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Marfan's syndrome with atrial septal defect rare clinical association

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Abstract
Marfan syndrome (MFS) is a systemic connective tissue disorder primarily caused by mutations in the *FBN1* gene, leading to widespread involvement of the cardiovascular, musculoskeletal, and ocular systems. Cardiovascular manifestations, especially aortic root dilatation and dissection, are the major contributors to morbidity and mortality. While valvular involvement such as mitral valve prolapse is relatively common, congenital heart defects like atrial septal defects (ASDs) are extremely rare in MFS and are not part of the diagnostic Ghent criteria. Limited literature exists on this association, especially in early childhood, raising questions about whether this is a coincidental finding or an underrecognized cardiac manifestation.

Keywords: Marfan syndrome, FBN1 mutation, atrial septal defect, congenital heart disease, pediatric cardiology

Introduction

Marfan syndrome (MFS) is a systemic connective tissue disorder caused by mutations in the *FBN1* gene, which encodes fibrillin-1, a glycoprotein essential for the formation of elastic fibers in connective tissue (Dietz *et al.*, 1991) [2]. This autosomal dominant condition exhibits wide phenotypic variability and affects multiple organ systems, notably the cardiovascular, skeletal, and ocular systems (Judge & Dietz, 2005) [4]. The global prevalence of Marfan syndrome is estimated at approximately 1 in 5,000 individuals, though this may be underreported due to variability in clinical expression (Loeys *et al.*, 2010).

Cardiovascular manifestations are the leading cause of morbidity and mortality in MFS and primarily involve the aortic root, with progressive aortic dilatation, aortic regurgitation, and risk of aortic dissection. Additionally, mitral valve prolapse, and less commonly, tricuspid or pulmonary valve involvement, may be present (Yetman *et al.*, 2003) [9]. However, congenital heart defects such as atrial septal defects (ASDs) are rarely reported in patients with MFS and are not part of the diagnostic criteria outlined in the revised Ghent nosology (Loeys *et al.*, 2010). The precise pathophysiological basis for such associations is unclear, but it is hypothesized that abnormal connective tissue development may occasionally impact septal formation during embryogenesis (Espínola-Zavaleta *et al.*, 2005) [3].

ASDs are one of the most common congenital cardiac anomalies in the general pediatric population, accounting for up to 10% of congenital heart disease cases (Mahony *et al.*, 1999) [6]. However, their coexistence with Marfan syndrome is extremely uncommon, and few cases have been documented in the literature. Notably, in MFS patients with ASDs, the structural fragility of the atrial wall poses significant procedural challenges, particularly if transcatheter closure is considered. For example, Loeffelbein *et al.* (2008) [5] reported atrial wall perforation following device placement in a child with Marfan syndrome, highlighting the potential complications associated with ASD intervention in this population.

Given the rarity of ASDs in MFS and their potential implications for management, early recognition through comprehensive echocardiographic evaluation is essential, especially in pediatric patients where symptoms may be absent.

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Small ASDs may be hemodynamically insignificant but still require long-term surveillance due to risks of right heart dilation, paradoxical embolism, and arrhythmias (Mahony *et al.*, 1999) [6]. In this report, we present a 7-year-old female with genetically confirmed Marfan syndrome who was incidentally found to have a small ostium secundum ASD, alongside classical systemic features such as lens subluxation and skeletal deformities. This case emphasizes the importance of considering atypical cardiac findings in the diagnostic and follow-up protocols for Marfan syndrome in children.

Case: 7 year-old female, from Kolhapur district of Maharashtra presented with complaints of dyspnea on exertion with chest pain radiating to back since 4-5 months . Upon general examination patient had a Tall stature with disproportionately long upper limbs (Dolichostenomelia). Detailed Anthropometric evaluation done and is as follows

Parameters	Value
Height	125cm
Weight	15Kg
Weight For Age	-2SD to -3SD
Height For Age	0 to +1 SD
BMI	18 Kg/m2
Arm Span	131 cm
Upper segment	58 cm
Lower Segment	67 cm
Us : Ls	0.86
Arm span: Height	1.048

Fig 1: Anthropometric evaluation of the patient showing tall stature, long arm span, and altered upper-to-lower segment ratio, consistent with skeletal manifestations of Marfan syndrome

Following anthropometric findings prompted us to evaluate patient in detail for Marfan's syndrome On General Examination Pulse - 98/min, regular, felt over right radial artery, high volume, equal on both side, no radio radial or radio femoral delay, no pulse apex deficit, all peripheral pulses well felt.

Blood Pressure

Limb	Right	Left
Upper	90/60 mmHg	90/60 mmHg
Lower	90 mmHg	90 mmHg

Peripheral signs of Aortic Regurgitation were not present in the patient:

Patient had Classical findings consistent with Systemic signs of Marfan's Syndrome. Following are systemic signs observed in the patient.

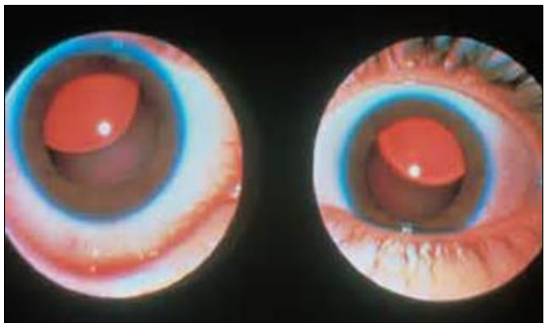


Fig 2: Minor superior temporal subluxation of lens in both eyes.

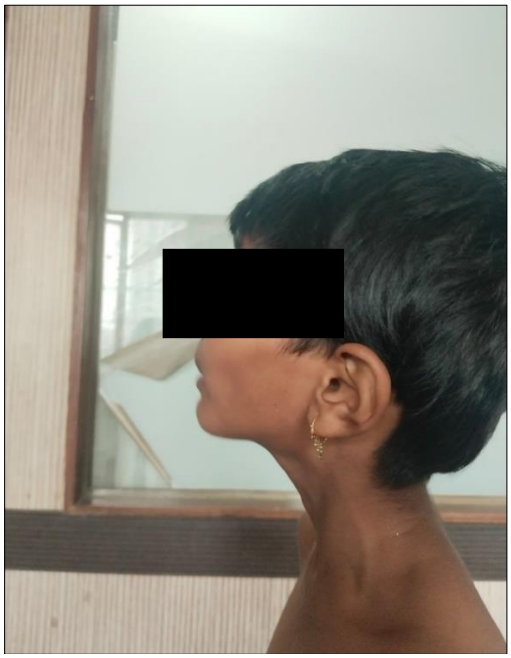


Fig 3: Flat Cheek - Malar hypoplasia

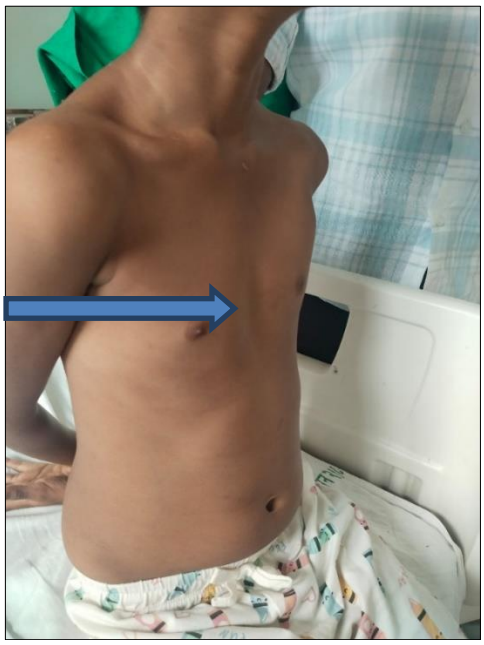


Fig 4: Pectus Excavatum (Arrow)

Fig 5: Steinberg sign - Thumb sign: Entire distal phalanx protrudes beyond ulnar border of clenched wrist with or without assistance to achieve maximum adduction

Fig 6: Arachnodactyly - long Fingers

Fig 7: Wrist Sign (Walker Murdoch sign) :Top of thumb covers entire finger nail of fifth finger

On Fundus examination patient was found to have Tessellated fundus - There is increased in visibility of choroid vessel and arcade vessels around fovea centralis

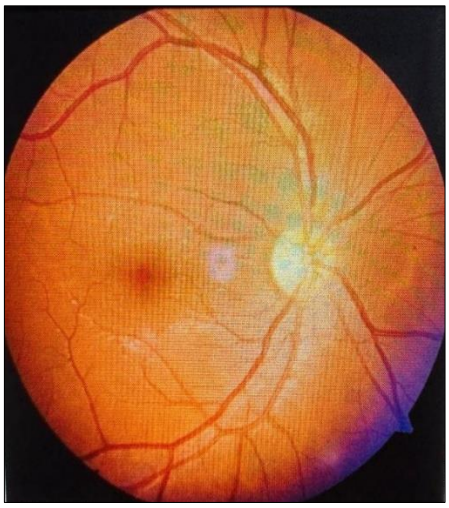


Fig 8: Fundus photograph showing tessellated fundus with increased visibility of choroidal vessels and arcade vessels around the fovea centralis, suggestive of ocular involvement in Marfan syndrome

Fig 9: Ophthalmic slit-lamp image highlighting superior temporal subluxation of the lens, a classical ocular feature in Marfan syndrome

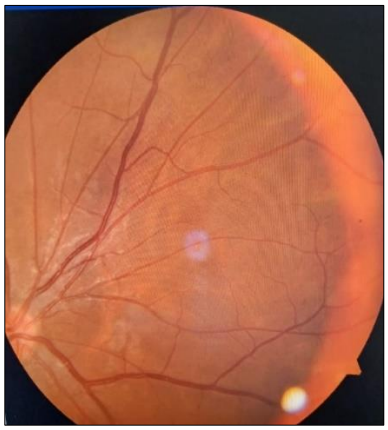


Fig 10: Chest X-ray (posteroanterior view) demonstrating cardiomegaly, along with systemic skeletal features including mild scoliosis and high-arched palate, consistent with Marfan phenotype

On cardiovascular systemic Examination patient was found to have, diffuse apex which is shifted downwards in 5th ICS medial to mid clavicular line; On palpation - No thrill or palpable heart sounds. Flow murmur of Grade III best heard in sitting and leaning forward position in full expiration with diaphragm on neoaortic area not radiating to apex
X-rays were done to document systemic findings and are as follows:

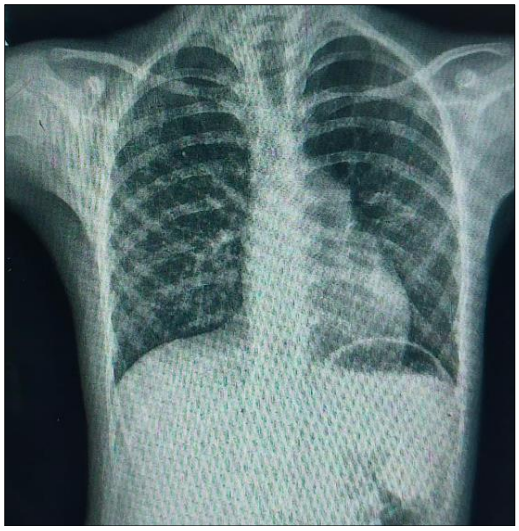


Fig 11: Mild Scoliosis; 10.2: High Arch palate

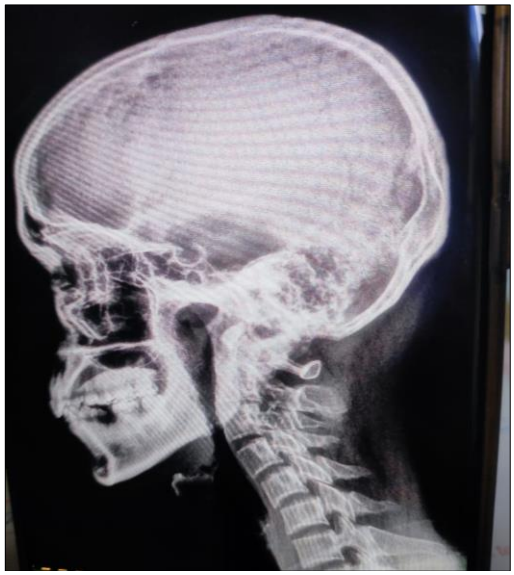
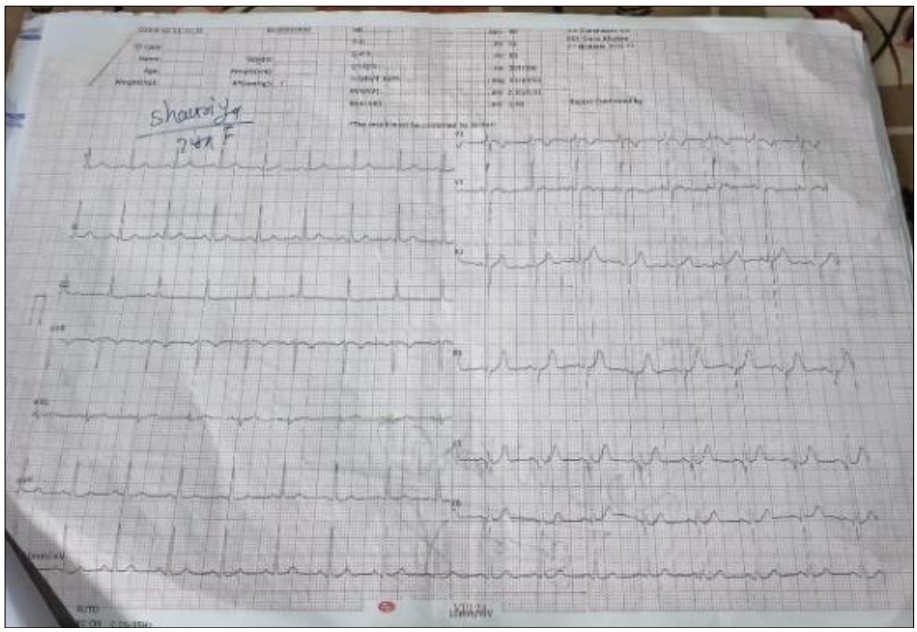


Fig 12: Mild Scoliosis; 10.4: High

ECG: Sinus Rhythm with No Significant ST segment change.



Patients Detailed 2 D ECHO was done and the findings are as follows:

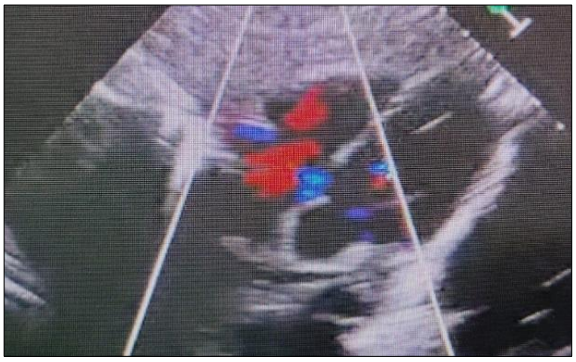


Fig 13: Subcostal View showing ASD of size 5 mm

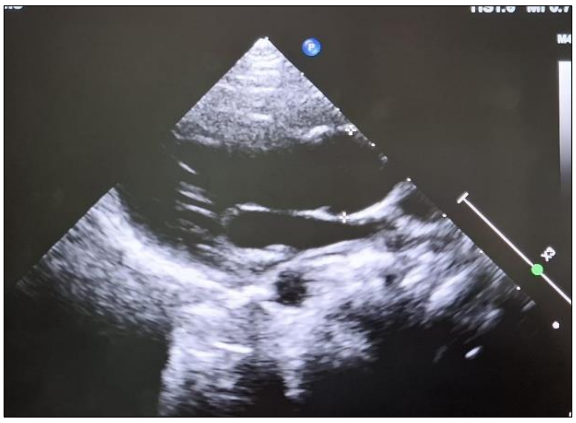


Fig 14: PLAX No dilatation of Aorta

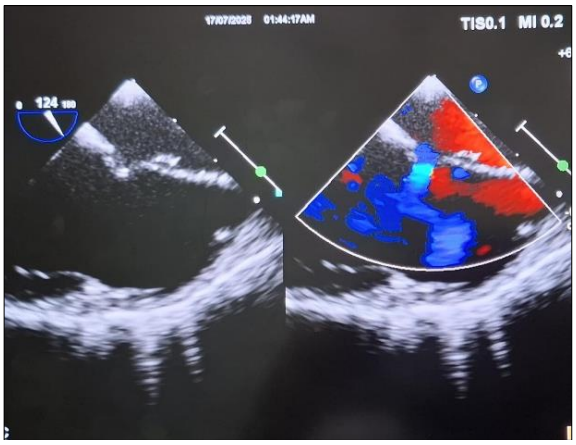


Fig 15: TEE showing ASD 5 mm size

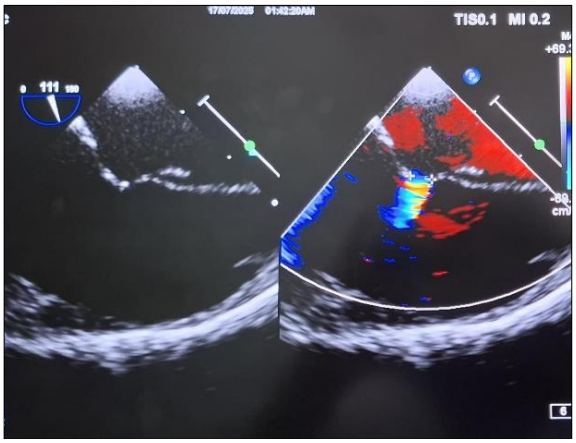


Fig 16: TEE showing ASD 5 mm size

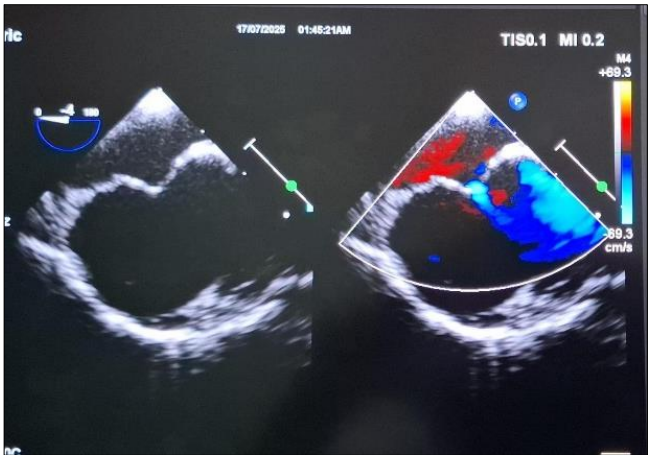


Fig 17: TEE showing ASD 5 mm size

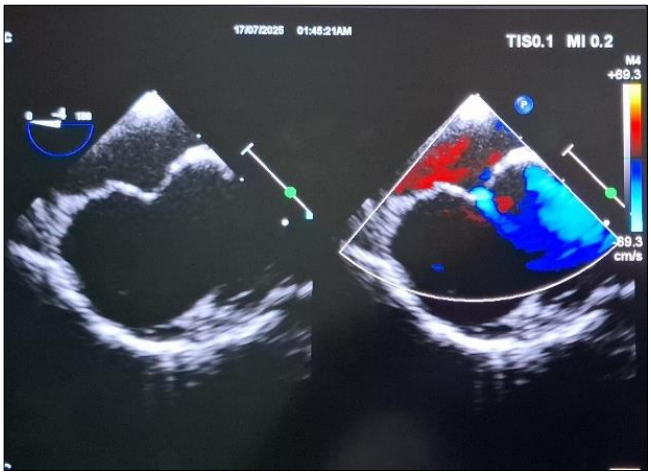


Fig 18: TEE showing ASD 5 mm size

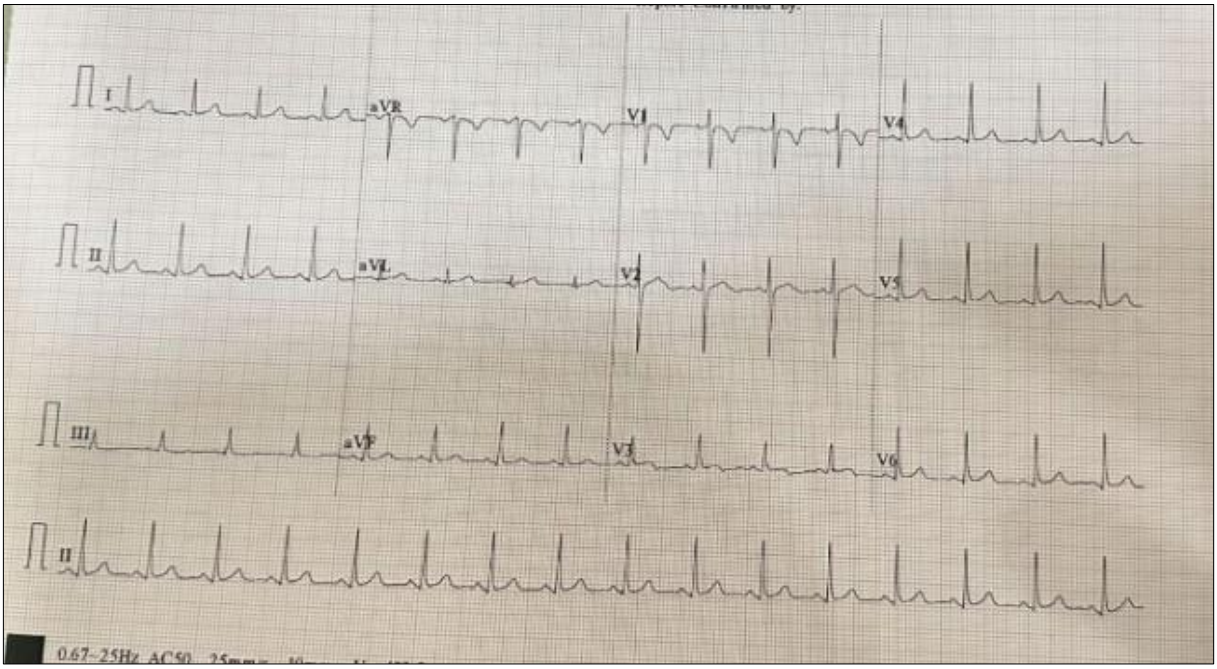


Fig 19: Apical 4 chamber view showing prolapsed AML; Apical 5 chamber view showing Dilated Aorta

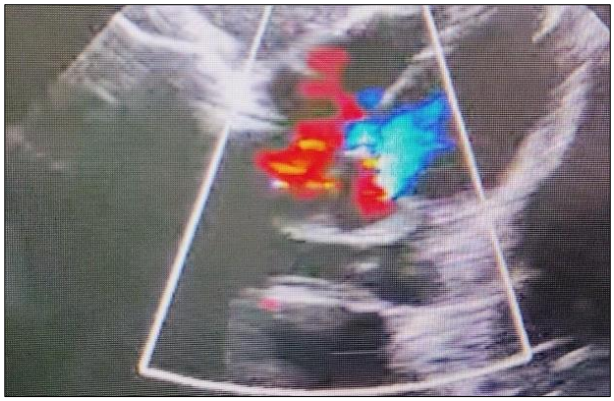


Fig 20: Subcostal view : ASD 5 mm size

After evaluating patient for components of Ghents Nosology. She had features which satisfied 8/20 criteria and they were as follows

Wrist and Thumb sign: 3 points
Pectus Excavatum: 1 point
Pes Planus: 1 point
Reduced upper segment to lower segment ratio and increased arm span to height with no severe scoliosis : 1 point
Scoliosis: 1 point

Discussion

Marfan syndrome (MFS) is a multisystem connective tissue disorder primarily characterized by mutations in the FBN1 gene, which encodes the extracellular matrix protein fibrillin-1. The cardiovascular system is predominantly affected, with aortic root dilation and valvular abnormalities accounting for most morbidity and mortality. In contrast, congenital cardiac anomalies such as atrial septal defects (ASDs) are rarely associated with MFS, especially in pediatric populations under 7 years of age, making our case particularly noteworthy.

Rarity and Clinical Significance of ASD in MFS

While ASDs are among the most common congenital heart defects in the general population, their occurrence in MFS patients is exceptionally rare. The classical cardiac phenotype of MFS centre on progressive connective tissue degeneration leading to aneurysmal dilatation of the aortic root and valvular dysfunction, which have a well-established pathophysiological basis. Conversely, ASDs arise from incomplete formation or fusion of the atrial septum during early embryogenesis, processes not directly linked to fibrillin-1 dysfunction.

Nonetheless, the extracellular matrix abnormalities characteristic of MFS might, in rare cases, influence cardiac septation. This hypothesis is supported by sporadic reports describing ASDs in pediatric MFS patients, although it remains unclear whether these defects represent coincidental congenital anomalies or a broader phenotypic spectrum of connective tissue dysregulation.

Implications for Diagnosis and Management

The identification of a 5 mm ostium secundum ASD in our 7-year-old patient with MFS underscores the importance of comprehensive cardiac evaluation beyond the aortic root and valvular apparatus. Small ASDs often remain asymptomatic and may be detected incidentally during routine echocardiography. In such cases, conservative management with close clinical and echocardiographic follow-up is generally appropriate.

However, ASD in the context of MFS warrants cautious surveillance due to potential complications such as paradoxical embolism, arrhythmias, or volume overload, which could exacerbate underlying cardiac vulnerability. Additionally, the fragile connective tissue in MFS may pose challenges if interventional closure becomes necessary, as highlighted by Loeffelbein *et al.* (2008) [5], who reported device-related atrial wall penetration during ASD closure in a pediatric MFS patient.

Literature Review and Future Directions

The scarcity of reported cases limits robust conclusions regarding the prevalence and natural history of ASDs in MFS. Yetman *et al.* (2003) [9] documented cardiovascular outcomes in pediatric MFS, noting the rare occurrence of septal defects alongside predominant aortic disease. Similarly, Attias *et al.* (2021) [1] emphasized the diversity of cardiovascular manifestations but did not identify ASD as a common feature.

Our case contributes to the limited pediatric literature, advocating for vigilant cardiac surveillance protocols that encompass detailed septal anatomy assessment in addition to standard aortic monitoring. Future studies with larger cohorts are essential to clarify the incidence, pathogenesis, and clinical course of ASDs in MFS, as well as to establish evidence-based guidelines for their management.

Conclusion

Marfan syndrome is predominantly characterized by aortic root dilation and valvular abnormalities, which constitute the main cardiovascular risks associated with the disease (Judge & Dietz, 2005; Attias *et al.*, 2021) [1, 4]. However, this case highlights that congenital anomalies such as atrial septal defects (ASDs), though rare, can also occur in pediatric patients with MFS, especially under 7 years of age. The presence of an ASD in such patients expands the recognized cardiac phenotype of MFS and necessitates comprehensive cardiovascular screening beyond the traditional focus on the aorta and valves (Yetman, Bornemeier, & McCrindle, 2003) [9].

Early identification of ASDs allows for careful hemodynamic assessment and timely decision-making regarding conservative management versus intervention. In small, asymptomatic ASDs, as seen in our patient, close echocardiographic surveillance is recommended to monitor defect size and potential complications such as right heart volume overload or arrhythmias (Mahony *et al.*, 1999) [6].

Given the fragile connective tissue architecture inherent to MFS, interventions such as device closure require cautious planning and expert cardiothoracic evaluation due to potential procedural risks (Loeffelbein, Schlensak, & Dittrich, 2008) [5].

This case underscores the need for heightened clinical vigilance for atypical cardiac anomalies in MFS, supporting comprehensive cardiac evaluation protocols in pediatric patients, including detailed assessment of septal anatomy. Further research and accumulation of case data are necessary to elucidate the prevalence, natural history, and optimal management strategies for ASDs in this unique population (Espínola-Zavaleta *et al.*, 2005; Attias *et al.*, 2021) [1, 3].

This case contributes to the limited but growing evidence suggesting that ASDs, though rare, may occur in pediatric patients with Marfan syndrome. The presence of an ASD in a 7-year-old girl with confirmed *FBN1* mutation emphasizes the need for detailed cardiac evaluation, beyond aortic assessment, as part of the diagnostic and monitoring process for MFS.

While the long-term significance of such findings remains unclear, early detection enables appropriate risk stratification and informs follow-up strategies. Further studies are needed to determine whether congenital septal defects represent part of the MFS phenotype or coincidental anomalies. Meanwhile, clinicians should remain vigilant for atypical cardiovascular findings in children with Marfan features

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