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Atypical Marfan Syndrome: Diagnostic Challenges and the Importance of a Multidisciplinary Approach

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ABSTRACT

Marfan syndrome is an autosomal dominant inherited connective tissue disorder, most commonly caused by mutations in the FBN1 gene. Its clinical manifestations involve the musculoskeletal, cardiovascular, and ocular systems. We report a challenging case of Marfan syndrome with atypical features and delayed diagnosis, involving a 27-year-old male who initially presented with atypical clinical features and was later diagnosed with Marfan syndrome through genetic testing. This case highlights the diagnostic challenges, the importance of comprehensive evaluation, and the role of multidisciplinary management in preventing fatal complications such as aortic dissection.

INTRODUCTION

Marfan syndrome is a rare autosomal dominant genetic disorder caused by mutations in the *FBN1* gene, which plays a crucial role in the formation of fibrillin-1, an essential structural component of elastin found in connective tissue.[1] The prevalence of Marfan syndrome is estimated to be approximately 1:5,000–1:10,000 in the general population, with no sex predilection.[2]

The main clinical manifestations include arachnodactyly, chest wall deformities, ectopia lentis, and aortic dilatation.[1,2] This disorder primarily affects the cardiovascular, musculoskeletal, and ocular systems, resulting in a wide range of clinical manifestations.[1,3] Cardiovascular complications, particularly aortic dissection, represent the leading cause of mortality in patients with Marfan syndrome.

Diagnosis is often challenging due to the marked variability in clinical presentation. Although the classic features are well recognized, atypical cases may lead to delayed diagnosis and suboptimal management. Early recognition and timely intervention are essential to prevent severe complications. Nevertheless, the diagnosis of Marfan syndrome can be established using the revised Ghent criteria, which integrate clinical findings, imaging studies, and genetic testing.[2]

CASE

A 27-year-old man presented to the clinic with complaints of chest pain, shortness of breath, and dizziness. The patient had a family history of cardiovascular-related deaths but no prior diagnosis of Marfan syndrome.

On physical examination, he exhibited a tall stature with an arm span greater than his height. To assess this, the patient was asked to stand with both arms extended laterally in an "arm span" position, which is commonly used to compare arm span with height. In patients with Marfan syndrome, one characteristic finding is an arm span exceeding body height. The patient appeared slender with long upper extremities, consistent with a marfanoid habitus (Figure 1).

Figure 1. The patient exhibited an arm span longer than his height.

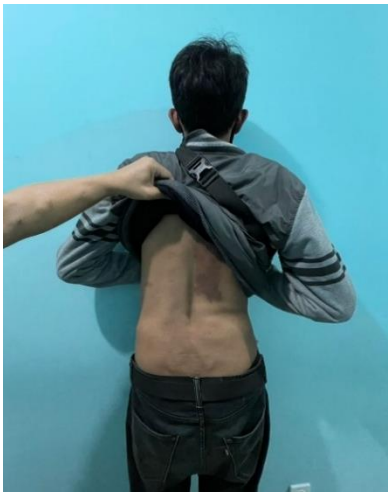


Figure 2. The patient's spine appeared prominent, indicating the presence of scoliosis.

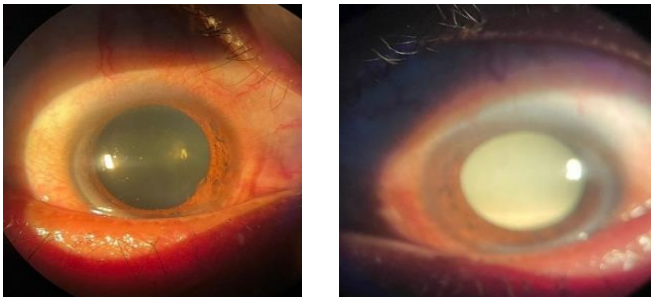
The spine appeared prominent, suggesting the presence of scoliosis, which is an abnormal curvature of the spine (Figure 2). Scoliosis or other spinal abnormalities constitute one of the major skeletal criteria in the manifestations of Marfan syndrome. Further evaluation is typically performed using radiological examination, such as spinal X-ray imaging, to assess the severity of scoliosis.

The fingers appeared long, slender, and tapering, consistent with the appearance of arachnodactyly (Figures 3 and 4). Arachnodactyly is one of the major skeletal manifestations included in the Ghent criteria for the diagnosis of Marfan syndrome. This finding reflects an underlying connective tissue abnormality that results in excessive longitudinal bone growth. However, these features are not always immediately recognized as signs of Marfan syndrome.

Figure 3. The patient's hand showing arachnodactyly (long, slender fingers).

Figure 4. The patient's hand photograph showing a positive Steinberg sign.

Ophthalmologic examination revealed evidence of ectopia lentis, or lens dislocation (Figures 5 and 6). Genetic testing identified a pathogenic mutation in the *FBN1* gene, supporting the diagnosis of Marfan syndrome.



Figures 5 and 6. The patient's eyes showing evidence of ectopia lentis (lens dislocation).

Although the presentation was not typical, further investigations confirmed systemic involvement, including joint hypermobility and mild

scoliosis. The patient's family history of premature cardiovascular death suggested an inherited predisposition, prompting genetic counseling and further family screening.

MANAGEMENT

The patient was initiated on beta-blocker therapy (atenolol) to reduce the risk of aortic dissection and to slow the progression of aortic dilatation.[4] The patient was scheduled for follow-up echocardiography and magnetic resonance imaging (MRI) every six months to detect any interval changes.

In addition to pharmacological management, the patient was advised to implement lifestyle modifications to reduce physical stress on the cardiovascular system. Education was provided regarding the restriction of strenuous physical activity and contact sports. Genetic counseling was offered to family members, and screening for potential manifestations of Marfan syndrome was recommended for relatives. Given the severity of aortic dilatation, the patient was considered for prophylactic aortic surgery.

Furthermore, physical therapy was initiated to address musculoskeletal symptoms, and the patient was closely monitored for signs of ocular complications, such as ectopia lentis or lens dislocation.

DISCUSSION

The diagnosis of Marfan syndrome can be challenging when clinical features are atypical. The majority of patients present with cardiovascular manifestations, such as aortic dilatation and an increased risk of aortic dissection, which can be life-threatening if not appropriately managed.[2] In this case, the patient's initial symptoms of chest pain and dizziness were initially attributed to other causes, resulting in a delayed diagnosis. Genetic testing plays a crucial role in confirming the diagnosis, particularly in cases with subtle or ambiguous clinical presentations.[1]

In the present case, the combination of physical characteristics—including a tall and slender habitus, long extremities (arachnodactyly), pectus excavatum, and scoliosis (Figures 1–4)—along with cardiovascular findings of aortic root dilatation provided strong evidence supporting the diagnosis of Marfan syndrome. Additionally, the presence of ectopia lentis or lens dislocation further strengthened the diagnosis (Figures 5 and 6).

Genetic analysis of *FBN1* mutations plays a significant role in confirming the diagnosis, especially in patients with subtle or borderline clinical manifestations.[1] However, in resource-limited settings, the revised Ghent criteria remain the primary standard for establishing the diagnosis.

Pharmacological therapy with beta-blockers is the standard approach to reduce the rate of aortic dilatation, while angiotensin II receptor blockers (ARBs), such as losartan, may inhibit the transforming growth factor-beta (TGF-β) pathway and provide additional benefit.[4]

Successful management of Marfan syndrome requires a multidisciplinary approach involving cardiologists, geneticists, ophthalmologists, and orthopedic specialists to monitor cardiovascular complications, ocular abnormalities (such as ectopia lentis), and skeletal deformities.[3]

Patient and family education regarding the restriction of strenuous physical activity, recognition of warning signs of aortic dissection, and the importance of regular follow-up is an integral component of long-term management.

CONCLUSION AND RECOMMENDATION

This case highlights the importance of maintaining clinical vigilance for Marfan syndrome, even in patients with minimal physical findings. Early diagnosis, appropriate pharmacological therapy, and regular monitoring can prevent life-threatening complications. Genetic testing and family screening are integral components of comprehensive management.

Patients suspected of having Marfan syndrome should undergo a thorough multidisciplinary evaluation, including cardiovascular imaging, ophthalmologic assessment, and genetic testing when available. Regular follow-up with echocardiography or advanced imaging is recommended to monitor aortic dimensions and guide timely intervention. Lifestyle modification, including avoidance of strenuous physical activity and contact sports, should be emphasized. In addition, genetic counseling and systematic screening of first-degree relatives are strongly recommended to enable early detection and preventive management.

ADVANCED RESEARCH

Further advanced research is warranted to improve early detection and risk stratification in patients with Marfan syndrome, particularly those with atypical or minimal clinical manifestations. Longitudinal studies investigating genotype–phenotype correlations of *FBN1* mutations may enhance prognostic accuracy and individualized management strategies. In addition, continued research into novel pharmacological therapies targeting molecular pathways such as transforming growth factor-beta (TGF-β) signaling may provide alternative or adjunctive treatment options to slow aortic disease progression. Advances in imaging techniques and biomarkers also hold promise for earlier identification of high-risk patients and optimization of timing for prophylactic surgical intervention.

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