presentation to the paediatric respiratory clinic, the aforementioned anomalies were noted. She was also found to be tachypnoeic and in respiratory distress with marked intercostal retractions and grunting. Peripheral oxygen saturation was 68% in room air and 99% on supplemental oxygen. Breath sounds were vesicular and course crepitations were heard in the right upper and middle lung zones.

Her weight (3 kg) was below the third centile for age and sex according to the WHO growth chart.

The pregnancy had been booked and the ante-natal care period was adversely uneventful. Spontaneous vaginal delivery was achieved at term, the baby had good APGAR scores and required no neonatal admission or care. She had been fully vaccinated for age according to the Nigerian National Programme for Immunisation.

Her full blood count revealed leucocytosis (11.4×10^3/UL) and anaemia (PCV of 23.4%). Serum electrolyte, urea and creatinine, and serum liver enzyme assay were all normal (Table 1).

Her chest X-ray however revealed extensive patchy opacities in the right upper and middle lung zones, in keeping with aspiration, cardiomegaly (CTR 66%) and abnormal fusion of the medial ends of the 3rd and 4th as well as the 5th and 6th ribs prior to their insertion into the sternum.

She was managed for aspiration pneumonitis with supplemental oxygen via nasal prungs, parenteral antibiotics, and steroids. She was fed through a nasogastric tube, to prevent further episodes of aspiration. Recovery was noted within a few days of admission as evidenced by the resolution of respiratory distress and fever.

The ophthalmologic assessment concluded the absence of the left eye. The patient was scheduled for audiometry to determine the functionality of the left ear.

She completed a course of antibiotics but continued to have poor oxygen saturation, dropping as low as 65% when attempts were made to wean her off oxygen necessitating an echocardiogram which revealed a 3.6 mm atrial septal defect. She was then commenced on oral diuretics as an anti-failure regimen and was being worked up for the closure of the cleft lip once her weight was up to 5 kg.

Her respiratory distress worsened 21 days into admission. It was noted that she vomited shortly after a feed of milk. Respiratory examination revealed

Table 1. Full blood count and serum electrolytes.

Full blood count	WBCC ($\times 10^3$/UL)	Granulocytes (%)	Lymphocytes (%)	Others (%)	Haemoglobin (g/dl)	Haematocrit (%)	MCV (fl)	Platelet ($\times 10^3$/L)
	11.4	87	10	3	7.1	23.4	85	121
Serum Electrolytes	**Sodium (mmol/L)**	**Potassium (mmol/L)**	**Chloride (mmol/L)**	**Bicarbonate (mmol/L)**	**Urea (mg/dl)**	**Creatinine (Umol/L)**		
	137	4.1	92	20	7	0.4		

reduced air entry in the right lung fields and a chest X-ray showed worse opacities in the right lung fields, confirming the suspicion that the child had aspirated milk.

She remained oxygen dependent and failed to improve significantly despite recommencing parenteral antibiotics and steroids. She eventually succumbed to the illness after spending 23 days on admission.

Her parents declined to have an autopsy done.

Diagnostic considerations in this case, in lieu of the facial abnormalities, were Goldenhar syndrome, anophthalmia plus syndrome, and Treacher Collins syndrome.

2. Discussion

Goldenhar syndrome or oculo-auriculovertebral syndrome (OAVS), is an uncommon congenital disorder that results from defects in the first and second brachial arches [1]. It is named after Dr. Maurice Goldenhar who first described the condition in 1952. The incidence of Goldenhar syndrome is approximately 1:35,000 - 1:56,000 with a male-to-female ratio of 3:2 [2]. The exact aetiology of Goldenhar syndrome is not yet fully elucidated and there is no consensus regarding this [1] [3]. Several risk factors have been associated with Goldenhar syndrome. These include chromosomal abnormalities, abnormal migration of neural crest cells as well as exposure to toxins in pregnancy such as thalidomide, cocaine, retinoic acid, and alcohol intake [3] [4]. In some cases, positive family history has been elucidated which suggests autosomal inheritance. Studies have thus proposed multifactorial causation of Goldenhar syndrome with involvement of multiple genes. Patients present with facial, ear, eye, and vertebral abnormalities as well as congenital heart defects [2]. The triad of mandibular hypoplasia, ocular dermoids, and an accessory tragus characterize the syndrome [2] [5]. Mounoud *et al.* [3] in 1975 reported a case of a 2 and half-year-old child with typical facial abnormalities from birth. His mother had ingested 10 mls of an oily vitamin A solution in the second month of pregnancy. Vitamin A as a teratogen can adversely affect neural crest cell formation and migration, processes that are relevant for the adequate formation of the branchial arch [3]. Goldenhar syndrome is most commonly unilateral (85%) and mostly affects the right side of the face [6]. In our case, the left side of the face was affected making this condition even more unusual. Systemic involvement can vary widely. Cardiovascular anomalies often involve cono-truncal abnormalities such as tetralogy of Fallot and ventricular septal defects [2] [7]. Our case however had an atrial septal defect. Cleft lip and palate, micrognathia (from mandibular hypoplasia), webbing of the neck, tracheoesophageal fistulas, and abnormalities of sternocleidomastoid muscle may be associated [2] [8]. Our patient also had cleft lip and palate with the abnormal fusion of the medial ends of ribs before insertion in the sternum. This buttresses the usefulness of radiographic investigations to support the clinical diagnosis.

Prenatal diagnosis is possible with considerable accuracy with ultrasound which may detect obvious defects. Since no specific genes have been linked to this syndrome, prenatal DNA testing cannot be used to diagnose the condition. The outcome of patients with Goldenhar syndrome is generally good but varies widely depending on the severity of the anomalies and whether correction of the anomalies has been done [5]. Differential diagnosis such as Treacher Collins Syndrome (TCS), Anophthalmia plus syndrome, Townes-Brocks syndrome and Nager syndrome should be considered in cases of Goldenhar syndrome in view of their similarities with respect to the facial abnormalities.

Treacher Collins Syndrome (TCS) usually presents with bilateral facial involvement [9] while a unilateral facial defect is the typical presentation in Goldenhar syndrome. Our patient presented with unilateral facial defect. A mutation of the TCOF1 gene on chromosome 5q31-34 is specifically linked to TCS [10] [11], as such, chromosomal analysis is an important tool in the diagnosis of TCS. Such chromosomal screening would have helped to rule out TCS in the index patient, though not specific for the diagnosis of Goldenhar syndrome.

Treatment is dependent on two major factors viz; the patient's age at the time of diagnosis and the systemic abnormalities present. As with Goldenhar syndrome, treatment is effective only when a multi-disciplinary approach is employed [9] [12]. Jaw reconstruction and the use of a distraction device can be offered in patients with mandibular hypoplasia and abnormalities of the maxilla from cleft palate [9]. Surgical repair of the cleft lip and palate as well as orthodontic intervention are also needful for the correction of other facial abnormalities. These are typically delayed until after jaw growth is completed. Ophthalmic and plastic surgical interventions are aimed at catering to the structural anomalies of the eyes and ears [12]. Growth failure when present is usually a result of under-nutrition which is a direct consequence of the difficulty with feeding, recurrent respiratory tract infections and aspiration, and obstructive sleep apnoea [9]. Our patient presented with difficulty with feeding, recurrent respiratory tract infections and aspiration pneumonia but did not show symptoms of obstructive sleep apnoea. Prognosis is good in cases without systemic illnesses but becomes guarded in such cases depending on the severity of systemic association [12] [13].

Anophthalmia Plus Syndrome (APS) is a very rare syndrome characterized by multiple organ malformation [14]. The most common findings are the absence of one or both eyes (unilateral or bilateral anophthalmia) or severe microphthalmia (abnormally small eyes), and cleft lip/palate both of which were present in our patient [6]. Other findings in patients with APS include wide-set eyes (ocular hypertelorism), colobomas of the eyes, congenital glaucoma, narrowed or uncanalised nostrils (choanal stenosis or atresia), low-set ears, neural tube defects, midline abdominal wall defects and clinodactyly [6]. Though the gene implicated is yet to be identified, it has been suggested that inheritance of APS is likely in an autosomal recessive manner. Although anophthalmia and/or microphthalmia associated with facial cleft are seen in other known syndromes that classically

present with other defining features such as limb abnormalities, and deafness among others. A diagnosis of APS may be considered when an individual presents with the most commonly reported signs and symptoms and other known syndromes with overlapping features have been ruled out [6] [14].

3. Conclusion

With similar facial abnormalities, a keen eye is often needed to distinguish these congenital syndromes. The genetic basis for some of them is yet unknown. The characteristic abnormalities in our patient enabled the diagnosis of Goldenhar syndrome. The severity of the oro-facial malformations poses a significant risk of frequent aspiration and respiratory illness in such patients which could be fatal, especially in the presence of other systemic congenital anomalies. Identification and management of such anomalies as well as adequate airway management are key to improving prognosis.

Ethical Approval

Ethical approval has been acquired and preserved by the authors.

Limitations

The absence of photographs is a limitation we attest to. Pictures would have aided the description of the anomalies in this child.

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Conflicts of Interest

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

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