Oculo-Auriculo-Vertebral Spectrum or Goldenhar Syndrome

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Introduction

The oculo-auriculo-vertebral spectrum or Goldenhar Syndrome is a congenital malformation syndrome originated from a first and second branchial arch development defect, which is typically presented with hemifacial microsomia, otic and/or ocular malformations and vertebral anomalies. It may also associate malformations of the heart, kidneys, central nervous system, digestive system, and skeletal system. The clinical presentations can vary from mild or minimal facial asymmetry to severe form with marked facial defects and internal organs involvement.

The European prevalence is less than 1 in 26,000 births, male infants are more commonly affected than female infants. The etiology is still unknown, but it has been described to be multifactorial, it includes both genetic and environmental factors, and there are cases that have been found to be related to the MYT1(20q13.33) gene.

Diagnosis is based on clinical findings. Microtia and/or mandibular hypoplasia associated with preauricular tags have been described as diagnostic criteria, but until present times there is no consensus on a minimum diagnostic criterion.

The differential diagnosis should be made with other syndromes including microtia and/or mandibular hypoplasia, such as Treacher Collins Syndrome, Townes-Brocks Syndrome, CHARGE Syndrome, Klippel-Feil Syndrome and Branchio-oto-renal spectrum disorders.

In this clinical case, the diagnosis, treatment and prognosis of the oculo-auriculo-vertebral spectrum is reviewed.

Clinical Case

A 48-year-old 16-week pregnant Nigerian woman without any personal or familiar risk factors and a couple with no history of consanguinity, with three previous healthy born children. In the second trimester screening the risk for trisomy 21 appeared to be 1 to 1, despite this result the patient rejected the invasive technique.

In the second trimester ultrasound was displayed a female fetus with hypoplasia of the ulna, agenesis of the radius and malposition of the club hand of the right upper limb, dorso-lumbar scoliosis with suspicion of hemivertebrae and right renal agenesis.

Despite prenatal pediatric counseling, the patient wished to continue with the pregnancy and kept rejecting the invasive technique, so it was decided to do ultrasound follow-up every 20 days.

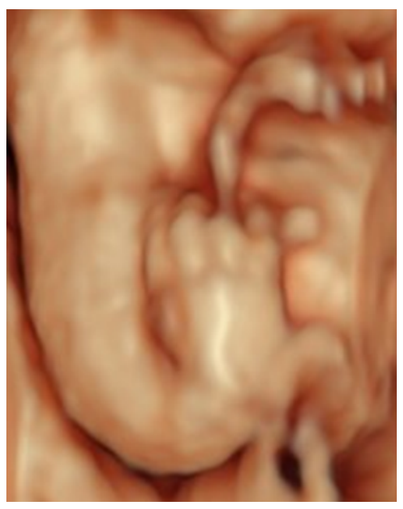

Image 1: Malposition of the club hand of the right upper limb (ECO3D)

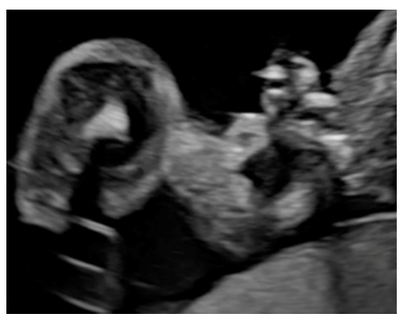

Image 2: Hypoplasia of the ulna

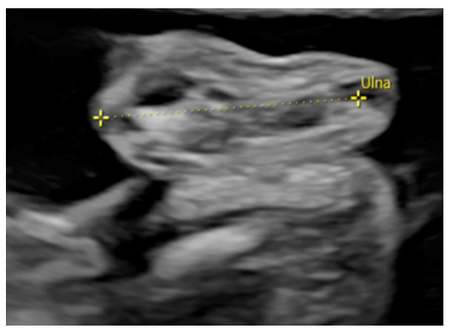

Image 3: Malposition of the club hand of the right upper limb and agenesis of the radius

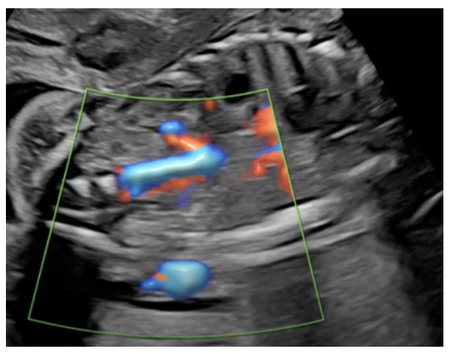

Image 4: Doppler absence of the right renal artery.

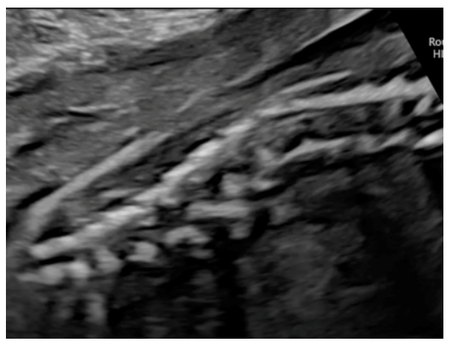

Image 5: Hemivertebrae and dorsolumbar scoliosis.

At week 37+3, due to suspicion of intestinal obstruction, by ultrasound imaging, with intestinal dilation and increased peristalsis and breech fetal presentation, it was decided to admit the patient to perform an external cephalic version and subsequent direct induction. After 5 hours of induction an urgent c-section was indicated due to risk of loss of fetal well-being. A 2705gr (p39) female infant was born with APGAR 9/10 and umbilical cord pH 7,20.

In the physical examination at birth multiple malformations were found:

- Agenesis of the right auricle and the external auditory canal
- Right mandibular hypoplasia with intact palate
- Short neck with pterygum colli
- Right thoracic hypoplasia
- Right radial and ulnar hypoplasia, clubby hand with radial deviation and camptodactyly of the IV finger
- Hypoplastic thumb
- Anterior anus and low perineal fistula

Image 6: Agenesis of the right auricle and right clubby hand with radial deviation.

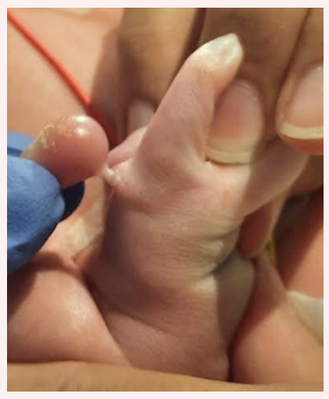

Image 7: Right camptodactyly of the IV finger

Complementary tests were made.

Thoracic and abdominal X-Ray: right thoracic hypoplasia with rib fusion, dorsal hemivertebrae and vertebral fusions at three heights at the dorsal and lumbar level with secondary scoliosis. Nasogastric tube in the stomach with dilation of the gastric chamber that suggests duodenal dilatation and aerated thin loops of normal caliber, with suspicion of duodenal membrane. There were signs of intestinal malrotation (inverted mesenteric artery and vein).

Right upper limb X-Ray: radial and ulnar hypoplasia, clubby hand with radial deviation, hypoplastic thumb and camptodactyly of the IV finger.

Echocardiography: small middle muscular ventricular septal defect and aneurysm of the fossa ovale.

Genetic studies: Normal qChip post 60K genomic hybridization study (no significant gains or losses of genomic material are detected) and molecular study using massive sequencing of the exome.

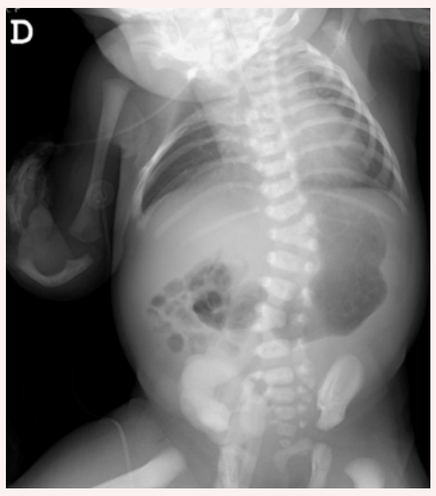

Image 8: Thoracic and abdominal X-Ray

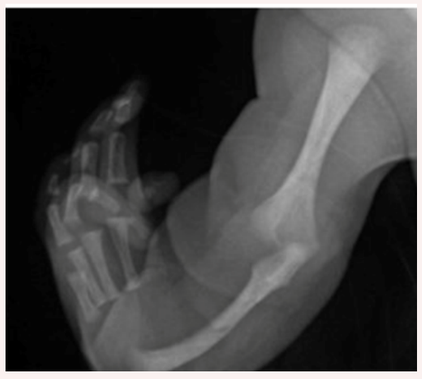

Image 9. Right upper limb X-Ray.

Given all these malformations the suspected diagnoses were the oculo-auriculo-vertebral spectrum or Goldenhar Syndrome, in the first place, and the VACTERL association.

At 21 days of life, she required laparotomic surgery due to intestinal malrotation and duodenal membrane-type duodenal atresia.

Discussion

The diagnosis of Goldenhar Syndrome is feasible starting from 14 weeks of pregnancy, especially in fetuses presenting the most severe end of the spectrum, fetal ultrasound allows detection of severe extracranial abnormalities and 3D ultrasound can identify milder defects. It is a sporadic onset disorder, but an autosomal dominant inheritance pattern has been described. Given its phenotypic heterogeneity, it is difficult to predict the severity and prognosis of the disease. The risk of recurrency in the next generation is 2-3%.

Treatment is challenging due to a large variety of clinical manifestations and differences in the severity of presentation, it requires a multidisciplinary approach and should be individualized to the anomalies of each patient.

Conclusion

The oculo-auriculo-vertebral spectrum is a rare congenital malformation syndrome of unknown etiology with a difficult prenatal diagnosis and has a highly variable prognosis depending on the severity of the malformations. A multidisciplinary approach is essential for the diagnosis and treatment of the patients.

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