ISSN 2692-5877
DOI: 10.46998/IJCMCR.2025.50.001239

International Journal of
Clinical Studies & Medical Case Reports

Review Article

Right-to-Left Shunting in Simple Atrial Septal Defect with Normal Pulmonary Artery Pressure: A Rare Cause of Cyanosis and Its Diagnostic Hurdles

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Received: February 24, 2025 **Published:** April 01, 2025

Abstract

Atrial Septal Defects (ASD) are congenital anomalies that typically lead to a left-to-right shunt due to the lower pressure in the right side of the heart. Cyanosis, a manifestation of systemic desaturation, generally occurs in the setting of elevated Pulmonary Artery Pressure (PAP) associated with ASD, resulting in bidirectional or right-to-left shunting. However, the occurrence of cyanosis in ASD patients with normal pulmonary artery pressure is an unusual and complex clinical phenomenon. This review explores the pathophysiology, diagnostic complexities, and management strategies for ASD-associated cyanosis in the absence of elevated PAP, emphasizing right-to-left shunting as the underlying cause. By exploring these rare mechanisms and their diagnostic hurdles, the article provides a comprehensive overview of the current understanding and approach to managing this intriguing condition.

Keywords: Simple Atrial Septal Defect; Normal Pulmonary Artery Pressure; Cyanosis
Abbreviations: ASD: Atrial septal defect; IAS: Inter Atrial Septum; PAP: Pulmonary Artery Pressure; SVC: Superior Vena Cava; IVC: Inferior Vena Cava; POS: Platypnea Orthodexia Syndrome; MRI: Magnetic Resonance Imaging

Introduction

Atrial septal defects (ASD) are among the most common congenital heart defects, representing about 10-15% of all congenital cardiac anomalies. ASDs are characterized by an abnormal communication between the right and left atria, typically resulting in a left-to-right shunt because the right atrium and ventricle have lower pressure compared to their left-sided counterparts. This condition increases the volume of blood entering the pulmonary circulation, leading to pulmonary over-circulation, right heart dilation, and in some cases, right heart failure. Over time, prolonged left-to-right shunting can result in the development of pulmonary hypertension (PH), further complicating the condition.

The occurrence of cyanosis in ASD is typically associated with elevated pulmonary artery pressures, leading to reversed or bidirectional shunting. However, in a small subset of patients, cyanosis occurs despite the absence of pulmonary hypertension. In these cases, right-to-left shunting can bypass the pulmonary vasculature, allowing deoxygenated blood to enter the systemic circulation, thereby causing cyanosis. This rare occurrence presents a significant challenge for clinicians due to its complex pathophysiological mechanisms and diagnostic difficulties. This review explores the rare phenomenon of right-to-left shunting in simple ASD with normal pulmonary artery pressures and its diagnostic hurdles.

Pathophysiology of Cyanosis in ASD with Normal Pulmonary Artery Pressure

In the typical scenario of ASD, a left-to-right shunt develops because of the difference in pressure between the left and right atria. This shunting leads to increased blood flow to the pulmonary circulation, potentially causing pulmonary over-circulation, right atrial and ventricular dilation, and progressive right-sided heart failure. However, cyanosis in ASD patients with normal pulmonary artery pressure remains an uncommon clinical occurrence. The presence of a right-to-left shunt, despite normal pulmonary pressures, allows deoxygenated blood to bypass the lungs and enter systemic circulation, resulting in hypoxemia and cyanosis.

Various mechanisms underlie this phenomenon:

1. Abnormal Venous Drainage and Atypical Anatomical Variants

A primary mechanism for right-to-left shunting in ASD patients with normal PAP is abnormal venous drainage. In some

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cases, particularly those involving sinus venosus-type ASDs, the inferior vena cava (IVC) may drain directly into the left atrium, bypassing the pulmonary circulation entirely. This anatomical anomaly can result from a malposition of venous structures, such as the superior vena cava (SVC)/IVC straddling or anomalous blood flow patterns, like an enlarged Eustachian valve or tricuspid regurgitation [1-3]. Such abnormalities cause preferential streaming of deoxygenated blood into the left atrium and subsequently into systemic circulation.

The IVC blood flow can preferentially reach the left atrium by targeting the lower portion of the interatrial septum (IAS), contributing to the development of a right-to-left shunt. When additional hemodynamic factors such as increased right atrial pressure (due to conditions like right heart failure, tricuspid regurgitation, or increased intrathoracic pressure during the Valsalva manoeuvre) occur, these factors can further exacerbate the right-to-left shunting. In such cases, deoxygenated blood bypasses the lungs and enters the systemic circulation, leading to cyanosis.

Furthermore, anomalies like a persistent left superior vena cava (SVC) draining into the coronary sinus, which in turn drains into the left atrium through an unroofed coronary sinus, may also lead to significant cyanosis in these patients. These anatomical variations can be difficult to detect, often leading to misdiagnosis or delayed diagnosis.

2. Elevated Right Atrial Pressures

Another potential contributor to right-to-left shunting in ASD patients is elevated right atrial pressure (RAP). This condition can arise from a variety of pathologies, including right ventricular (RV) abnormalities such as RV infarction, RV diastolic dysfunction, or RV cardiomyopathy [4-7]. Additionally, conditions such as positive pressure ventilation (PPV) with high positive end-expiratory pressure (PEEP) or severe pulmonary stenosis can lead to increased RAP (8, 9). When RAP exceeds left atrial pressure, deoxygenated blood is directed through the ASD into the left atrium, bypassing the pulmonary circulation and leading to cyanosis.

The clinical presentation of elevated RAP often includes symptoms of right heart failure or systemic venous congestion. In such cases, right-to-left shunting is exacerbated by the high RAP, resulting in systemic desaturation even in the absence of pulmonary hypertension.

3. Inferiorly Positioned ASD and Abnormal Venous Return

The anatomical location of the ASD significantly influences the direction of the shunt. When the ASD is positioned in the inferior part of the atrial septum, venous return from the IVC can preferentially flow into the left atrium, particularly when the defect is large or multiple fenestrations exist [8]. This results in deoxygenated blood bypassing the lungs and entering the systemic circulation. This phenomenon is particularly pronounced when there is an abnormal venous return or when the ASD is sufficiently large to allow multiple pathways for blood to flow from the right atrium to the left.

In patients with inferiorly located ASDs, it is crucial to assess the size of the defect and the presence of any associated structural anomalies that might further influence blood flow dynamics and contribute to right-to-left shunting.

4. Platypnea-Orthodeoxia Syndrome (POS)

Platypnea-Orthodeoxia Syndrome (POS) is a rare but significant cause of cyanosis in patients with ASD. In POS, patients experience postural cyanosis, particularly in an upright position. This phenomenon results from the gravitational shift of blood flow from the right atrium to the left atrium through the ASD when the patient assumes an upright posture. This shift is accentuated when there are structural anomalies like aortic aneurysms, loculated pericardial effusions, or in patients who have undergone lobectomy [10-15]. The upright position exacerbates right-to-left shunting due to a decrease in venous return to the right atrium and a subsequent increase in the pressure gradient favouring right-to-left flow through the ASD. The mechanism is best understood as a pressure imbalance between the right and left atria that occurs due to the body's position, resulting in systemic desaturation.

5. Eisenmenger Syndrome

Eisenmenger syndrome, which is typically associated with pulmonary hypertension, can also contribute to cyanosis in ASD patients. In cases where there is longstanding left-to-right shunting, pulmonary vascular resistance gradually increases, and the shunt direction can reverse to right-to-left. This condition, known as "Eisenmenger physiology," is usually accompanied by elevated PAP and the subsequent development of cyanosis [16]. However, in the case of ASD with normal PAP, this phenomenon is not the primary cause of cyanosis. It is important to distinguish Eisenmenger syndrome from other causes of right-to-left shunting in ASD patients with normal pulmonary pressures.

Diagnosis of Cyanosis in ASD with Normal Pulmonary Artery Pressure

Diagnosing cyanosis in ASD patients with normal pulmonary artery pressure is a complex process that requires a detailed clinical evaluation and the use of advanced diagnostic tools. Given the rarity of this presentation, a high degree of clinical suspicion is essential. The following diagnostic approaches are crucial for identifying right-to-left shunting in ASD patients:

1. Clinical Assessment

A comprehensive clinical history is vital in identifying ASD patients at risk for cyanosis. Symptoms such as exertional dyspnea, cyanosis, and clubbing can be indicative of systemic desaturation, which may be associated with right-to-left shunting. Physical examination findings such as cyanosis or oxygen desaturation in the absence of pulmonary hypertension should raise suspicion for abnormal venous drainage or elevated right atrial pressures. Reviewing the patient's past medical history, including any previous cardiac interventions, is essential to understanding the potential underlying causes of right-to-left shunting.

2. Echocardiography

Echocardiography is the cornerstone of ASD diagnosis. In typical cases, it demonstrates a left-to-right shunt. However, in cases where abnormal venous drainage or inferiorly located ASDs are present, the direction of the shunt may be reversed. Saline contrast echocardiography, or bubble study, is particularly valuable in detecting right-to-left shunting. During this procedure, microbubbles injected into the venous system appear in the left atrium and subsequently enter the systemic circulation, providing clear evidence of a right-to-left shunt. Additionally, Doppler studies can help assess the direction and velocity of blood flow through the ASD, further supporting the diagnosis.

3. Cardiac Catheterization
Cardiac catheterization remains a definitive diagnostic tool for assessing hemodynamics in complex cases. It allows for precise measurements of pulmonary artery pressure and right atrial pressure, which can confirm the presence of normal PAP and further support the diagnosis of right-to-left shunting. Oxygen saturation levels can be measured at different points in the heart, and a significant drop in oxygen saturation between the right atrium and left atrium suggests the presence of a right-to-left shunt. This procedure can also be used to assess the effectiveness of potential closure methods, including balloon occlusion testing.

4. Balloon Occlusion Test
Balloon occlusion testing is a helpful diagnostic technique that can assess the hemodynamic significance of the ASD. By temporarily occluding the defect, the test evaluates whether the closure of the ASD improves oxygen saturation levels. If oxygen saturation increases significantly after balloon occlusion, it suggests that the ASD is contributing to cyanosis and confirms the presence of a right-to-left shunt [17].

5. Magnetic Resonance Imaging (MRI)
Magnetic resonance imaging (MRI) provides high-resolution imaging of the heart's anatomy, offering detailed views of the atrial septum and any associated structural abnormalities. MRI can identify fenestrated septa, abnormal venous drainage, or other anatomical factors that contribute to right-to-left shunting. Additionally, MRI can evaluate the size of the ASD, assess the atrial septal morphology, and aid in pre-procedural planning for closure.

Management of Cyanosis in ASD with Normal Pulmonary Artery Pressure

The management of ASD with cyanosis and normal PAP is focused on correcting the underlying anatomical defect and improving systemic oxygenation. Treatment options depend on the severity of symptoms, the size of the defect, and the presence of associated complications

1. Conservative Management
In asymptomatic patients or those with mild symptoms, a conservative approach with regular follow-up and clinical monitoring may be appropriate. Patients should be closely monitored for any changes in symptoms or progression of the condition. Regular echocardiograms and clinical assessments are recommended to track disease progression and any potential changes in the direction of shunting.

2. Percutaneous Closure
For patients with significant cyanosis or right-to-left shunting, percutaneous ASD closure is the preferred treatment. This minimally invasive procedure involves the placement of a device to close the ASD, preventing further systemic desaturation. Percutaneous closure offers several advantages, including a lower risk of complications and a faster recovery time compared to traditional surgery. Pre-procedural assessment using imaging studies and balloon occlusion testing is essential to ensure successful device placement and to minimize the risk of complications such as device embolization.

3. Surgical Closure
In cases where percutaneous closure is not feasible, or if complications arise, surgical closure may be required. Surgical closure involves patching the ASD with a synthetic material or pericardium. This approach is typically reserved for patients with complex ASD anatomies, such as multiple fenestrations, or when percutaneous closure is not possible due to technical factors. Although surgical closure carries a higher risk than percutaneous methods, it remains an effective option for patients with significant clinical symptoms.

4. Post-Closure Management
Postoperative follow-up is essential to monitor for residual shunting or complications such as arrhythmias or thromboembolic events. Patients may require long-term anticoagulation therapy to reduce the risk of stroke or other complications associated with ASD closure. Regular echocardiograms should be performed to ensure the success of the procedure and detect any residual defects.

Conclusion

Cyanosis in patients with ASD and normal pulmonary artery pressure is a rare and complex clinical challenge. Understanding the multifactorial mechanisms that contribute to right-to-left shunting in these patients is crucial for accurate diagnosis and appropriate management. Advanced diagnostic imaging, including saline contrast echocardiography, MRI, and cardiac catheterization, along with careful pre-procedural planning, are essential for achieving successful outcomes.

In most cases, percutaneous or surgical ASD closure can effectively resolve the right-to-left shunt, improving oxygen saturation and leading to favourable long-term outcomes. Awareness of this rare phenomenon will aid clinicians in better diagnosing and managing patients with ASD and cyanosis despite normal pulmonary artery pressures.

Learning Objectives
- Understand the pathophysiology of right-to-left shunting in ASD with normal pulmonary artery pressure.
- Identify the diagnostic challenges and techniques necessary for diagnosing cyanosis in such cases.
- Review the management strategies, including percutaneous and surgical ASD closure, to improve clinical outcomes.

Declarations:
Ethical approval and consent to participate: Not applicable
Consent to publish: Not applicable
Availability of data and material: Not applicable
Competing interests: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.
Funding: The author(s) received no financial support for the research, authorship, and/or publication of this article.
Author contribution:
UDK: Conceptualization; Methodology; Supervision; Writing—original draft; Writing—review and editing.
NT: Conceptualization; Methodology; Supervision; Writing—original draft; Writing—review and editing
SKM: Conceptualization; Methodology, Validation; Writing—original draft.
All authors reviewed the paper and approved the final version of the manuscript.
Acknowledgements: None

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