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Case Report

Marfan Syndrome in Mid-Adulthood: A Detailed Case Report of a 47-Year-Old Female Patient

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ABSTRACT

Marfan syndrome is a hereditary connective tissue disorder with an autosomal dominant inheritance pattern, affecting the cardiovascular system, eyes, and musculoskeletal structure. While often diagnosed in childhood, late diagnosis, especially in middle-aged individuals, can complicate prognosis and treatment, leading to serious health issues. We present the case of a 47-year-old female with Marfan syndrome, who initially presented with complaints of chest pain, shortness of breath, and joint laxity. Physical examination revealed features characteristic of Marfan syndrome, including tall stature, arachnodactyly, and scoliosis. Echocardiography showed severe aortic root dilation and mitral valve prolapse, requiring immediate medical attention. Despite intensive treatment aimed at stabilizing her cardiovascular status, the patient's condition progressively deteriorated. Complications, including acute aortic dissection, were noted, which ultimately led to her demise during treatment. This case underscores the challenges in diagnosing and treating Marfan syndrome, particularly regarding cardiovascular issues, when identified late. The patient's delayed presentation led to more severe disease progression, limiting intervention effectiveness. To reduce the risk of life-threatening complications like aortic dissection, routine screening and early treatment for individuals with Marfan syndrome are crucial. The late diagnosis of Marfan syndrome in middle-aged individuals poses considerable risks, particularly concerning cardiovascular issues. This case underscores the critical necessity for early identification of the condition and emphasizes the importance of proactive cardiovascular surveillance, which can enhance patient outcomes and diminish the likelihood of mortality among those affected.

Keywords: Marfan syndrome, Aortic dissection, Cardiovascular complications, Late diagnosis, Connective tissue disorder, Mitral Valve Prolapse.

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INTRODUCTION

Marfan syndrome is a genetic disorder inherited in an autosomal dominant manner, primarily impacting connective tissue. This condition is predominantly marked by a range of abnormalities that influence the musculoskeletal system, cardiovascular system, and ocular structures.[1,2] The occurrence of Marfan syndrome is estimated to be around 1 in every 5,000 individuals, with approximately 26% of affected cases lacking any familial history of the condition. Diagnosis primarily relies on the Ghent criteria alongside a comprehensive clinical evaluation. Despite advancements in early diagnosis and improved medical and surgical interventions that have extended the median life expectancy from 40 to around 70 years, individuals affected by Marfan syndrome still experience significant morbidity.[3,4] Abnormalities in Fibrillin-1, a crucial Extracellular Matrix (ECM) protein that forms microfibrils, lead to significant alterations in ECM structure and disrupt the balance of matrix homeostasis. This disruption is responsible for the diverse clinical presentations associated with Marfan syndrome, which can affect various systems, including ocular, musculoskeletal, and, most critically, the cardiovascular system. While the most prominent clinical features observed during examinations typically include lens subluxation and musculoskeletal deformities such as arachnodactyly, the long-term outlook for patients is predominantly influenced by cardiovascular complications.[5]

Individuals affected by underlying systemic disorders frequently lack awareness of their condition, which can result in unexpected and severe health complications during adulthood, particularly those related to cardiovascular issues.[6] The enlargement of the aortic root may result in congestive heart failure. In contrast, aortic aneurysms pose a significant risk of rupture, representing the leading cause of mortality among patients diagnosed with Marfan syndrome.[7] The diagnosis is often contemplated in adults exhibiting a slender physique, elongated limbs, arachnodactyly, and pectus abnormalities, with scoliosis occasionally present. Additional clinical indicators, including a high-arched palate

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accompanied by dental crowding, skin striae, and the recurrence of hernias or pneumothorax, may further heighten the suspicion.[8]

This report details the case of a 47-year-old woman recently diagnosed with Marfan syndrome, who presented with a range of significant cardiovascular issues, such as inverted T-waves, mitral valve prolapse, severe mitral regurgitation, and advanced left ventricular dysfunction. Despite receiving initial medical treatment, the patient suffered three cardiac arrest episodes, which ultimately led to her death. This case illustrates the severe cardiac complications linked to Marfan syndrome. It emphasizes the urgent necessity for careful monitoring and prompt intervention in individuals with undiagnosed or late-presenting connective tissue disorders that may lead to life-threatening cardiovascular incidents.

CASE DESCRIPTION

A 47-year-old woman was hospitalized due to primary symptoms of dyspnea, pervasive fatigue, and a burning sensation in her chest that persisted for two days. Her medical history reveals a diagnosis of hypertension and mitral valve prolapse, both of which have been present since 2010. The patient has previously been on several medications, including Sacubitril/Valsartan at a dosage of 24/26 mg taken twice daily, Bisoprolol 5 mg once daily, and a combination of Torsemide/Spironolactone at 10/50 mg once daily. Additionally, she takes Ferrous Ascorbate/Folic Acid at 100/1.5 mg, Vitamin D with Zinc in the afternoon, and Pantoprazole/Domperidone at 40/30 mg each morning. Furthermore, her surgical history is notable for the plating of the right tibia and fibula, which occurred four months before her admission.

Figure 1 shows the oral assessment of a patient with Marfan syndrome with an increased number of teeth and distinctive facial features. This condition often leads to craniofacial irregularities, such as dental overcrowding and a high-arched palate, as seen in this case.

Figures 2a and 2b typically exhibit elongated fingers and a larger palm, indicative of arachnodactyly. Their foot also shows a slender, elongated structure with hyperextended toes, reflecting the syndrome's characteristic elongated appendages.

The patient's medical history indicates a diminished appetite and irregularities in her menstrual cycles. She stands at 6 feet tall and weighs around 88 kg, resulting in a Body Mass Index (BMI) of 26.3, categorizing her as overweight. Upon physical examination, signs of pallor and esotropia in the left eye were observed. A preliminary diagnosis of Coronary Artery Disease (CAD) was established, and the initial treatment plan involved the immediate intravenous administration of Pantoprazole at a dosage of 40 mg and Ondansetron at 4 mg.

Laboratory assessments indicated several key findings: a Packed Cell Volume (PCV) of 27.2%, a Mean Corpuscular Volume (MCV) of 68.2 fL, a Mean Corpuscular Hemoglobin (MCH) of 23 pg, and a Mean Corpuscular Hemoglobin Concentration (MCHC) of 33.8 g/dL. The hemoglobin concentration was measured at 9.2 g/dL, while the white blood cell count stood at 11,300 cells per cumm. Additionally, the chloride level was recorded at 107 mEq/L, with NT-Pro BNP at 13,364 pg/mL and high-sensitivity Troponin at 1071 pg/mL. An electrocardiogram demonstrated sinus tachycardia, the presence of an abnormal Q-wave, an inverted T-wave, trigeminy of premature ventricular contractions, and a prolonged QT interval. Furthermore, a two-dimensional echocardiogram revealed a dilated aorta accompanied by moderate aortic regurgitation, mitral valve prolapse, severe mitral regurgitation, moderate tricuspid regurgitation, and Pulmonary Arterial Hypertension (PAH), with a Right Ventricular Systolic Pressure (RVSP) measured at 60 mmHg.

The conclusive diagnosis identified was Mitral Valve Prolapse (MVP) accompanied by severe mitral regurgitation, mild dysfunction of the left ventricle, severe Pulmonary Arterial Hypertension (PAH), and the presence of Marfan syndrome. The therapeutic regimen comprised intravenous administration of Furosemide at a dosage of 20 mg, Pantoprazole at 40 mg, Fondaparinux sodium subcutaneously at 2.5 mg, and Cefoperazone/Sulbactam at 1.5 g. Additionally, oral medications included Rosuvastatin/Aspirin at 10/75 mg, Metoprolol at 12.5 mg, and Eplerenone at 25 mg. A STAT intravenous infusion of Sodium Bicarbonate at 100 mL was also administered, alongside a Noradrenaline infusion at a rate of 20 mL/hr, a Dopamine infusion (comprising 1 amp and 45 mL of normal saline) at 5 mL/hr, and a Nitroglycerine infusion at 1.5 mL/hr. On the 5th day of her hospital stay, the patient experienced shortness of breath, with a respiratory rate recorded at 25 breaths per minute. This was subsequently followed by two episodes of cardiac arrest during the night, necessitating Cardiopulmonary Resuscitation (CPR). Laboratory results indicated a serum creatinine level of 2.5 g/dL, while her blood pressure was critically low at 93/36 mmHg, and her haemoglobin level had decreased to 6.9 g/dL. Additionally, her blood pH was measured at 6.93, with a Pa. CO_2 of 27 mmHg and Serum Bicarbonate levels at 6.6 mEq/L. On the morning of the sixth day, the patient suffered another cardiac arrest, again requiring CPR, after which she became unconscious. At this point, her blood pressure, pulse rate, and oxygen saturation levels were unreportable. Alarmingly, her serum creatinine level surged to a dangerous 13 mg/dL, ultimately leading to her demise due to acute kidney injury, compounded by metabolic acidosis and cardiorenal syndrome.

DISCUSSION

Marfan syndrome is a genetic disorder characterized by a range of systemic effects that significantly impact both the physical appearance and overall quality of life of individuals affected by the condition. The limitations imposed by reduced physical

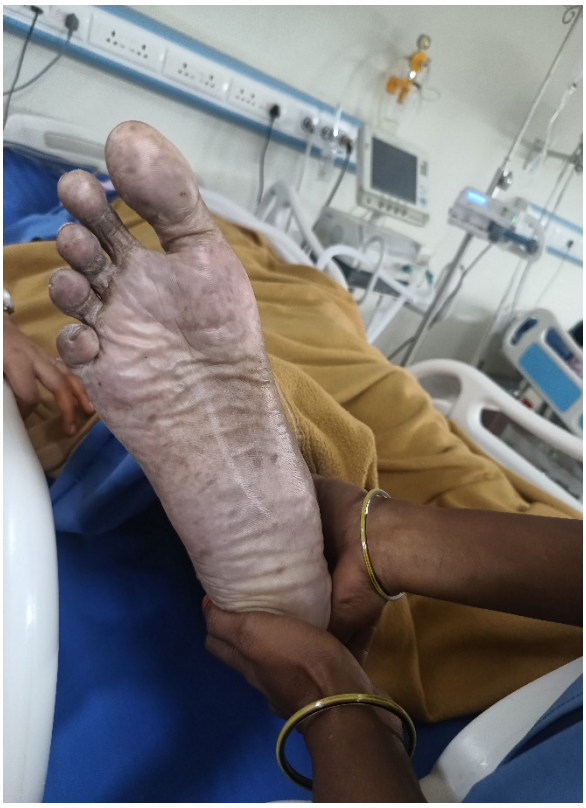

Figure 1: The oral assessment of a patient with Marfan syndrome with an increased number of teeth and distinctive facial features. This condition often leads to craniofacial irregularities, such as dental overcrowding and a high-arched palate, as seen in this case.

Figure 2a, 2b: Typically exhibit elongated fingers and a larger palm, indicative of arachnodactyly. Their foot also shows a slender, elongated structure with hyperextended toes, reflecting the syndrome's characteristic elongated appendages.

capabilities and aesthetic concerns can restrict life opportunities for these patients, often resulting in feelings of frustration and diminished self-worth. Oral manifestations commonly observed in these individuals include maxillary constriction, dental crowding, and cross-bites, which frequently prompt patients to seek aesthetic interventions.[9] Additionally, these cases may present with a high-arched palate that is linked to a narrow nasal airway, leading to compensatory mouth breathing. This alteration in breathing patterns can affect natural head posture, contributing to the development of adenoid facies. Furthermore, increased resistance in the nasal airway heightens the risk of obstructive sleep apnea, further complicating the health challenges faced by those with Marfan syndrome.[10]

Cardiovascular complications represent the most critical challenges associated with Marfan syndrome, significantly influencing both prognosis and survival rates. These complications encompass a range of abnormalities, including dilation of the aortic root, aortic regurgitation, aortic dissection, and the formation of aortic aneurysms, with the ascending aorta being the most frequently affected area, although the descending aorta may also be involved. In the case of our patient, mild mitral regurgitation and tricuspid regurgitation were observed.[11]

The establishment of a diagnosis necessitates a thorough clinical assessment, supported by defined diagnostic criteria. The Ghent criteria incorporate elements such as family and genetic history, the involvement of various organ systems-primarily the skeletal, cardiovascular, and ocular systems-and the classification of clinical signs as either major or minor.[12] Major criteria are distinctive to Marfan syndrome and are infrequently observed in the general population. According to these established criteria, a diagnosis of Marfan syndrome is confirmed in a patient with a clear family history when there is significant involvement of one organ system (skeletal, cardiovascular, or ocular) alongside the involvement of a second organ system. Conversely, in cases where the patient lacks a first-degree relative with a definitive diagnosis of Marfan syndrome, the presence of major criteria in at least two distinct organ systems, along with the involvement of a third system (skeletal, cardiovascular, or ocular), is required for a diagnosis of Marfan syndrome.[13]

The clinical observations in this case report correspond with established complications associated with Marfan syndrome, notably its link to Mitral Valve Prolapse (MVP) and pronounced Mitral Regurgitation (MR), alongside Left Ventricular Dysfunction (LVD). In individuals with Marfan syndrome, MVP frequently arises from structural irregularities in the mitral valve, primarily attributed to myxomatous degeneration, which is a defining feature of MVP in disorders affecting connective tissue. Research indicates that such degeneration can result in significant MR, which adversely affects left ventricular performance and often leads to the progressive LVD noted in this patient.[14] The presence of severe LVD and MR in Marfan syndrome heightens the likelihood of sudden cardiac incidents, as the hemodynamic strain imposed by these abnormalities on the heart can contribute to the cardiac arrests experienced by this individual.

Furthermore, existing literature highlights that T-wave inversions, commonly observed in individuals with Marfan syndrome, may serve as indicators of left ventricular strain or the presence of underlying fibrosis. This observation is particularly significant as it may be associated with heightened mortality risks in patients with Marfan syndrome, especially when coupled with severe mitral valve pathology. The occurrence of T-wave inversion in this patient, in conjunction with recurrent cardiac arrests, emphasizes the aggressive nature of the disease in certain instances and its capacity to precipitate life-threatening cardiac complications. Research indicates that Marfan patients exhibiting such cardiac characteristics, particularly as they advance in age, are often at an

elevated risk for negative health outcomes, thereby underscoring the necessity for more vigilant monitoring and timely surgical interventions in the earlier phases of the disease to enhance overall prognosis.[15]

The patient's death underscores the serious cardiac complications associated with Marfan syndrome. This is particularly relevant in situations where issues like severe mitral regurgitation, mitral valve prolapse, and left ventricular dysfunction go untreated or worsen over time, potentially leading to fatal outcomes. Relating this case to the established literature, it is clear that despite the intricate genetic underpinnings of Marfan syndrome, vigilant surveillance for early signs of valvular and ventricular irregularities is essential in mitigating the risk of serious cardiac issues, as demonstrated in this instance.

Marfan syndrome is a genetic disorder with varying symptoms among individuals, even within families. It is present from birth, but many show few early symptoms, which often become more apparent with age. Lifestyle factors and complications like aortic dilation can affect this progression. A lack of significant health issues before age 47 may indicate a milder form of the syndrome. Some individuals may remain asymptomatic or undiagnosed until adulthood.[16] The onset of symptoms at 47 years may reflect natural progression or age-related changes. This variability underscores the importance of regular monitoring and timely intervention to manage potential complications, even in those with mild or no symptoms.

CONCLUSION

This case highlights the urgent need for prompt diagnosis and proactive treatment in individuals with Marfan syndrome to prevent serious cardiac issues. Due to the high risk of mitral valve prolapse, significant mitral regurgitation, and left ventricular dysfunction, a comprehensive management strategy is essential. This should include regular monitoring, appropriate medications, and timely surgeries. Early detection and intervention, such as using beta-blockers to reduce hemodynamic strain or scheduling elective mitral valve repair, are crucial for improving patient outcomes. The case emphasizes the importance of diligent follow-up and personalized treatment plans to slow disease progression and prevent severe complications, revealing significant gaps in managing undiagnosed or late-presenting Marfan syndrome.

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CONFLICT OF INTEREST

The authors affirm that there are no conflicts of interest associated with this research. Every facet of the study, encompassing data gathering, analysis, and interpretation, was carried out autonomously, free from any personal or financial affiliations that might be viewed as a potential conflict.

AUTHOR CONTRIBUTIONS

Dr. Pavan Kumar Yanamadala, Madhuri Akasapu, and Pradeepthi Bokka were key contributors to this manuscript. Dr. Pavan Kumar Yanamadala developed the conceptual framework and oversaw the case analysis, providing insights into clinical findings and treatment strategies. Madhuri Akasapu conducted extensive data gathering, performed a literature review, and drafted the manuscript to align it with relevant case literature. Pradeepthi Bokka interpreted the data, improved the manuscript's organization, and participated in critical revisions to enhance clarity and rigour. Their collaborative efforts presented a comprehensive perspective on Marfan syndrome, emphasizing the importance of early diagnosis and personalized care.

PATIENT CONSENT

In alignment with established ethical standards, informed consent was secured from the patient's family member, given that the patient was receiving intensive care throughout the treatment duration. The consent specifically permitted the utilization of the patient's clinical information and images for publication, with a commitment to uphold confidentiality and safeguard the patient's privacy in all disseminated materials.

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