CASE

A 12 year old girl presented to Refugees Health Center with low back pain and abnormality of chest form. She had an eye operation that they couldn’t describe well. On her physical examination: she was above-average height, and had disproportionately long, slender limbs with thin, weak wrists and long fingers and toes (Fig 1,2). Beside a heart murmur (systolic and diastolic, 3-4/6), she had abnormal lateral curvature of the spine (scoliosis), thoracic lordosis, protrusion (pectus carinatum) of the sternum (Figure 3,4), abnormal joint flexibility, a high-arched palate with crowded teeth and an overbite (Figure 5,6), flat feet, hammer toes. She had speech disorders resulting from symptomatic high palates and small jaws. She had a family history of consanguineous marriages (parents and first degree relatives) also she describes two family members with similar apperarence and complaints.

Question: Given the patient's complaints, history and the physical appearance, which one of the following would be the most likely diagnosis?

a) Loeys–Dietz Syndrome
b) Kashin-Beck Disease
c) Klinefelter Syndrome
d) Marfan Syndrome
e) Ehlers-Danlos Syndrome

OLGU

12 yaşındaki bir kız, bel ağrısi ve göğüs anormallığı ile Mülteci Sağlık Merkezi'ne başvurdu. İyi tarif edemediği bir göz ameliyatı geçirmiştir. Fiziksel muayenesinde: boyu ortalamanın üstündeydi ve orantısız olarak uzun ince, ince bilekler, uzun parmaklar ve ayak parmakları olan ince bacaklara sahipti (Şekil 1,2). Kalp üfürümünün (sistolik ve diyastolik, 3-4/6) yanı sıra omurganın anormal lateral eğriliği (skoloz), torasik lordozis, sternumun çıkıntısı (pectus carinatum) (Şekil 3,4), anormal eklem esnekliği, yüksek kavisli bir damak ve dişlerde bozukluk olmakla beraber (Şekil 5,6), düz tabanlık ve çekic parmakları vardı. Yüksek damaklar ve küçük çenelerden kaynaklanan semptomatik konuştma bozuklukları vardı. Akrabalık evlilikleri (ebeveynler ve birinci dereceden akrabalar) olan bir aile geçmişine sahipti ve iki aile üyesinde daha benzer görünüm ve yakınmalar tarifiyordu.

Soru: Hastanın yakınmaları, hikayesi ve fiziksel görünümüne dayanarak, en olası tanıниз aşağıdaki den hangisidir?

a) Loeys–Dietz Sendromu
b) Kashin-Beck Hastalığı
c) Klinefelter Sendromu
d) Marfan Sendromu
e) Ehlers-Danlos Sendromu

Corresponding Author / İletişim için
Assoc. Prof. Dr. Dilek Toprak
SBÜ Şişli Hamidiye Etfal Training and Research Hospital, Family Medicine Clinic, İstanbul
E-mail: dilekt66@yahoo.com
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The answer is: d) Marfan Syndrome

Marfan Syndrome is an autosomal dominant genetic disorder of the connective tissue. Many different signs and symptoms are variably associated with Marfan syndrome. The most prominent of these affects in various degrees, the skeletal, cardiovascular, and ocular systems, but all fibrous connective tissue throughout the body can be affected (1,2).

Marfan syndrome affects males and females equally, and the mutation shows no ethnic or geographical bias. Estimates indicate about 2-3 per 10,000 individuals have Marfan syndrome. Most individuals with Marfan syndrome have another affected family member. Approximately 15–30% of all cases are due to de novo genetic mutations; such spontaneous mutations occur in about one in 20,000 births (1-3).

The two primary features of Marfan syndrome are vision problems caused by a dislocated lens (ectopia lentis) in one or both eyes and an aortic aneurysm or aortic dissection. The major sign that would lead a doctor to consider an underlying condition is a dilated aorta or an aortic aneurysm. Fatigue, shortness of breath, heart palpitations, racing heartbeats, or chest pain radiating to the back, shoulder, or arm may accompany. Cold arms, hands, and feet can also be linked to Marfan syndrome because of inadequate circulation. A heart murmur,
abnormal reading on an ECG, or symptoms of angina can indicate further investigation (2,3).

Pulmonary symptoms are not a major feature of Marfan syndrome, but spontaneous pneumothorax is common. Other possible pulmonary manifestations of Marfan syndrome include sleep apnea and idiopathic obstructive lung disease (4).

Patients may have limited range of motion in the hips due to the femoral head protruding into abnormally deep hip sockets (2).

Most of the readily visible signs are associated with the skeletal system. Many individuals with Marfan syndrome grow to above-average height, and some have disproportionately long, slender limbs with thin, weak wrists and long fingers and toes. Besides affecting height and limb proportions, people with Marfan syndrome may have scoliosis, thoracic lordosis, pectus excavatum or pectus carinatum, abnormal joint flexibility, a high-arched palate with crowded teeth and an overbite, flat feet, hammer toes, stooped shoulders, and unexplained stretch marks on the skin (1,4).

The diagnosis of Marfan syndrome is based on family history and a combination of major and minor indicators of the disorder, rare in the general population, that occur in one individual. Also it can be diagnosed often based on the Ghent criteria (2-4).

There is no cure for Marfan syndrome, it is treated symptomatically. The goal of treatment is to slow the progression of aortic dilation and damage to heart valves by eliminating arrhythmias, minimizing the heart rate and minimizing blood pressure.

Management often includes the use of beta blockers such as propranolol or if not tolerated calcium channel blockers or ACE inhibitors. Surgery may be required to repair the aorta or replace a heart valve. It is recommended that hard exercise be avoided (3,4).

Regular checkups to monitor the health of the heart valves and the aorta is necessary. The goal of treatment is to slow the progression of aortic dilation and damage to heart valves by eliminating arrhythmias, minimizing the heart rate and minimizing blood pressure (1,2).

Lens dislocation in Marfan syndrome with the lens being kidney-shaped and resting against the ciliary body. Other signs and symptoms affecting the eye include increased length along an axis of the globe, myopia, corneal flatness, strabismus, exotropia and esotropia.

Due to dural ectasia, lower back pain, leg pain, abdominal pain, other neurological symptoms in the lower extremities, or headaches – symptoms which usually diminish when lying flat can occur (1,2,4). This symptom was the prime complaint of our patient.

Surgery may be needed for progressive aortic aneurysm and spinal abnormalities and ocular problems. Recurrent pneumothoraces also might require chest surgery.

Differential Diagnosis

Many other disorders can produce the same type of body characteristics as Marfan syndrome. Genetic testing and evaluating other signs and symptoms can help to differentiate them. The differential diagnosis of Marfan Syndrome from the other choices:

a) Loeys-Dietz syndrome: It is an autosomal
dominant genetic connective tissue disorder. The disorder is marked by aneurysms in the aorta, often in children. Cardiac defects and club foot may be noted at birth. Findings of hypertelorism (widely spaced eyes), bifid or split uvula, bifid uvula or cleft palate, arterial tortuosity and skin findings such as easy bruising or abnormal scars may distinguish Loys-Dietz from Marfan syndrome (1,5).

b) Kashin-Beck disease: The clinical manifestations are related to decrease in growth and multiple joint damage. The worst form of the disease starts at childhood (age 2–3 years) and may result in dwarfism. Signs of symmetrical severe articular deformities caused by primary epiphyseal destruction are followed by severe cartilage destruction resulting in restriction of movements and metaphyseal enlargement. The distal joints of the upper and lower limbs are most often and most severely affected. Frequently involved joints are the ankle-, wrist-, knee- and elbow joint. Patients experience arthritic pain, morning stiffness, shortened fingers, deformed and/or enlarged joints, with limited motion in the extremities (2,6).

c) Klinefelter syndrome: In XXY (Klinefelter) syndrome no associated lens dislocation or aortic aneurysm. Mental deficiency and hypogonadism accompanied the clinic. Also karyotype reveals extra X chromosome in Klinefelter syndrome (4,7)

e) Ehlers–Danlos syndrome (EDS): EDS is caused by a defect in the structure, production, or processing of collagen or proteins that interact with collagen. In EDS Joint hypermobility more common presentation. Type IV variety, which most commonly affects the aorta, is characterised by thin skin and bleeding disorders with increased bruising. Differential diagnosis can be done by Skin biopsy for abnormal collagen and DNA testing for gene mutation (8).

In Marfan syndrome, the joints are very mobile and similar cardiovascular complications occur. People with EDS tend to have a "Marfanoid" appearance (e.g., tall, skinny, long arms and legs, "spidery" fingers). However, physical appearance and features in several types of Ehlers-Danlos Syndrome also have characteristics including short stature, large eyes, and the appearance of a small mouth and chin, due to a small palate. The palate can have a high arch, causing dental crowding. Blood vessels can sometimes be easily seen through translucent skin, especially on the chest (1,8).

Besides thin skin with visible veins; easy bruising; small joint laxity; rupture of hollow organs as well as medium- and large-size arteries, skin biopsy for abnormal collagen and DNA testing for gene mutation can be used for differentiating these diseases (1,2,4,8).

References