Genetic Counseling in a Case of a Pregnant Woman with Goldenhar Syndrome (Oculoauriculovertebral Spectrum)

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Goldenhar Syndrome also known as oculoauriculovertebral spectrum (OAVS) is a rare syndrome characterized by hemifacial microsomi, microtia, epibulbar dermoids, ear malformations and hemivertebrae. The mode of inheritance is clearly unknown and mostly polygenic etiology. The aim of this presentation is to present this young mother with oculoauriculovertebral spectrum and related problems. Most of the individuals with this syndrome do not notice themselves before the time of diagnosis. For that reason, we followed this patient's pregnancy and performed cesarian section due to cephalopelvic disproportion. The enlighting of these patients with this syndrome is very important for the evaluation of this family and for the future pregnancies.

Key Words: Goldenhar syndrome, Oculoauriculovertebral spectrum, Pregnancy, Cardiovascular malformations, Ventricular septal defect

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Introduction

Goldenhar Syndrome (oculoauriculovertebral spectrum) is characterized by multisystemic malformations such as craniofacial, vertebral, cardiac, renal, and central nervous system anomalies. The most typical facial malformations are characterized with epibulbar dermoids, microtia, mandibular hypoplasia. The classical facial aspect described as facial microsomia and the other associated anomalies are probably caused by developmental defects of the first and second brachial arches.[1] The etiology of these developmental defects seems to be heterogeneous.

OAVS has a prevalence ranging from 1:3.500 to 1:7.000 live births, and male-female gender ratio is 3:2.[1] Although most cases are sporadic, familial inheritance has also been reported.[1] The frequency of associated cardiovascular malformations has been estimated to be between 5-58%.[2] In the medical literature, several studies have shown that fertility is not affected in patients with this syndrome.

In this report, we describe a case of 20-year-old pregnant woman with classical features of Goldenhar syndrome, her antenatal course and postpartum period.

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Case Report

A 20-year-old woman, gravida 1, parity 0, at 14 weeks' gestation was referred to Hacettepe University because of multiple malformations.

She had a height of 135 cm (<3p), a weight of 50 kg (3-10p). Her physical examination revealed facial asymmetry, microtia and preauricular skin tag on the right ear (Figure 1.), malocclusion of the jaw, mandibular hypoplasia (Figure 2.), severe kyphoscoliosis (Figure 3.) and right-sided hearing problems. She was diagnosed as a sporadic case of OAVS as there were not any similar findings of other family member. She denied a history of in utero exposure to known teratogenic agents or consanguinity between her parents. She was demonstrating age-appropriate mental and speech development with no signs of mental retardation.

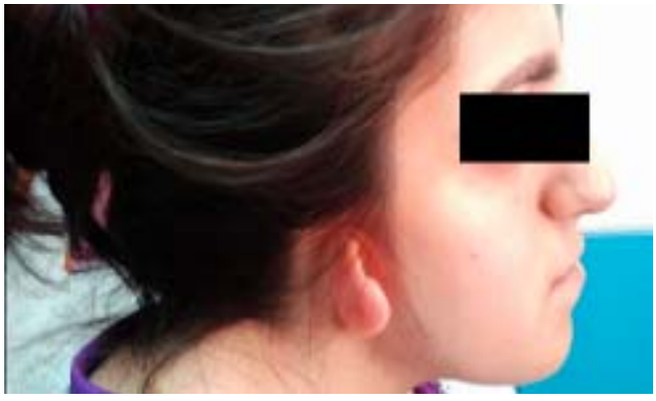

Figure 1: Lateral view of the face showing ear malformations, including microtia and preauricular tags. (The patient's signed informed consent authorizing the publication of these pictures.)

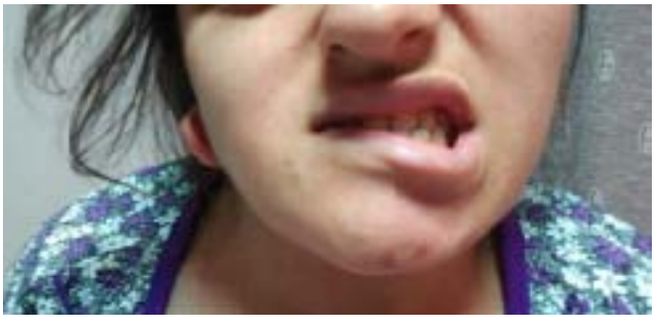

Figure 2: Frontal view of the face showing marked facial asymmetry and malocclusion. (The patient's signed informed consent authorizing the publication of these pictures.)

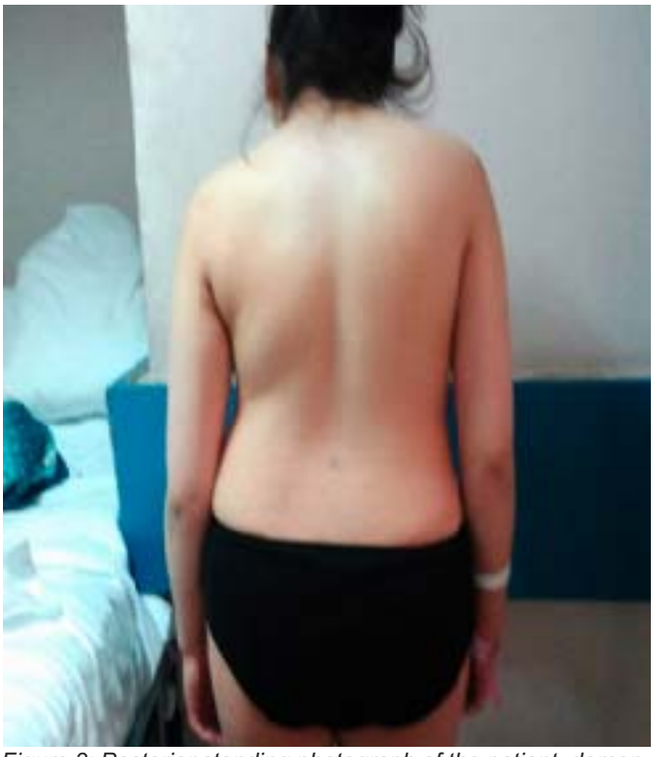

Figure 3: Posterior standing photograph of the patient, demonstrating severe kyphoscoliosis. (The patient's signed informed consent authorizing the publication of these pictures.)

Her blood pressure and heart rate were in normal ranges. Cardiac auscultation revealed normal S1 and S2, while S3 and S4 were not audible. Grade 2-3/6 holosystolic murmur was detected at the left sternal border of the 3rd intercostal space. The electrocardiogram was normal but transthoracic echocardiography revealed small ventricular septal defect, a thin aneuvrismatic interatrial septum, minimal mitral valve insufficiency, minimal tricuspit insufficiency with normal systolic functions. Her cardiac function was evaluated by echocardiograms performed in every month.

Peripheral blood chromosome analysis was normal, 46, XX. Genetic counseling regarding the inheritance patterns, possible ways of expression and pregnancy outcome was given.

Her triple screen test revealed low risk and second trimester ultrasound scan showed normal findings. At 20th gestational week, fetal echocardiography was performed showing normal fetal cardiac conditions. At 26 weeks' she had a screening glucose challange test with a normal result. She was kept under close cardiac and obstetric surveillance. Serial prenatal sonographies were found within normal limits.

Patient was evaluated for cardiac functions every month. She showed no symptoms of cardiac deterioration including dyspnea, fatigue or palpitation. Her blood pressure kept in normal ranges, echocardiograms showing no cardiac decompansation.

At the 39th week patient presented with increased uterine contractions and gush of fluid. Her pelvic examination revealed cephalopelvic disproportion so a cesarian section was planned. Difficult intubation was expected in patients because of the facial and oral anomalies. Thus, epidural anesthesia was performed by an expert anesthesiologist. She delivered a female baby weighting 3080g (25-50 p) with 9 and 10 Apgar scores at 1st and 5th minutes respectively. She was kept under close monitoring postoperatively. Her vital signs were normal. Post operative echocardiogram showed no cardiac deterioration. Her baby had a normal phenotype with no signs of facial or skeletal abnormalities. Echocardiogram of the baby showed normal neonatal cardiac findings. The patient and the baby subsequently did well, and on second postpartum day they were discharged home, with planned follow-up with the cardiologist.

Discussion

In 1952, Goldenhar analyzed 3 new cases in addition to 16 cases previously reported, and described oculoauricular dysplasia with the major triad of epibulbar tumor, auricular appendage and aural fistula.[3] In 1963, Gorlin et al investigated over 40 previously reported cases and joined the name 'oculoauriculovertebral dysplasia', featuring epibulbar dermoids and/or lipodermoids, auricular appendices and pretragal blind-ended fistulas, and vertebral anomalies.[4] Our case had microtia and preauricular tag on the right ear, facial asymmetry, malocclusion, mandibular hypoplasia, and severe kyphoscoliosis showing all aspects of the syndrome.

The frequency of cardiovascular malformation in Goldenhar syndrome is 5-58%, showing great variability.[2] The common cardiovascular malformations are ventricular septal defect and tetralogy of Fallot.[2] OAVS should be kept in mind when cardiac malformations accompanies dismorphic facial ocular and vertebral features. The case reported here had small ventricular septal defect, minimum mitral valve insufficiency, minimum tricuspit insufficiency with normal systolic functions, thin aneuvrismatic interatrial septum.

In the medical literature there are hypothesis corcerning development of this syndrome, in 1998 Nakajima et al. reported that the cause is the abnormalities of the first and second branchial arches.[2] In 1981 Russell et al. pointed out that Goldenhar syndrome might result from mesodermal deficiencies caused by impairment of primitive streak cell migration, because the organs showing the dysplasia spectrum of this syndrome are derived from the mesoderm.[5] It is also reported that reported autosomal dominant inheritance of Goldenhar syndrome,[2] but there is no family history of this syndrome in the present case.

It is very interesting that reproduction abnormalities influenced this syndrome. It is known that the safety of assisted reproductive technology (ART) is a major concern.[6] Beksac et al. reported that OAVS might be associated with ART.[6] Horsthemke et al. reported that there is a bidirectional relationship between twinning and OAVS.[7] Since we do not know the underlying etiology and pathogenesis of OAVS, there are common arguments that not only twinning may increase the risk of OAVS, but also the embyologic defect in OAVS may casue twinning, or they may have a common basis.[7] Since our case is a spontaneus pregnancy, the assisted reproductive technology and OAVS relationship hypothesis is not an appropriate explanation.

Engiz et al. reported case series of 31 patients with Goldenhar syndrome. They performed karyotype analysis to 29 of them. One patient with severe mental and motor retardation had 47,XX,+der (22) t (11.22) (q23; q11) karyotype.[8] Balcı et al. also suggested to screen every patient with OAVS for 22q11 deletion using array technology since the distal 22q11.2 region could be a candidate gene for this syndrome.[9] Karyotype analysis of our patient revealed to be normal. To keep in mind that, since penetrance is not known, karyotype analysis should be performed.

In conclusion, we have reported the antenatal course and postpartum period of a pregnant woman with Goldenhar syndrome. The presented case had a spontaneous pregnancy and the antenatal course was uneventful. The fetal imaging studies showed normal developing fetus without any anatomic defect. During cesarian section epidural block was performed by an expert anestesiologist due to risk of difficult intubation. After delivery, the baby and the mother did well and discharged at second postpartum day. Because patients with Goldenhar syndrome may have associated cardiac defects and performance of anesthesia to these patients requires expert anesthiologists, they should be referred to tertiary hospitals.

Goldenhar Sendromu (Oküloaurikülovertebral Spektrum) Olan Gebe Bir Olguda Genetik Danışmanlık

Oküloaurikülovertebral spektrum (OAVS) olarak da bilinen Goldenhar Sendromu hemifasyal mikrozomi, mikroti, epibulbar dermoidler, kulak malformasyonları ve hemivertebra ile karakterize nadir bir sendromdur. Kalıtım şekli kesin olmamakla beraber, genellikle poligenik kalıtım üzerinde durulmaktadır. Bu yazıda oküloaurikülovertebral spektrumu olan genç hamile bir hastanın problemleri tartışılacaktır. Bu sendromu taşıyan pek çok kişi, tanı anına kadar hastalığının farkında değildir. Bu nedenle, biz bu hastayı gebeliği boyunca takip ettik ve sefalopelvik uyumsuzluk nedeniyle sezaryen ile doğumunu gerçekleştirdik. Ailenin değerlendirilmesi ve sonraki gebeliklerin seyri için bu sendromu taşıyan hastaların aydınlatılması çok önemlidir.

Anahtar Kelimeler: Goldenhar sendromu, Oküloaurikülovertebral spektrum, Gebelik, Kardiyovasküler malformasyonlar, Ventriküler septal defekt

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