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Marfan Ailment

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Introduction

Marfan syndrome is a connective tissue abnormality that leads to various system diseases, such as enlargement of the long bones and problems with the skin, heart, and eyes [1]. The condition is either caused by a novel mutation or an inherited mutation of the fibrillin-1 gene (FBN1). Both mutations are phenotypically identical [2]. The heritable variant is inherited by an autosomal dominant pattern, which means that the disease can be caused by a single copy of the defective gene [3,4]. People who don't have a positive family history of the condition can nonetheless get the disease from de novo mutations. 25% of Marfan syndrome cases are believed to be caused by a novel mutation in the FBN1 gene, although these cases are less common than those with inherited mutations [5,6]. The prevalence of Marfan syndrome varies from 1 in 5000 to 1 in 10,000; there is no discernible racial, ethnic, or gender preference [7].

Features of Phenotypic

Tall stature with long, slender arms and legs are common skeletal anomalies linked to Marfan syndrome. Two further distinguishing phenotypic characteristics are arachnodactyly [8]. An elongated, narrow face, an arched palate, overcrowding in the teeth, scoliosis, and hyperflexibility are common characteristic features of this disorder [9]. Myopia is the most frequent ocular disease associated with Marfan syndrome, and roughly 60% of affected individuals have ectopia lentis, or lens displacement from the pupil's center [10]. Additionally, there is a higher chance of retinal detachment, glaucoma, and early cataract development in those who have this illness [11].

The heart, eyes, blood vessels, and skeleton are the primary areas affected by MFS. Individuals diagnosed with MFS typically have a stature characterized by elevated height and a slender physique,

accompanied by abnormally elongated limbs, digits, and extremities. Marfan syndrome can result in varying degrees of damage, ranging from minor to severe [12].

Although the majority of individuals with MFS inherit the condition from a parent, 25% of patients acquire the disease due to a spontaneous mutation in the gene (FBN1) responsible for producing the connective tissue protein fibrillin-1 [13]. Fibrillin-1 is a predominant component of elastic fibers and functions as a matrix glycoprotein. Less than 10% of patients exhibit the classic symptoms, most likely because of either a complete deletion of the gene or a change in its regulation [14].

The etiology of aortic dilatation in MFS is a complex phenomenon. Fibrillin-1 serves as a controller of TGF-beta availability, resulting in the occurrence of inflammation, fibrosis, and the activation of specifically MMP-2, various matrix metalloproteinases (MMPs), and MMP-9 [15]. The weakening of the aortic wall is caused by an elevated release of matrix metalloproteinases (MMP), cytokines, chemokines, prostaglandin derivatives, and fragments resulting from the destruction of elastic fibers [16]. The combination of these variables, along with a decrease in collagen, diminishes the structural strength of the aorta and results in the expansion of an aneurysm. Preliminary investigations conducted on a mouse model of MFS have demonstrated this process [17]. In comparison, mutant mice that received propranolol treatment showed just a modest decrease in the rate of aortic root dilation [18].

Individuals diagnosed with MFS have hyperplasia of the long bones and increased laxity in their joints. Some individuals experience decreased joint mobility, specifically in the elbow and fingers. Individuals diagnosed with Marfan syndrome exhibit greater height compared to the average population [19]. They exhibit dolichostenomelia, which refers to the condition of having extremities that are excessively lengthy in relation to the length of the trunk [20].

MFS is a genetic condition of the connective tissue that is inherited in an autosomal dominant manner. It is characterized by severe symptoms in the skeletal, ophthalmic, and cardiovascular systems, which tend to worsen as a person ages [21]. It also shows significant heterogeneity in its presentation within families and between different families. Gonad mosaicism, a rare occurrence, can lead to the birth of many affected kids. Although uncommon, documented cases of gonad mosaicism exist [22]. FBN1 missense mutations, insertions, and deletions, as well as variants that cause loss of expression from one allele, are responsible for MFS [23].

The Berlin diagnostic criteria of 1988 were amended and formalized as the Ghent nosology in 1996 to improve the consistency and prognostic value of diagnosing MFS. By utilizing nosology, it is possible to determine which individuals with a physique resembling Marfan syndrome are prone to cardiovascular complications. These individuals require consistent monitoring and preventative medical and surgical interventions [24].

It is produced as a precursor weighing 375 kD, which undergoes processing and is then released into the extracellular matrix (ECM). The majority of fibrillin-1 mutations are missense, indicating a dominant-negative impact on the synthesis of microfibrils. Ectopia lentis is often linked to missense mutations that result in cysteine substitutions within the epidermal growth factor–like domains of the protein [25].

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