Marfan Syndrome

What is Marfan syndrome?

Marfan syndrome is an inherited condition that affects the strength of connective tissues in the body. These tissues provide the framework that holds the body together and play an important role in growth and development. Because connective tissue is found throughout the body, patients with Marfan syndrome have problems with a number of systems including bones, joints, eyes, heart, blood vessels, nervous system, skin, and lungs.

Marfan syndrome affects both sexes and all ethnic groups. About 1 in 5000 people are born with the disorder, and an estimated 200,000 individuals in the United States are currently diagnosed with it.

What causes Marfan syndrome?

It is caused by a mutation in the gene FBN1 that creates problems in a protein called fibrillin-1. Fibrillin-1 is an essential component of connective tissue. Three out of every four people with Marfan syndrome inherit the disorder from a parent with the disease. One out of four have a spontaneous mutation in the gene — meaning neither parent has Marfan syndrome.

How is Marfan syndrome inherited?

It is an autosomal dominant condition. This type of inheritance means each new child of an affected parent has a fifty percent chance of inheriting the disease. Spontaneous mutations in the FBN1 gene account for approximately 25% of cases. The likelihood of such a mutation is quite uncommon, occurring in about 1 of 20,000 births.

What are the clinical features of Marfan syndrome, and how is it diagnosed?

The diagnosis of Marfan syndrome remains a clinical one. There is a wide range of variability in the manifestations of the disease within and among families. Also, many individuals without the syndrome have one or more clinical features that may suggest that they may have Marfan syndrome, which can be the reason for a referral to be worked up for Marfan syndrome. Such common features include tall and thin stature, heart murmurs, or eye problems. A person is diagnosed with Marfan syndrome when they have a number of the clinical signs of this disease.

Is there a genetic test for Marfan syndrome?

There is genetic testing for the mutation in the fibrillin-1 gene, FBN1. The results of the testing are not always straightforward. If a person undergoes genetic testing, he or she would work with a genetic counselor to understand the results.

What are the ocular features of Marfan syndrome?

Most people with Marfan syndrome suffer from nearsightedness, or myopia, and abnormal curvature of the eye, or astigmatism. These can be notably high since the connective tissue defect can affect the cornea, lens, and growth of the eye. Other signs and symptoms include ectopia lentis (see below), corneal thinning, flattened corneal curvature, cataracts, glaucoma, strabismus, and retinal detachment.

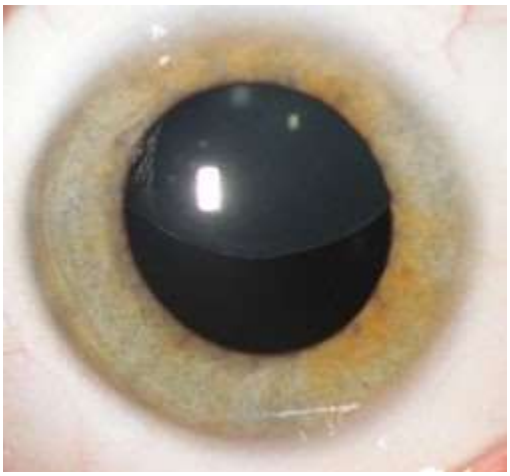

Fig. 1: Subluxated lens (ectopia lentis).

What is ectopia lentis?

Ectopia lentis is a shift in the location of the lens inside the eye (i.e., lens subluxation). The lens moves from its normal location in the eye so that the person is not looking through the center of their lens. It can be progressive such that the person may be looking through the edge of the lens or through an area where there is no lens as time goes on. This dislocation is caused by weakness in the connective tissue that holds the lens in place (zonules). Ectopia lentis occurs in roughly 60% of individuals with Marfan syndrome and is one of the major criteria for the clinical diagnosis of this condition [See figures 1 and 2]. If a person does not have dislocated lenses, though, it does not mean that they do not have Marfan syndrome.

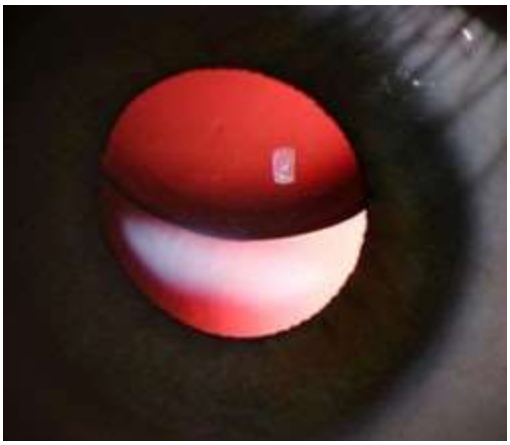

Fig. 2: Same lens as Fig. 1 with retroillumination (a different kind of lighting).

How does Marfan syndrome affect the heart and blood vessels?

Many of the symptoms of Marfan syndrome are striking, but the most serious problems associated with the Marfan syndrome involve the heart and blood vessels. There can be problems with one of the valves in the heart called the mitral valve. The valve leaflets are too large and can bow in the wrong direction. This is called mitral valve prolapse (MVP). In individuals with MVP, the mitral valve makes a click as it moves backward, which is a sound that can be detected with a stethoscope when a doctor listens to the heart. In about ⅓ of people with MVP, blood leaks backward through the valve (mitral valve regurgitation), producing a heart murmur that can also be heard through a stethoscope. A few individuals with mitral regurgitation develop symptoms like breathlessness, an irregular pulse (causing palpitations), or extreme tiredness.

A second problem can occur with the aorta (the major blood vessel coming off of the heart). Some enlargement of the aortic root is found in nearly everyone with Marfan syndrome. A substantial (about two inches) dilatation of the aorta (i.e., an aneurysm) can result in two things: an abnormal backflow of blood into the heart (aortic regurgitation) or a tear in the middle layer of the aorta (dissection). Dissecting aortic aneurysms are the most frequent cause of death in persons with Marfan syndrome.

How does Marfan syndrome affect the skeletal system?

Most patients are evaluated for Marfan syndrome because of their skeletal manifestations. A person with the disorder will usually be tall, thin, and loose jointed. Frequent signs of the disease include long, slender fingers and toes (arachnodactyly) and flat arches (pes planus). Curvature of the spine (scoliosis and kyphosis) and protrusion or indentations of the breastbone (pectus carinatum and excavatum) are also common problems. The roof of the mouth (palate) may be highly arched, causing dental crowding, and the face may seem narrow and elongated. Persons with Marfan syndrome may also demonstrate an arm-span-to-height ratio greater than 1.05.

How does Marfan syndrome affect the skin?

Marfan syndrome may lead to striae, or bands of thin wrinkled skin. Initially, they appear red, but they can become purple and white. They tend to appear in areas prone to stress — such as the shoulders, hips, and lower back.

How does Marfan syndrome affect the lungs?

Decreased flexibility in the air sacs of the lungs can be detected in nearly everybody with the disease, but mostly it does not pose a serious problem. One out of twenty people diagnosed with the condition experience the feeling of breathlessness or chest pain as a direct result of the spontaneous collapse of the lung (spontaneous pneumothorax). Some people with Marfan syndrome also suffer from sleep disorder due to abnormal breathing.

Is Marfan syndrome curable?

There is no cure for Marfan syndrome at this time. However, with early detection and awareness, we can improve the quality of life and life expectancy of a person with Marfan syndrome.

What is the prognosis for persons with Marfan syndrome?

Individuals with Marfan syndrome can develop severe orthopedic, cardiovascular, and ocular challenges, but medical and surgical advancements have increased the life span of people with Marfan syndrome dramatically over the last two decades. In 1972 the average life expectancy was about 45 years, now the average life expectancy is about 70 years.

How should Marfan syndrome patients be monitored?

- Annual echocardiograms and regular follow-up with a cardiologist to monitor the heart
- Initial comprehensive eye exam with regular ophthalmologic follow up, particularly paying attention to the status of the lens, refractive errors, and retinal health
- Careful monitoring of the skeletal system
- Lifestyle adjustments: avoidance of strenuous activities and contact sports

What cardiovascular treatments are used for Marfan syndrome patients?

The use of beta-blocker agents, medications used to prevent progressive enlargement of the aorta and treat high blood pressure, have become an essential aspect of cardiovascular management. Individuals with Marfan syndrome are advised to refrain from heavy lifting and forceful activity. In the case of aortic regurgitation or significant dilation of the aortic root, surgical repair may become necessary.

What skeletal treatments are used for Marfan syndrome patients?

A back brace is often recommended for children with moderate scoliosis (between 20º– 40º). If the curve becomes severe (> 40º), surgery is usually considered to prevent further complications. The sole treatment for pectus excavatum or carinatum is surgery. Management for pes planus is not ordinarily required, but special cushions, inserts, or orthotics may help. Wearing comfortable shoes is also recommended.

What ocular treatments are used for Marfan syndrome patients?

Comprehensive ophthalmologic care is necessary to achieve the best possible vision in people with Marfan syndrome. Patients with subluxated lenses are treated with glasses or contact lenses whenever possible. If the visual acuity cannot be improved with these options, surgery may be necessary to optimize vision. Individuals with cataracts require lens extraction with or without placement of an intraocular lens. Glaucoma may require treatment with medications or surgery. If there is a retinal detachment, surgery will be required to fix the problem.

When should the dislocated lens be removed in Marfan syndrome patients?

Removal of clear, dislocated lenses in children remains a difficult decision to make. There is a general consensus that they should be removed if they are interfering significantly with vision by causing large degrees of astigmatism that cannot be corrected with glasses or contact lenses. Lens extraction in children with Marfan syndrome, however, does have an increased risk of complications during and after surgery, including retinal detachment.

Where can I find more information about Marfan syndrome?

Please visit the National Marfan Foundation website. A large number of frequently asked questions have been answered by experts in the field, and there are links to resources for parents and children. They also host an annual conference.

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