CASE REPORT

Goldenhar syndrome: a rare diagnosis with possible prenatal findings

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SUMMARY

Goldenhar syndrome is a rare congenital disease associated with hemifacial hypoplasia as well as ear and ocular defects. Sometimes it is also associated with vertebral and other bone defects, cardiac malformations and central nervous system anomalies. Its aetiology is not yet clarified in the literature. We present a case of multiple malformations detected in the morphology ultrasound (at 22 weeks of gestation), namely absent nasal bones, micrognathia and absent left radius, among other defects. Genetic counselling, fetal brain MRI and cardiac sonography, which showed ventricular septal defect, were performed. 11 syndromes with poor fetal or neonatal prognosis were identified as possible diagnosis, using a genetic database and the couple asked for a medical termination of pregnancy. Postmortem examination has shown features consistent with Goldenhar syndrome.

BACKGROUND

Goldenhar syndrome or hemifacial microsomia is a birth defect with incidence of 1 in 3000–5000 newborns that involves the first and second branchial arch derivatives. It was described by Goldenhar for the first time, in the 50s, as a triad of mandibular hypoplasia, epibulbar dermoids and preauricular tags.[1]

Gorlin *et al*[2] found an association between this syndrome and vertebral anomalies and named it oculoauriculovertebral dysplasia. Typically, it affects the external and middle ear, jaw, maxilla, soft tissues and muscles in the affected side. In some cases, it can affect the orbit, eye, nose or neck. In 85% of the cases is unilateral and in 50% can be associated with other systemic features such as cardiac, vertebral and central nervous system malformations. This syndrome can also be associated with ipsilateral radial defects.[1]

The aetiology of this syndrome is not known but it could be related to an anomaly in the blood supply of the branchial arches during the seventh week of pregnancy. Other hypothesis is an anomaly in the migration of neural crest cells migration.[1 3]

Most of the cases are sporadic but autosomal dominant inheritance was already reported. It is a frequently observed variability of clinical expression within families.[4] The genes involved are not yet known, so genetic diagnosis is not possible. Some environmental factors have been related to the syndrome, such as the use of some vasoactive drugs, maternal diabetes and assisted reproduction techniques.[3 5]

It is possible to suspect the syndrome in prenatal ultrasonography. The prognosis depends on the combination of malformations and systemic associated defects.[1 3]

The case described below matches the features of Goldenhar syndrome and represents a rare birth defect in which a multidisciplinary approach, involving obstetrics (fetal medicine), medical genetics, paediatric cardiology and pathology, was crucial to reach the diagnosis.

CASE PRESENTATION

A 37-year-old pregnant woman, Caucasian, married, with no consanguinity story and without relevant personal or family background. Her first pregnancy was uneventful with the birth of a healthy newborn, 17 years before.

The routine first-trimester prenatal ultrasound performed at 11th week showed a fetus without visible nasal bones, increased nuchal translucency (3.86 mm) and positive biochemical screening. Amniocentesis was performed and the karyotype was normal (46, XX). On the second trimester ultrasound, other dysmorphic features such as micrognathia (figure 1) and absent left radius (figure 2) were identified. Fetal growth was in the normal range. The couple was referenced to our hospital to attend a medical genetics appointment and counselling.

INVESTIGATIONS

In medical genetics appointment, research for micrognathia and radium agenesis in a genetics database (London Medical Database Dysmorphology database), found 69 syndromes, some of them associated with congenital heart defects, mental retardation and central nervous system alterations. Fetal brain MRI showed no anomalies, except uncertainty of

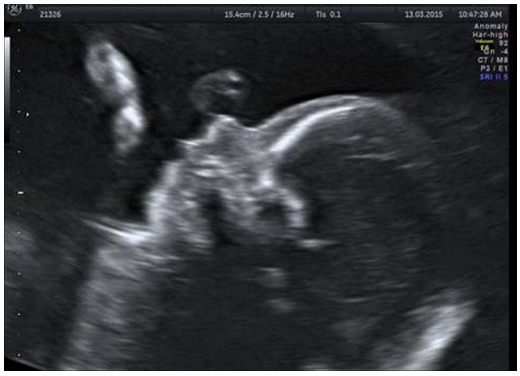

Figure 1 Micrognathia.

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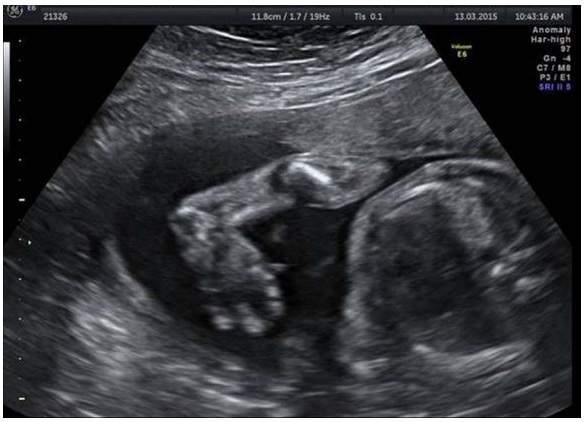

Figure 2 Absent left radius.

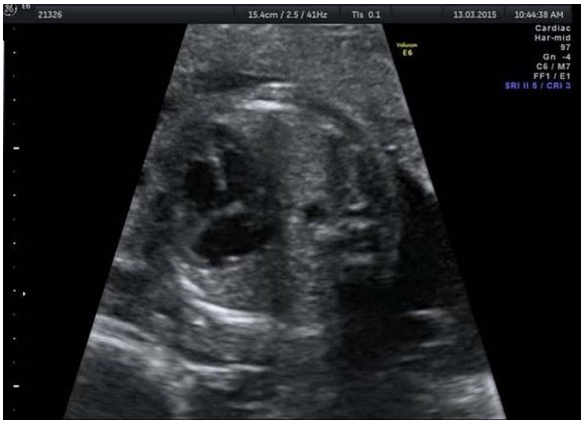

Figure 3 Interventricular communication.

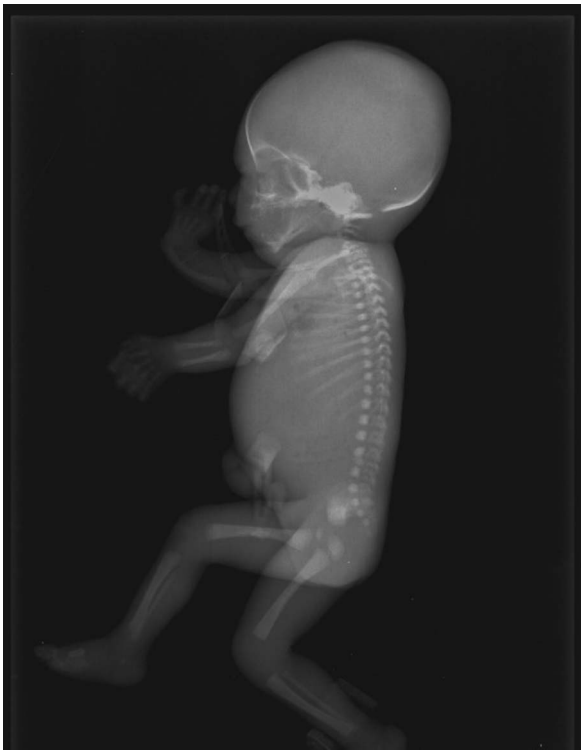

Figure 4 Absent left radius and left thumb in X-ray.

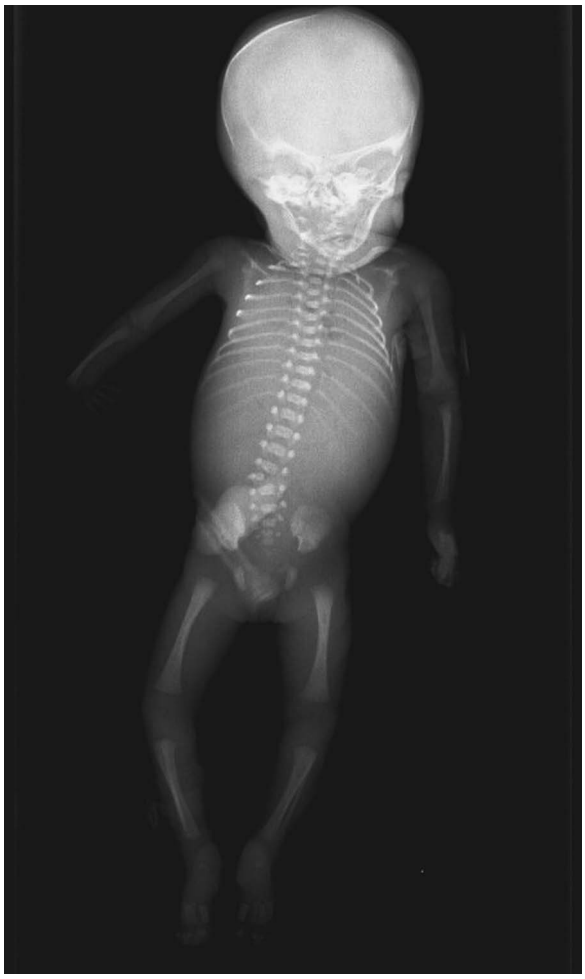

Figure 5 Lumbar hemivertebra in X-ray.

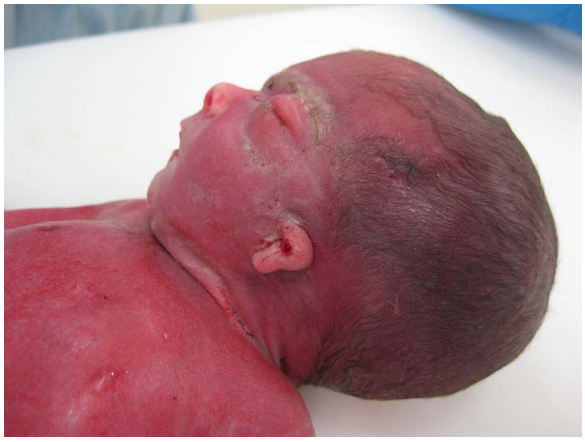

Figure 6 Hemifacial hypoplasia in autopsy.

nasal bones' presence. Fetal echocardiography showed a large subaortic interventricular communication (figure 3). The case was sent to the prenatal diagnosis unit of our hospital and an obstetric ultrasound corroborated the previous findings and added a peculiar facies, a low implantation of the ears and polyhydramnios. Adding these findings to the genetic database, 11 syndromes with poor prognosis were identified. Of note, Goldenhar syndrome was not among them.

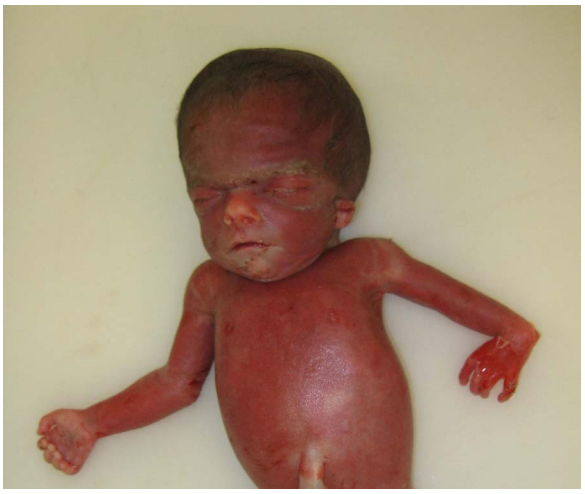

Figure 7 Hemifacial hypoplasia and forearm deformity in autopsy.

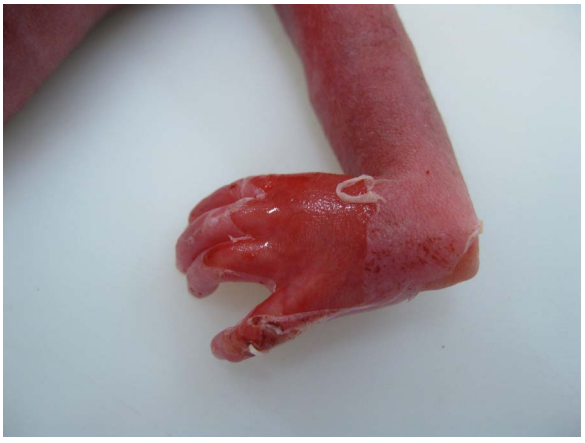

Figure 8 Absence of left thumb in autopsy.

OUTCOME AND FOLLOW-UP

A multidisciplinary discussion concluded that the fetus presented a multiple malformation syndrome, with poor clinical prognosis, although without definitive diagnosis. After counselling, the couple decided to request a medical termination of pregnancy at 23 weeks of gestation.

The postmortem X-ray showed absence of left radius, left thumb (figure 4) and a lumbar hemivertebra (L5; figure 5). The autopsy showed left hemifacial hypoplasia, low implantation of the ears, left microtia, left micrognathia, palatine cleft, short left forearm, absence of left thumb and interventricular communication (figures 6–8). The dysmorphic findings are consistent with Goldenhar syndrome.

This case report demonstrates that congenital complex syndromes are a challenging diagnosis. A multidisciplinary team with interaction between medical genetics, obstetrics (fetal medicine), paediatric cardiology and pathology was crucial to achieve prenatal suspicion of a severe malformation syndrome and a more accurate diagnosis after autopsy and X-ray examination.

DISCUSSION

Hemifacial microsomia or Goldenhar syndrome includes unilateral malformation of the external ear, hemifacial hypoplasia with epibulbar dermoid and vertebral anomalies. There are no consensual diagnostic criteria and it is a clinically heterogeneous birth defect.[6] Several cases of this rare syndrome were already reported in the literature, but timely diagnosis remains a challenge.

Saraux *et al*[7] reported two sisters with Goldenhar syndrome, with healthy, unrelated parents. The karyotype was normal. Touliatou *et al* described detailed clinical features of 17 Greek patients with Goldenhar syndrome, including a pair of monozygotic twins. The most constant findings were auricular defects (94%), facial anomalies (76%), ocular anomalies (65%) and conductive hearing loss (76%). Most features were unilateral (70%) and ipsilateral to the affected side of the face.[8] Digilio *et al*[9] studied the frequency and characteristics of congenital heart defects in 87 patients with this syndrome. Congenital heart defects were diagnosed in 28 (32%) of the patients.

One of the challenges of this syndrome is absence of a genetic diagnosis to confirm prenatal suspicion. Moreover, the diversity of phenotypic presentations of the syndrome leads to a lack of consensus in the minimum criteria for the diagnosis and uncertainty of the prognosis. Indeed, the prognosis might be relatively good or considerably poor depending on the severity of malformations and affected organs.

Learning points

- Goldenhar syndrome is a rare birth defect with unknown aetiology.
- Prenatal suspicion is possible but no genetic diagnosis is yet available.
- The prognosis depends on the presented malformations and association with systemic defects.
- Multidisciplinary evaluation is essential to reach this challenging clinical diagnosis.

Contributors BR and JI wrote the clinical case; MG-R took the pictures, followed the couple in genetics appointment and reviewed the manuscript; AC followed the couple in prenatal diagnosis and reviewed the manuscript. All authors were present and followed the case when it took place.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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