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Marfan Syndrome

Description of the Mutation:

Marfan syndrome is a disorder that impacts the connective tissue of the body. This disorder is a consequence from a mutation in the fibrillin-1 gene, also known as FBN1 gene. The mutations that occur within the FBN1 gene have to do with single nucleotide deletions. In a study conducted on 26 Marfan syndrome patients, it was found that most of the patients with severe Marfan syndrome symptoms had in-frame deletions of the FBN1 gene within the exons 30-56. Furthermore, patients with deletions in exon 6 displayed mild Marfan syndrome symptoms (Jiacheng et al. 2017). Thus, this information suggests that there are different phenotypes that can be expressed depending on where the deletion is made on the FBN1 gene. Additionally, it is noticed that the in-frame deletions located in the middle of the FBN1 gene display more severe symptoms in Marfan syndrome patients than the deletions located on the terminal ends of the gene. Adding on, in a study conducted on a pregnant woman who died from Marfan syndrome, it was found that her autopsy revealed that she had developed aortic dissection from Marfan syndrome and that she had a single base deletion of exon 39 in her FBN1 gene (Aquila et al. 2020). This information supports that haploinsufficiency of the FBN1 gene is a prevalent form of identifying that an individual has Marfan syndrome, but also the severity of these single nucleotide deletions within the gene.

Discussion of the Transmission:

Marfan syndrome is autosomal dominant and can be inherited from a single parent or both parents that have the disorder. In Marfan syndrome, the abnormal gene is considered to be

more dominant than the normal gene. Thus, this means that there can be a fifty percent chance of a parent with Marfan syndrome to pass this genetic disorder to their children. In a case involving a child that was born with Marfan syndrome, it was reported that his father, his grandfather from his father's side, his two sisters, and his two brothers were diagnosed with the Marfan syndrome disorder. The child's grandfather died from aortic dissection, while his father and his siblings also displayed common symptoms of the disorder such as a weakened aorta and changes in vision. It was reported that there was a mutation in exon 63 for each of these family members diagnosed with the disorder (Mastromoro et. al 2020). In this case, it is shown how a single parent, who also inherited the disorder from his father, is dominant because the abnormal gene was able to transmit the Marfan syndrome disorder to over fifty percent of their children, including the same kind of mutation and phenotypes that were being expressed. In another case involving a child affected by Marfan syndrome, it was reported that the child's mother displayed common phenotypes of the disorder and the child died after four months due to heart failure, which is a common symptom of Marfan syndrome. Their analysis displayed an inherited FBN1 mutation on exon 49 of both of their genes (Laurianne et. al 2016). This report demonstrates that most cases that involve the transmission of Marfan syndrome are usually neonatal, which would explain why there is the inheritance of the same exact mutation between the parent and the child. The transmission of this disorder can be extremely severe because of its dominance in affecting the connective tissues of the body, which would explain why in many cases the newborn child does not live for long.

Symptoms:

The symptoms of Marfan syndrome vary depending on the person, but also depending on what area throughout the body they are experiencing problems with their connective tissue. Some individuals experience mild symptoms that are hardly noticeable, while others experience more severe symptoms that can be detrimental or deadly. In a case of an adolescent with

Marfan syndrome, the adolescent has the severe conditions of scoliosis, ectopia lens, and weakened aorta. Based on her physical examination, she has a tall stature with fingers and toes that are much longer than normal (Delk et. al 2023). These symptoms presume that the adolescent is experiencing issues with the connective tissues in her spinal area, the walls of her aorta, and in her lens. These symptoms are considered to be severe because they may develop into other issues that are fatal if her aorta ruptures. Her physical examination reveals that she may have been transmitted of this disorder during her neonatal period. The mild symptoms of Marfan syndrome include a headache, loose joints, a blurry vision, abdominal pain, and longer than normal fingers, toes, hands, and legs (Handisides et. al 2019). These symptoms are less severe and would make it difficult to distinguish if a person had Marfan syndrome, besides the most common symptom of having long fingers, toes, and legs. Thus, all symptoms of Marfan syndrome involve an impact on the connective tissue, which supports everything that needs to function in our body.

Epidemiology:

Marfan syndrome is a rare condition that develops during the prenatal period, however, its distinctive characteristics are sometimes not noticed until the infant reaches their teenage or adult years. This genetic disorder occurs in 1 in 5,000 individuals and it occurs equally in both males and females (Pyeritz 2019). Therefore, since the condition occurs equally in both sexes, it also occurs equally in all racial groups and the condition can only be passed onto the child if either one of its parents is a carrier or actually has the disorder. In the first studies done on Marfan syndrome, it was expected that an individual with this disorder would not make it past the prenatal period with severe symptoms and the age of 32 with mild symptoms. Today, individuals with this disorder have managed to double this theory with the appropriate treatments and depending on where the disorder is located in the body (Pyeritz 2019). Thus, the individuals with more severe symptoms, such as a disruptive aorta, are more prone to being a

part of the individuals who do not live for long. As previously stated, Marfan syndrome is found to affect the connective tissues throughout the body, however, the abnormalities are more prevalent in the cardiovascular area and the spine. Most individuals with Marfan syndrome develop an aortic disease, cardiac valve disease, and scoliosis (Andersen et. al 2022). Therefore, Marfan syndrome most commonly affects the areas that can be detrimental to an individual if not treated properly or paid attention to. Although it is a rare condition, it is still a condition that can be extremely fatal if severe symptoms are developed.

Screening:

To determine whether an individual has Marfan syndrome or is a carrier for the disorder, it is common to have a genetic screening test performed by a doctor. The most accurate way to receive information on a person with Marfan syndrome is to do the Sanger test, the next generation test, and then the multiplex ligation-dependent probe test (Orphanet 2020). The Sanger sequencing test focuses on the nucleotide sequence of DNA to test for any heritable mutations. The next generation sequencing test focuses on the sequencing of both DNA and RNA to detect mutations. The multiplex ligation-dependent probe amplification test allows for the screening of mutations in the fibrillin-1 gene and it is more commonly done on individuals who have received unclear information from the sanger and the next generation sequencing tests (Orphanet 2020). Thus, these genetic tests are more commonly performed on adults that have already developed symptoms of Marfan syndrome. To determine if a fetus is at risk for Marfan syndrome or if they already have the syndrome due to their family history, an echocardiogram is performed to analyze their heart and its different structures while it is beating. An echocardiogram is the only form of testing the fetus for Marfan syndrome, but it is also the most appropriate because it is a noninvasive procedure. (Richer et.al 2016). Since the echocardiogram is more commonly used to detect abnormalities in the heart, it would specifically focus on whether the fetus has developed aortopathy, a severe symptom of Marfan

syndrome. Thus, there are no other procedures that are usually performed on the fetus to test for Marfan syndrome because it can lead to harmful defects.

Treatment:

A cure for Marfan syndrome does not exist, however, individuals with Marfan syndrome are able to form a treatment plan that can help reduce the symptoms or prevent other severe symptoms from developing. For individuals that have aortopathy, a severe symptom of Marfan syndrome that can be fatal, it is more common to do an open heart surgery to prevent aortic rupture. After the surgery, there are follow ups that are set to occur annually (Nicholls 2017). Thus, these follow ups allow for the doctors to determine how much the symptoms have been reduced, but also if the individual is at risk for other symptoms. The individuals that refuse the cardiac surgery for the treatment of aortopathy, usually use medications. The medications used do not guarantee the symptoms will reduce as much as they would with open heart surgery. However, it has been found that medications with beta blockers and angiotensin receptor blockers are significant in reducing the symptoms of aortopathy. There are also other medications that can be taken to relieve pain or to reduce inflammation (Bhatt 2015). Therefore, these medications reduce the temporary stress that is placed on the heart to prevent aortic rupture. For the individuals with minor symptoms of Marfan syndrome, it is recommended that they perform lifestyle changes that are beneficial to their health. These lifestyle changes could include moderate physical exercise and a healthier diet with less grease. To strengthen the muscles, it is common for individuals with Marfan syndrome to also utilize physical therapy (Stachurska 2017). Thus, a treatment plan for Marfan syndrome allows the individuals with the disorder to successfully restrain the severities to be able to live comfortably.

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