

## A Case Report of Ehlers-Danlos and Goldenhar Syndromes

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### Abstract

A 23-year-old Thai female presented with skin laxity and delayed wound healing. Physical examination revealed asymmetry of face and hypertelorism of both eyes. Microtia of right ear, right periauricular pit, multiple fish mouth and cigarette paper scars were found. There were hyperextension of elbows and knees, 10 degrees and 15 degrees, respectively, Passive hyperflexion of the 5th finger more than 90 degrees was demonstrated. According to Villefranche's criteria, she had all major criteria for the diagnosis of Ehlers-Danlos syndrome, classic type. She also had hemifacial microsomia and ocular abnormalities that were compatible with Goldenhar syndrome. To our knowledge, a case of Ehlers-Danlos syndrome associated with Goldenhar syndrome has never been reported. This article presents the case of co-occurrence of these two rare syndromes.

**Keywords:** Ehlers-Danlos; Goldenhar syndrome

### Introduction

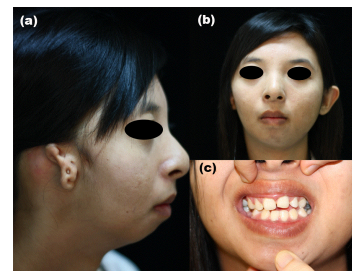
Ehlers-Danlos Syndrome (EDS) is an inherited syndrome that has a variety of genetic and clinical aspects. The genetic defect causes abnormality in biosynthesis and structure of collagen type I, III, or V, which lead to skin, joint, blood vessel and internal organ abnormalities [1]. In 1997, there were six subgroups, based on phenotype, inheritance pattern and underlying biochemical and molecular defects [2]. Currently, at least 11 subgroups of EDS have been reported [1,3].

Goldenhar syndrome is a rare congenital anomaly in developing defect of the first and second branchial arches, which was first described in early 1950's. Its prevalence was reported to be approximately 1:3000 to 1:5000 live births [4]. It is also described as Oculo-auriculo-vertebral dysplasia and hemifacial microsomia [5].

### Case Report

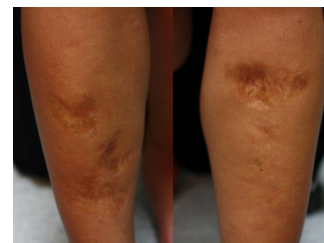
A 23-year-old Thai female presented with cutaneous hyperextensibility and delayed wound healing since childhood. Her skin could be stretched and bruised easily. Moreover, she was noticed to have asymmetrical face with small right pinna and loss of hearing in the same affected site. Past history revealed normal labor with birth weight of 2,200 grams. Congenital cleft palate requiring surgical closure was detected. She denied any history of joint pain, joint dislocation and joint subluxation. She had normal competency in learning and mental health. Her mother was the only family member who also had similar skin laxity and delayed wound healing phenotype.

Physical examination showed asymmetry of face and hypertelorism of both eyes. The fundoscopic examination of both eyes was normal. Microtia of the right ear, right periauricular pit, right maxilla and right mandibular hypoplasia and malocclusion of teeth were presented (Figure 1).



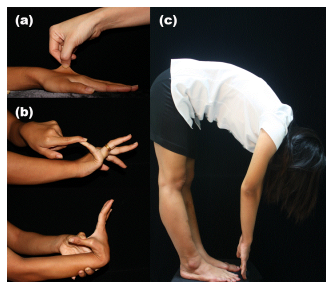
**Figure 1:** Microtia and preauricular pits of right ear (a) facial asymmetry (b) malocclusion of teeth (c).

Multiple fish mouth and cigarette paper scars along the shin areas were found (Figure 2).



**Figure 2:** Multiple fish mouth and cigarette paper scars along both legs.

Her skin showed hyperextensibility and hyperextension of both elbows and knees, 10 degrees and 15 degrees, respectively, and passive hyperflexion of the 5<sup>th</sup> finger more than 90 degrees were demonstrated (Figure 3). The skull X-ray showed hypoplasia of the right mandible but the vertebrae were normal.



**Figure 3:** Hyperextensible skin (a), passive dorsiflexion of the 5<sup>th</sup> finger >90° (b), hyperextension of both knees 15°(c).

## Discussion

Ehlers-Danlos syndrome (EDS), classic type is characterized by skin hyperextensibility, delayed wound healing with widened atrophic scars or fish mouth scars, and joint hypermobility. Using Beighton's scale to evaluate joint hypermobility, our patient did have bilateral passive dorsiflexion of the fifth finger >90° (2 points), bilateral hyperextension of the elbows >10° (2 points) and bilateral hyperextension of the knees >10° (2 points). Score more than 5 out of 9 as in our patient defines joint hypermobility. According to the diagnosed criteria of EDS by Villefranche in 1997, our patient had all major criteria which were (i) skin hyperextensibility, (ii) widening atrophic scar, (iii) joint hypermobility and (iv) positive family history. Three minor criteria including smooth and velvety skin, easy bruising and tissue extensibility and fragility were also demonstrated in our patient. Three major criteria are highly specific for the diagnosis of classic EDS [6]. Hence, she was diagnosed as EDS, classic type.

The prevalence of classic EDS (OMIM #130000) is approximately 1:20,000. It usually inherits in autosomal dominant mode and is caused by a mutation in type V collagen genes, COL5A1 or COL5A2. Type V collagen is a minor fibrillar collagen that widely present in tissues such as skin, bone, tendon, cornea, placenta and fetal membranes. Characteristic facial features which include epicanthic folds, excess skin over the eyelids, dilated scars, and premature aging of the face can be found in classic type of EDS [1]. From literature review, there is a new proposed type which is EDS with craniofacial characteristics, multiple congenital contractures, progressive joint and skin laxity, and multisystem fragility-related manifestations. Kosho et al. reported 6 cases of EDS with craniofacial abnormalities. All patients had hypertelorism, blue sclera and spinal deformities such as kyphoscoliosis or scoliosis [7]. Five of them had facial asymmetry. However, none of them reported microtia as characterized in our patient. There are other organ systemic involvements in EDS; musculoskeletal, neurologic, and cardiovascular systems. Joint hypermobility leads to major articular complications, such as habitual subluxation and dislocation of the joints. The joints that are mostly affected include shoulder, patella, digits, hip, radius, and clavicles. In neurologic disorder, primary muscular hypotonia causing delayed motor development and motor disturbance can be presented. In contrast, cardiovascular manifestation is not common in classic type of EDS [1].

Goldenhar syndrome, which was first described in 1952, is an uncommon inherited condition. Other several terms are used to describe this rare syndrome such as oculo-auriculo-vertebral (OAV)

dysplasia, 1<sup>st</sup> and 2<sup>nd</sup> branchial arch syndrome and hemifacial microsomia [5]. The incidence is between 1:3500 and 1:5600, with male and female ratio of 3:2. Multifactorial pathogenesis including nutritional and environmental factors has been proposed to cause disturbances of blastogenesis and development defects. It is possible that there are abnormal embryonic vascular supplies with disruption of mesodermal migration or some other factors leading to defective formation of the branchial and vertebral systems. Most of the cases are sporadic, although autosomal dominant and autosomal recessive inheritance has been reported. There is no genetic test to confirm Goldenhar syndrome. The diagnosis is based on clinical features. Classical triad includes ocular, auricular and vertebral disturbances. However, the cardinal findings most consistently present are facial asymmetry, mandibular or maxillary asymmetry and ear anomalies, whereas vertebral defect and epibulbar choristoma may or may not be presented [8]. Ocular changes comprise microphthalmia, epibulbar dermoids, lipodermoids and coloboma while pre-auricular tag, hearing loss, and microtia can be found as aural features. Vertebral anomalies include scoliosis, hemivertebrae, and cervical fusion. Eighty-five percent of the cases had unilateral facial abnormalities such as hypoplasia of the zygomatic, mandibular and maxillary bones [4]. Our patient presented with right hemifacial microsomia, microtia, periauricular pits, malocclusion of the teeth and unilateral hearing loss of right ear which reflect the impair development of 1<sup>st</sup> and 2<sup>nd</sup> brachial arches. No vertebral anomalies were detected.

To our knowledge, a case of EDS in association with Goldenhar syndrome has never been reported. Chromosome 9 and X translocation has been reported in one case of EDS and the inversion of chromosome 9 has been shown in another case of Goldenhar syndrome [9,10]. Chromosome study was done in our patient and revealed normal karyotype. Therefore, these two syndromes in our patient likely do not have any association through chromosomal abnormality. In conclusion, we reported the case of co-incidence of Ehlers-Danlos syndrome, classic type, and Goldenhar syndrome.

## Learning point

1. Ehlers-Danlos syndrome (EDS) is an inherited syndrome that causes abnormality in biosynthesis and structure of collagen type I, III, and V.
2. Goldenhar syndrome is a rare congenital anomaly in developing defect of the first and second branchial arches.
3. To our knowledge, a co-incidence of these two rare syndromes has never been reported.
4. The case of co-incidence of EDS and Goldenhar syndrome is presented in this article.

## MCQ

1. Which is (are) tissue (s) that contains type V collagen?  
a) Skin b) Bone c) Cornea d) Fetal membrane e) All of the above  
Ans. E.
2. What are the triad abnormalities of Goldenhar syndrome?  
a) Ocular, auricular and vertebral defects b) Ocular, auricular and cutaneous defects c) Ocular, cutaneous and vertebral defects d) Auricular, cardiac and vertebral defects e) Auricular, cutaneous and vertebral defects  
Ans. A.

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