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Review

Marfan syndrome: An eyesight of syndrome☆

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ABSTRACT

Marfan syndrome (MFS), a relatively common autosomal dominant hereditary disorder of connective tissue with prominent manifestations in the skeletal, ocular, and cardiovascular systems, is caused by mutations in the glycoprotein gene fibrillin-1 (FBN1). Aortic root dilation and mitral valve prolapse are the main presentations among the cardiovascular malformations of MFS. The revised Ghent diagnostics nosology of Marfan syndrome is established in accordance with a combination of major and minor clinical manifestations in various organ systems and the family history. The pathogenesis of Marfan syndrome has not been fully elucidated. However, fibrillin-1 gene mutations are believed to exert a dominant negative effect. The treatment includes prophylactic β-blockers and angiotensin II-receptor blockers in order to slow down the dilation of the ascending aorta and prophylactic aortic surgery. Importantly, β-blocker therapy may reduce TGF-β activation, which has been recognized as a contributory factor in MFS. The identification of a mutation allows for early diagnosis, prognosis, genetic counseling, preventive management of carriers and reassurance for unaffected relatives. The importance of knowing in advance the location of the putative family mutation is highlighted by its straightforward application to prenatal and postnatal screening. The present article aims to provide an overview of this rare hereditary disorder.

Contents

Abbreviation: MFS, Marfan syndrome; TGF-β, Transforming growth factor; FBN1, Fibrillin-1 gene; AT1R, Angiotensin II type 1 receptor.

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Introduction

In 1896 Antoine Marfan (French pediatrician) first described the Marfan syndrome (MFS) in a five and half-year-old girl (Van de Velde et al., 2006). MFS (OMIM #154700) is an inherited, autosomal dominant disorder with a high degree of clinical variability that affects many parts of the body like skeletal, ocular and cardiovascular systems etc. (Haneline and Lewkovich, 2007). MFS affects males and females equally and the mutation shows no ethnic or geographical or gender bias. Flo Hyman (Olympic silver medalist in Women's Volleyball 1984), Jonathan Larson (author and composer of *Rent*), Vincent Schiavelli (an actor and spokesperson for the National Marfan Foundation), Niccolò Paganini and Robert Johnson (Musicians and composers) and former American President Abraham Lincoln manifested several key clinical features of MFS (science.jrank.org., 2010; www.marfan.org., 2010). The estimated prevalence of the disease ranges from 1 in 5000 to 1 in 10,000 live newborns (Faivre et al., 2007; Pearson et al., 2008). Myopia is the most common ocular feature and the displacement of the lens from the center of the pupil observed in approximately 60% of affected individuals. People with MFS are at increased risk for retinal detachment, glaucoma, and early cataract formation (Ahram et al., 2009). The skeletal system involvement is characterized by bone overgrowth and joint laxity. The extremities are disproportionately long for the size of the trunk (dolichostenomelia). Approximately 25% of MFS patients have cutaneous features and no craniofacial dysmorphology. The major sources of morbidity and early mortality in the MFS relate to the cardiovascular system. Cardiovascular manifestations include dilatation of the aorta at the level of the sinuses of Valsalva, a predisposition for aortic tear and rupture, mitral valve prolapse (MVP) with or without regurgitation, tricuspid valve prolapse (TVP) and enlargement of the proximal pulmonary artery (Geva et al., 1987). Pregnancy can be dangerous for women with MFS, especially if the aortic root exceeds 4.0 cm. Complications include rapid progression of aortic root enlargement and aortic dissection or rupture during pregnancy, delivery and the postpartum period (Silverman et al., 1995). In this manuscript, we are discussing the molecular pathogenesis, genetics, diagnosis as well as the current therapeutic strategy of the disease.

Genetic insight of the disease

The gene linked to the MFS disease was first identified by Francesco Ramirez at the Mount Sinai Medical Center in New York City in 1991 (Brown, 2008). The majority of cases of MFS (MFS1) are caused