CASE REPORT OLGU SUNUMU

DOI: 10.5336/ophthal.2023-100339

Ophthalmological Approach to a Goldenhar Syndrome Patient with a Perimembranous Cardiac Defect First Diagnosed in an Eye Clinic

İlk Tanısı Göz Hastalıkları Kliniğinde Konan Perimembranöz Kardiyak Defektli Goldenhar Sendromu Hastasına Oftalmolojik Yaklaşım

Burak ÖZKAN[a], Nihan BAHADIR[b], Emrah UĞURLU[c], Emre TIRAŞÇI[d]

[a]Yunus Emre State Hospital, Clinic of Ophthalmology, Eskişehir, Türkiye
[b]Erciş Şehit Rıdvan Çevik State Hospital, Clinic of Cardiology, Van, Türkiye
[c]Erciş Şehit Rıdvan Çevik State Hospital, Clinic of Ear Nose Throat Diseases, Van, Türkiye
[d]Erciş Şehit Rıdvan Çevik State Hospital, Clinic of Physical Medicine and Rehabilitation, Van, Türkiye

ABSTRACT A 17-year-old male patient presented with the complaint of an enlarging and irritating mass in the left eye. He was discovered to have a left limbal dermoid and forniceal dermoid. External examination revealed minimal facial asymmetry and ipsilateral hemifacial microsomia and preauricular skin tag. The limbal dermoid area was operated with the diagnosis of oculo-auriculo-vertebral spectrum (OAVS) or Goldenhar syndrome, and ventricular septal defect was diagnosed in the cardiology clinic and he was referred for surgical repair. Limbal dermoid and phenotypic spectrum of the OAVS, a wide-ranging disorder helped identify the effects that could affect all systems.

Keywords: Goldenhar syndrome; limbal dermoid; ocular surface; perimembranous cardiac defect

ÖZET On yedi yaşındaki erkek hasta, sol gözünde büyüyen ve rahatsız edici kitle şikâyeti ile başvurdu. Sol limbal ve alt kapak forniks alanında dermoid görüldü. Dış muayenede minimal yüz asimetrisi, ipsilateral hemifasiyal mikrozomi ve preauriküler cilt eklentisi görüldü. Limbal dermoid bölge okülo-aurikülo-vertebral spektrum (OAVS) veya Goldenhar sendromu tanısıyla opere edilen hastaya kardiyoloji kliniğinde ventriküler septal defekt tanısı konularak cerrahi onarım için yönlendirildi. Limbal dermoid ve olgunun fenotipik özellikleri, tüm sistemleri etkileyebilecek bir tablo olan OAVS içinde etkilenmelerin belirlenmesinde önemli bir belirleyicidir.

Anahtar Kelimeler: Goldenhar sendromu; limbal dermoid; oküler yüzey; perimembranöz kalp defekti

Goldenhar syndrome or oculo-auriculo-vertebral spectrum (OAVS) is a rare congenital defect involving primary and secondary branchial dysgenesis.[1] Classic findings such as limbal dermoid, mandibular hypoplasia with facial asymmetry, auricular malformations and vertebral abnormality are observed.[1,2] Other ocular findings; choristoma, microphthalmia, iris and retinal coloboma. Facial asymmetry and maxillary and mandibular hypoplasia, accessory tragus, external auditory canal atresia, and scoliosis are other findings.[1-3] Cardiac pathologies include atrial septal defects (ASD), ventricular septal defects (VSD), patent ductus arteriosus (PDA), Tetralogy of Fallot (ToF), double inlet left ventricle, aortic stenosis, pulmonary artery stenosis and bicuspid aortic valve, double outlet right ventricle (DORV), coarctation of aorta, transposition of the great arteries (TGA).[4,5] Our case is an eye clinic patient with asymptomatic car-

TO CITE THIS ARTICLE:
Özkan B, Bahadır N, Uğurlu E, Tıraşçı E. Ophthalmological approach to a Goldenhar syndrome patient with a perimembranous cardiac defect first diagnosed in an eye clinic. Turkiye Klinikleri J Ophthalmol. 2024;33(3):190-4.

Correspondence: Burak ÖZKAN
Yunus Emre State Hospital, Clinic of Ophthalmology, Eskişehir, Türkiye
E-mail: burakozkanmd@yahoo.com

Peer review under responsibility of Turkiye Klinikleri Journal of Ophthalmology.

Received: 18 Nov 2023 ***Received in revised form:*** 05 May 2024 ***Accepted:*** 06 May 2024 ***Available online:*** 10 May 2024

diac pathology diagnosed at a late age. Our aim is to introduce the OAVS, which is necessary to add a systemic approach to the ophthalmological approach.

CASE REPORT

A 17-year-old male patient presented with complaints of decreased vision level in his left eye (LE) and a mass on the anterior surface of the eye (Figure 1A, Figure 1B). Anterior segment examination of the LE with a elevated, non-pigmented deeply infiltrating the stroma, inferotemporal limbo-conjunctival epibulbar dermoid lesion with hair follicle in its surface, measuring approximately 5.6x8.6 mm and an accessory tragus on the same side (Figure 1C). The patient's best corrected visual acuity (BCVA) was 20/20 in the right eye and 2/20 (LE cycloplegic refractive error +5.25 -5.75x145) in the LE. The patient's posterior segment examination was normal. Intraocular pressure was measured as 12/14 mmHg (Goldmann Applanation Tonometer). There was no limitation in eye movements. Clinical findings and history were consistent with OAVS or Goldenhar syndrome. Excisional biopsy was performed on the limbal dermoid and forniceal lipodermoid area in the LE, with covered using a conjunctival advancement flap of 10-0 nylon suture. It was observed that the corneal stroma tissue under the excised mass was extremely thin. The results of the pathological study revealde: "Epidermis and dermis-like squamous epithelium on the surface, thick collagen bands, sebaceous glands and hair follicles underneath has been followed" On the tenth postoperative day, there was mild ocular hyperemia in the LE, nephelion in the inferotemporal corneal area with remnants of the infiltrative lesion (Figure 1D). Two months after surgery, a quiescent eye, local conjunctival hyperemia, and fluorescein-negative cornea were observed with a small inferior temporal nephelion (Figure 1E). Postoperative refractive error decreased but final BCVA remained 2/20 (LE cycloplegic refractive error +2.50 -2.75x145).

Our patient was diagnosed with Goldenhar syndrome due to the presence of a typical epibulbar dermoid finding as well as other clinical symptoms. Genetic tests were requested for confirmation, but this service was not available in the current location

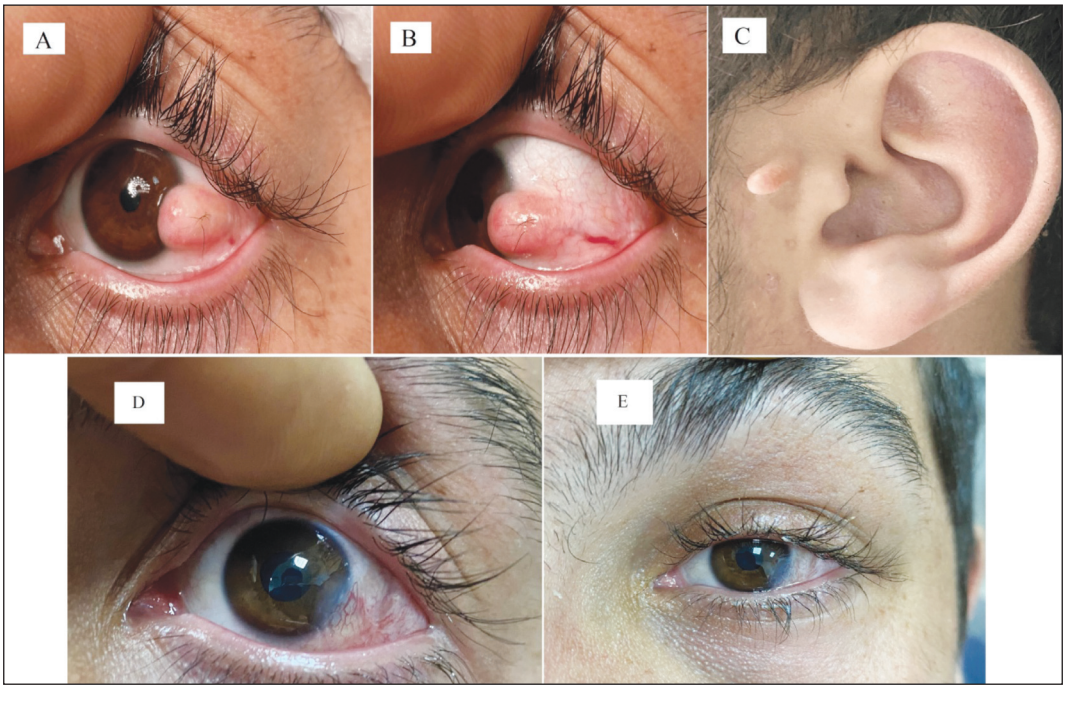

FIGURE 1: A-B) Limbal dermoid appearance; **C)** Accessory tragus; **D)** Postoperative appearence: 10th day postoperative **E)** 60th day postoperative-corneal leukoma at the lesion excision site.

and the patient and his relatives did not want to have genetic tests. In addition, our patient did not have a family history of this spectrum. The patient who was very satisfied with the final ocular result both aesthetically and spiritually.

After diagnosis of OAVS, our patient without symptoms of wheezing, tachypnea, respiratory distress or cyanosis was examined for cardiac problems that may accompany. On electrocardiography, his heart rate was 90 beats per minute, right axis with incomplete right bandle branch block, normal intervals including corrected QT of 0.39 s. In echocardiographic examination a VSD on perimembraneous outlet septum- 11 mm in diameter and with left to right shunt (Figure 2). Systolic phase functions were in normal range (ejection fraction 66% and shortening fraction 36%). Using Spectral Doppler interrogation on the parasternal long axis image, the pressure gradient across the defect was calculated 88 mmHg (Figure 2). The velocity of tricuspid valve regurcitation was measured as 3.49 m/sn with second degree tricuspid valve regurgitation (Figure 2). Left ventricle was dilated to an end-diastolic diameter of 59 mm. The maximum gradient was measured 50 mmHg in the subaortic region due to the subaotic membrane structure extanding at LVOT 3 mm below the aortic valve and due to aortic valve prolapse, first degree aortic regurgitation was observed. Perimembranous defects may self-closing because of apposition of contiguous tissue from the leaflets of the tricuspid valve; but defects that failure to spontaneously close and have possibility of development of aortic valvar prolapse always require transcatheter or surgical closure.[6] During the examination at the orthopedic clinic, the patient's anteroposterior spine radiograph revealed right-facing scoliosis in the thoracic region with a 15-degree cobb angle (Figure 3). For this report and images, written informed consent forms were obtained from the patient and his family to be published.

DISCUSSION

Limbal dermoids are rare benign choristomas that are congenital and often diagnosed at birth.[5] Choristomas are generally stable and nonprogressive solid masses covered with conjunctival epithelium. They are comprise of dermal and epidermal tissue and appendages. In some cases, they do not reduce the visual quality and are operated only for aesthetic concerns. In some

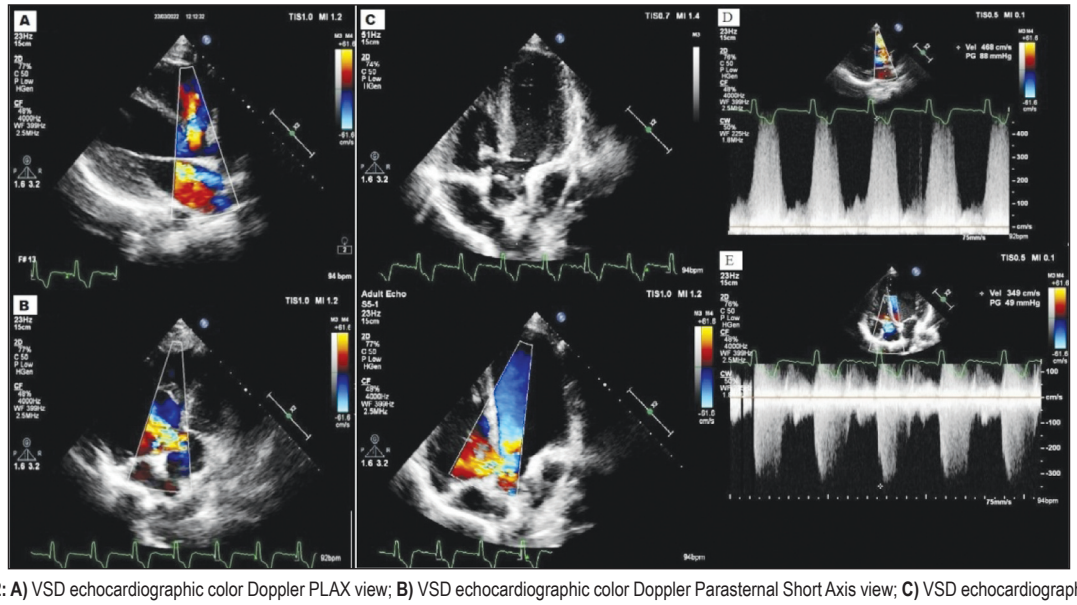

FIGURE 2: A) VSD echocardiographic color Doppler PLAX view; **B)** VSD echocardiographic color Doppler Parasternal Short Axis view; **C)** VSD echocardiographic 2D and color Doppler Apical five chamber view; **D)** The pressure gradient through VSD by using Doppler echocardiography at PLAX view; **E)** The velocity of tricuspid valve regurcitation by using Doppler echocardiography at Apical four chamber view.
VSD: Ventricular septal defects; PLAX: Parasternal Long Axis.

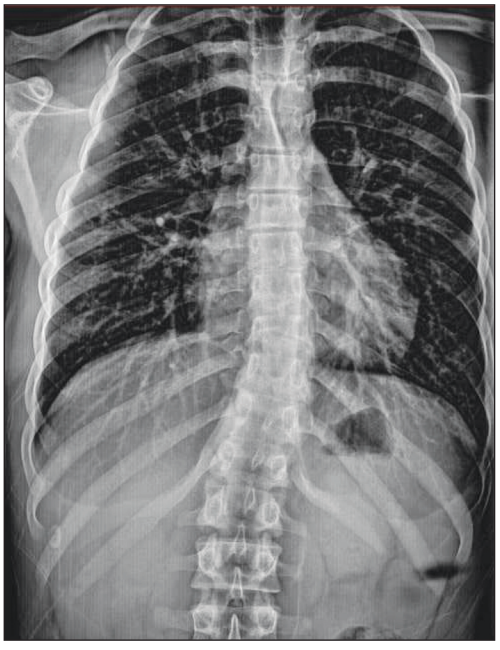

FIGURE 3: Right-facing scoliosis in the thoracic region with a cobb angle of 15 degrees on the anterior-posterior X-ray of the spine.

cases, it causes astigmatism, amblyopia and ocular motility limitation.[7] Our case had both high astigmatism and amblyopia development. Astigmatism is the most common sequelae that reduces visual quality in this spectrum. It has been suggested that epibulbar dermoid often occurs in the inferotemporal quadrant, with the second most common in the superotemporal region.[7]

There are several autosomal dominant and sporadic-occurring syndromes overlapping with OAVS.[8] Various etiologies have been reported for the OAVS, environmental causes containing hereditary and various chromosomal abnormalities (Table 1).[5,9]

In one study, cardiac defects were detected in 39.4% of patients; including ToF, atrioventricular septal defect, secundum ASD, TGA, PDA, pulmonary atresia (PA) with intraventricular communication, cor triatriatum and pulmonary artery

TABLE 1: Syndromes with overlapping findings that should be considered in the differential diagnosis of the oculoauriculovertebral spectrum.

Syndrome	Ocular features	Systemic features	Pattern of inheritance
Oculoauriculovertebral spectrum	Epibulbar dermoid Eyelid coloboma Microphthalmia/anophthalmia Aniridia	Vertebral abnormalities External ear abnormalities Hemifacial macrosomia Cardiac, anorectal, nervous, urogenital and pulmonary abnormalities	Most sporadic
Branchiooculofacial syndrome	Cataracts Strabismus Nasolacrimal dysgenesis Hypertelorism and Ptosis	External to inner ear abnormalities Conductive hearing defect Branchial skin defects Facial asymmetry and muscle atrophy Microphthalmia/anophthalmia Cleft palate/lift	Autosomal dominant
Treacher Collins Franceschetti syndrome	Down-slanting palpebral fissures Lower lid and iris colobomas Refractive errors and amblyopia Periorbital muscle anomalies	Mandibulofacial dysostosis External ear abnormalities Cleft palate	Autosomal dominant
Townes Brock syndrome	Iris coloboma Duane anomaly	Imperforate anus External ear abnormalities/pre-auricular tags Visceral abnormalities (cardiac, renal, urogenital)	Autosomal dominant
CHARGE syndrome	Coloboma Microphthalmia	Ear abnormalities Choanal atresia Cleft palate/lift Visceral malformations (Cardiac, tracheoesophageal, cranial nerve, urogenital) Growth retardation	Autosomal dominant

stenosis.[10] In their large series of 87 patients, Digilio et al. found that 32% of patients had heart defects.[5] They reported that most common defrcts were conotruncal/outflow deformities (39%) containing TGA, DORV, ToF, PA with VSD, double aortic arch and coarctation of aorta.[5] Although there is no specific cardiac pathology, a wide range of cardiac abnormalities have been presented to be associated with OAVS. ToF and septal defects are frequent.[6] The patient was referred to the tertiary center for cardiac catheterization, VSD closure and subaortic membrane resection, due to our center secondary level health center.

Our patient, who came to our ophthalmology clinic with complaints of low vision and an eye mass, actually had a life-threatening cardiac pathology. Therefore, a complete systemic evaluation and multidisciplinary approach are required in these patients. Additionally, genetic analysis and prenatal counseling to determine the inheritance pattern will be helpful for future pregnancies.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Burak Özkan, Nihan Bahadır;* ***Design:*** *Burak Özkan, Nihan Bahadır;* ***Control/Supervision:*** *Burak Özkan;* ***Data Collection and/or Processing:*** *Burak Özkan, Nihan Bahadır, Emre Tıraşçı;* ***Analysis and/or Interpretation:*** *Burak Özkan, Nihan Bahadır, Emre Tıraşçı, Emrah Uğurlu;* ***Literature Review:*** *Burak Özkan, Nihan Bahadır, Emrah Uğurlu;* ***Writing the Article:*** *Burak Özkan, Nihan Bahadır;* ***Critical Review:*** *Burak Özkan, Nihan Bahadır;* ***References and Fundings:*** *Emrah Uğurlu, Emre Tıraşçı;* ***Materials:*** *Emrah Uğurlu, Emre Tıraşçı.*

REFERENCES

1. Bogusiak K, Puch A, Arkuszewski P. Goldenhar syndrome: current perspectives. World J Pediatr. 2017;13(5):405-15. [Crossref] [PubMed]
2. Schmitzer S, Burcel M, Dăscălescu D, Popteanu IC. Goldenhar Syndrome - ophthalmologist's perspective. Rom J Ophthalmol. 2018;62(2):96-104. [Crossref] [PubMed] [PMC]
3. Hofmann E, Detterbeck A, Chepura T, Kirschneck C, Schmid M, Hirschfelder U. Oculoauriculovertebral spectrum and maxillary sinus volumes : CT-based comparative evaluation. J Orofac Orthop. 2018;79(4):259-66. English. [Crossref] [PubMed]
4. Morrison PJ, Mulholland HC, Craig BG, Nevin NC. Cardiovascular abnormalities in the oculo-auriculo-vertebral spectrum (Goldenhar syndrome). Am J Med Genet. 1992;44(4):425-8. [Crossref] [PubMed] `~
5. Digilio MC, Calzolari F, Capolino R, Toscano A, Sarkozy A, de Zorzi A, et al. Congenital heart defects in patients with oculo-auriculo-vertebral spectrum (Goldenhar syndrome). Am J Med Genet A. 2008;146A(14):1815-9. [Crossref] [PubMed]
6. Balaban İ, Bilgici MC, Baysal K. A new association of Oculoauriculovertebral spectrum and persistent fifth aortic arch -double lumen aorta: a case report. BMC Pediatr. 2022;22(1):102. [Crossref] [PubMed] [PMC]
7. Walker BA, Saltzman BS, Herlihy EP, Luquetti DV. Phenotypic characterization of epibulbar dermoids. Int Ophthalmol. 2017;37(3):499-505. [Crossref] [PubMed]
8. Lin AE, Haldeman-Englert CR, Milunsky JM. Branchiooculofacial Syndrome. 2011 May 31 [updated 2023 Sep 28]. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, Amemiya A, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. [PubMed]
9. Tasse C, Böhringer S, Fischer S, Lüdecke HJ, Albrecht B, Horn D, et al. Oculo-auriculo-vertebral spectrum (OAVS): clinical evaluation and severity scoring of 53 patients and proposal for a new classification. Eur J Med Genet. 2005;48(4):397-411. [Crossref] [PubMed]
10. Rosa RF, Dall'agnol L, Zen PR, Pereira VL, Graziadio C, Paskulin GA. Espectro óculo-aurículo-vertebral e malformações cardíacas [Oculo-auriculo-vertebral spectrum and cardiac malformations]. Rev Assoc Med Bras (1992). 2010;56(1):62-6. Portuguese. [Crossref] [PubMed]