

A "Dual-Hit" Pathophysiology in a Giant Pulmonary Artery Aneurysm: The Intersection of Behçet's Disease and Atrial Septal Defect-Induced Pulmonary Arterial Hypertension

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ABSTRACT

Background: Pulmonary artery aneurysm (PAA) is an exceedingly rare but life-threatening vascular anomaly, typically defined by a diameter exceeding 40 mm in females or 1.5 times the upper limit of normal [1,2]. While Behçet's disease (BD) classically induces distal PAAs via vasculitis, congenital shunts predominantly cause proximal PAAs due to chronic hemodynamic stress [1,2].

Case Presentation: A 53-year-old woman with an established diagnosis of BD and an uncorrected 15 mm atrial septal defect (ASD) presented in July 2024 with severe dyspnea and chest pain. Her main pulmonary artery measured 44 mm. Because her pulmonary vascular resistance (PVR) exceeded 5 Wood units, surgical ASD closure was contraindicated. She was managed medically with macitentan, spironolactone, and furosemide, which significantly improved her functional capacity. She was subsequently lost to follow-up. In August 2026, she returned with recurrent symptoms. Despite stable pulmonary hemodynamics and an inactive inflammatory state (C-reactive protein 2.49 mg/L), imaging revealed a staggering anatomical expansion of the PAA to 84.2 mm. Recognizing the extreme risk of rupture associated with aneurysms >55 mm or those exhibiting rapid growth [1,7], she was urgently referred for surgical graft replacement.

Conclusion: The striking coexistence of ASD-induced PAH and inactive BD points toward a "dual-hit" pathophysiology. Chronic hemodynamic shear stress synergizes with the underlying inflammatory fragility previously established by BD, culminating in extraordinary central aneurysm formation. This case critically highlights that anatomical aneurysmal expansion can progress rapidly despite clinical and hemodynamic stabilization on pulmonary vasodilator therapy.

Keywords

Pulmonary Artery Aneurysm, Behçet's Disease, Pulmonary Arterial Hypertension, Atrial Septal Defect, Dual-Hit Hypothesis, Vascular Remodeling.

Introduction

A pulmonary artery aneurysm (PAA) is defined as a focal dilatation of all three layers of the vessel wall, typically exceeding

40 mm in females or measuring greater than 1.5 times the upper limit of normal [1,2]. It is an exceptionally rare clinical entity, with an estimated prevalence of 1 in 14,000 autopsies [1,2]. PAAs can be systematically classified into high-pressure and low-pressure groups based on their underlying etiology and intravascular hemodynamics, with high-pressure variants being disproportionately responsible for fatal complications such as dissection and rupture [1].

Behçet's disease (BD) is a multisystem inflammatory disorder known to cause low-pressure, predominantly peripheral or distal PAAs due to severe neutrophilic vasculitis and inflammation of the vasa vasorum [2-4]. Conversely, conditions that increase pulmonary blood flow, such as an atrial septal defect (ASD), generate sustained hemodynamic shear stress that typically causes proximal or main PAAs [1,2].

The pathological vascular remodeling seen in these overlapping states is highly complex. Chronic exposure to high shear stress and disturbed blood flow prevents normal endothelial morphological adaptation, leading to progressive structural remodeling and impaired barrier function [3]. When these mechanical forces overlap with an inherently fragile, inflamed vessel wall, the risk of catastrophic aneurysmal expansion increases exponentially. We present a highly unusual case of an 84.2 mm giant main PAA in a patient afflicted with both BD and ASD-associated PAH. This presentation illustrates the compounding effects of inflammatory vascular fragility and unrelenting mechanical hemodynamic stress, alongside the vital clinical lesson that anatomical progression may occur despite successful hemodynamic control.

Case Presentation

A 53-year-old woman with a documented history of Behçet's disease initially presented to our cardiology clinic in July 2024, complaining of exertional dyspnea, shortness of breath, and chest pain. An initial 12-lead electrocardiogram (ECG) revealed normal sinus rhythm with a complete right bundle branch block (RBBB). Transthoracic echocardiography (TTE) demonstrated right ventricular (RV) dilatation, an uncorrected 15 mm ASD, and moderate tricuspid regurgitation.

To precisely evaluate her hemodynamics, coronary angiography and a right heart catheterization (RHC) were performed. The RHC revealed a mean pulmonary arterial pressure (mPAP) of 30 mmHg and a pulmonary vascular resistance (PVR) of 5.3 Wood units. Concurrent imaging measured the main pulmonary artery diameter at 44 mm. Because the PVR exceeded the definitive threshold of 5 Wood units, surgical closure of the ASD was contraindicated. A medical management strategy was subsequently initiated, consisting of the endothelin receptor antagonist macitentan (10 mg daily), spironolactone (25 mg daily), and furosemide. Under this regimen, the patient's functional capacity notably increased, and her symptoms completely resolved; however, she was subsequently lost to clinical follow-up for a two-year period.

In August 2026, the patient was readmitted to the emergency department following the recurrence of severe chest pain and exertional dyspnea. Clinical examination revealed no evidence of an active Behçet's disease flare. Laboratory investigations demonstrated a normal C-reactive protein (CRP) level of 2.49 mg/L, confirming the absence of acute systemic inflammation. High-sensitivity Troponin I was mildly elevated at 22.4 pg/mL (reference range: 0-15.6 pg/mL).

A repeat TTE and RHC were performed to assess for disease progression. Strikingly, the 2026 hemodynamic parameters showed no significant difference compared to the 2024 measurements. The TTE confirmed an estimated systolic pulmonary arterial pressure (sPAP) of 50 mmHg and a Tricuspid Annular Plane Systolic Excursion (TAPSE) of 14 mm, indicating persistent but stable right ventricular strain. A chest radiograph, however, prominently displayed a massive enlargement of the main pulmonary artery segment (Figure 1).

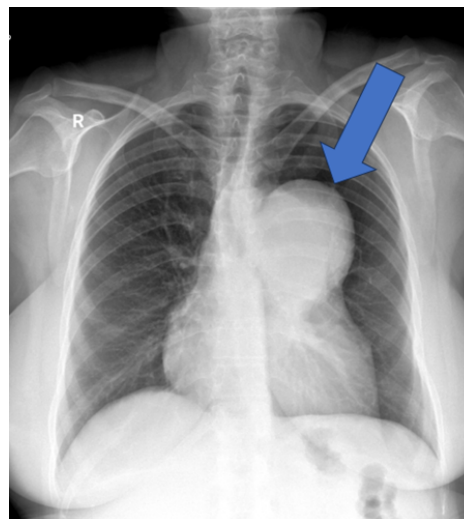


Figure 1: A posteroanterior chest radiograph demonstrating pronounced enlargement of the main pulmonary artery segment (indicated by the blue arrow), accompanied by significant expansion of the right heart structures.

Coronary and pulmonary angiography confirmed the profound vascular distortion (Figure 2). To definitively assess the anatomy, a computed tomography pulmonary angiogram (CTPA) was obtained. The CTPA unequivocally confirmed a giant aneurysmal dilatation of the main pulmonary artery. The central lumen of the aneurysm measured an extraordinary 84.2 mm in its maximum diameter (Figure 3).

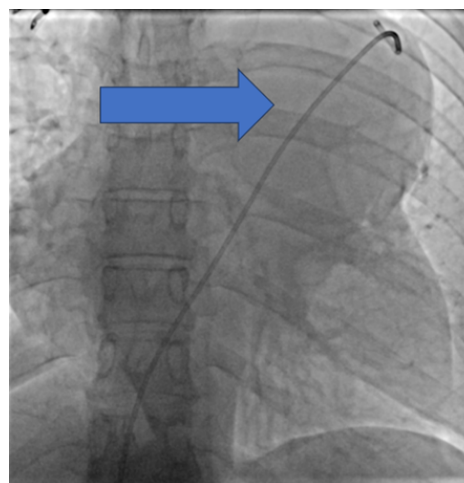


Figure 2: Diagnostic right heart catheterization and pulmonary angiography exposing a massive aneurysmal dilatation of the pulmonary artery (highlighted by the blue arrow).

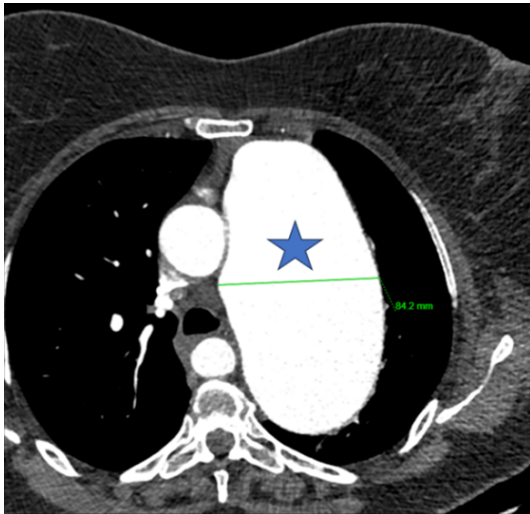


Figure 3: An axial view from a computed tomography pulmonary angiogram (CTPA) confirming the presence of a giant pulmonary artery aneurysm. The central lumen of the aneurysmal sac (marked with a blue star) expanded from a baseline of 44 mm in 2024 to an astonishing 84.2 mm in its maximum diameter (delineated by the green measurement line) over a two-year period.

This represented a staggering anatomical expansion of approximately 40 mm over a 24-month period, occurring despite stable pulmonary pressures. Current surgical guidelines indicate that operative repair should be strongly considered when a PAA exceeds 55 mm, or when the expansion rate exceeds 5 mm in 6 months, to prevent fatal rupture [7]. Given the extreme dimensions and the rapid growth rate, the multidisciplinary consensus determined that the patient faced an imminent risk of catastrophic rupture. She was immediately referred for urgent cardiothoracic surgery. Her macitentan therapy was deliberately continued throughout the preoperative period to preserve functional capacity and maintain RV hemodynamics. The complete chronological progression of the patient's clinical presentation, hemodynamic parameters, anatomical changes, and management strategy over the two-year period is summarized in Figure 4.

Discussion

The natural history of PAAs in the setting of Behçet's disease is fundamentally driven by profound vasa vasorum inflammation and immune system dysregulation [3,4]. In PAH, excessive local secretion of pro-inflammatory cytokines compromises the structural integrity of the arterial wall [3]. However, the unprecedented size (84.2 mm), the specific proximal location, and the extraordinarily rapid growth of the aneurysm observed in our patient strongly point toward a compounding pathophysiological mechanism.

We hypothesize that this massive aneurysmal dilatation was propagated by a "dual-hit" mechanism. The initial "hit" stems from the underlying autoimmune vasculitis inherent to BD, which structurally weakened the pulmonary arterial wall. Notably, our patient exhibited no clinical or biochemical signs of an acute

vasculitic flare (CRP 2.49 mg/L) at presentation. This suggests that the second "hit"—the chronic, unrelenting mechanical burden imposed by the ASD and the resulting high-pressure PAH—acted as the primary active driver for expansion.

A critical clinical lesson from this case is the clear dissociation between hemodynamic stability and anatomical progression. The patient's functional capacity improved and her RHC parameters remained remarkably stable between 2024 and 2026 under macitentan therapy. Yet, the aneurysm grew from 44 mm to 84.2 mm—an alarming expansion rate of roughly 20 mm per year. A growth rate exceeding 2 mm/year is considered a high-risk characteristic for dissection or rupture [1] [cite: 9]. The continuous subjection of a structurally fragile vessel to elevated pulmonary pressures (sPAP 50 mmHg) and high shear stress overwhelmingly accelerated this severe central aneurysmal remodeling, regardless of the pharmacological control of the PVR [1,3].

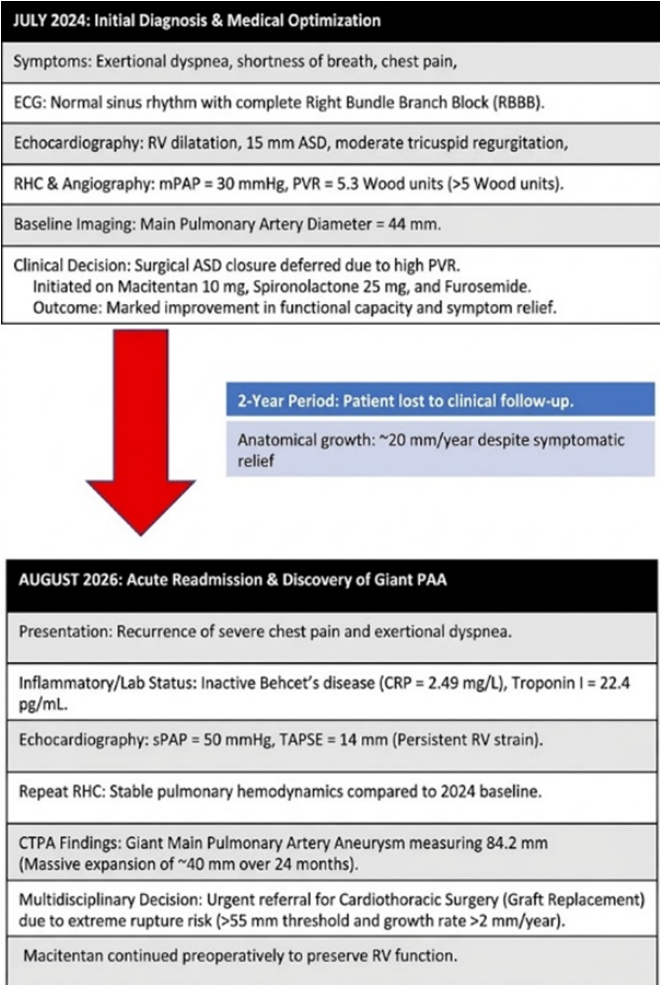


Figure 4: Timeline outlining the clinical course, diagnostic workup, hemodynamic parameters, and management decisions of the patient from initial presentation in July 2024 to acute readmission in August 2026. Note the significant anatomical expansion of the main pulmonary artery aneurysm (from 44 mm to 84.2 mm) over the two-year period despite clinical and hemodynamic stabilization on targeted pulmonary vasodilator therapy.

The differential diagnosis for rapidly expanding or massive PAAs includes mycotic aneurysms, primary lung tumors, and pulmonary artery intima sarcoma [6]. Intima sarcoma, in particular, can masquerade as chronic thromboembolic pulmonary hypertension or arteritis [6]. However, the patient's established history of BD and congenital heart disease makes the inflammatory-hemodynamic etiology the most plausible.

The clinical management of giant PAAs is notoriously complex. While distal or peripheral PAAs may occasionally be managed with endovascular coil embolization or vascular plugs [5], recent surgical consensus indicates that operative repair via graft replacement should be recommended for central PAAs >55 mm [7]. Dimensions beyond these thresholds correlate strongly with airway compression, left main coronary artery compression, and sudden unexpected death [7]. For a giant proximal PAA measuring 84.2 mm, conservative management is highly perilous. Aneurysmorrhaphy (excision of the aneurysmal wall followed by primary closure) is generally discouraged in patients with concomitant PAH due to the high risk of recurrent dilatation of the preserved native tissue [7]. Therefore, the multidisciplinary team's decision to pursue urgent surgical graft replacement aligned perfectly with the most robust available evidence for managing high-risk PAAs [7]. Due to institutional limitations, an 18F-FDG PET-CT scan could not be performed, which serves as a minor limitation in definitively ruling out subclinical metabolic activity within the vessel wall.

Conclusion

This remarkable case underscores the critical imperative of recognizing overlapping etiologies in patients presenting with complex vascular pathologies. The profound synergistic impact of mechanical right heart pressure overload combined with historical autoimmune-mediated vasculitic wall degradation can facilitate the formation of exceptionally massive, central pulmonary artery aneurysms. Crucially, this case demonstrates that immense anatomical expansion (>20 mm/year) can occur even when functional capacity and hemodynamics are stabilized with pulmonary vasodilator therapy. PAAs exceeding 55 mm, or those exhibiting rapid growth, demand prompt evaluation and urgent surgical graft replacement to avert life-threatening complications [1,7].

Patient Perspective

"Two years ago, I visited the cardiology clinic with complaints

of shortness of breath and chest pain. Following the initial tests, my doctors informed me that I had pulmonary hypertension and explained the associated risks. I was also told that there was a hole in my heart, but it could not be surgically closed at that time. I took my prescribed medications regularly and paid close attention to my diet. Within a week, my shortness of breath significantly improved, and I was able to perform my daily activities with ease, although I still experienced some breathlessness during strenuous physical exertion.

However, two months before my scheduled two-year follow-up, my symptoms began to worsen again, prompting me to visit the outpatient clinic early. The new tests revealed a severe enlargement in my lung vessels. My medical team clearly explained that the vessel could rupture at any moment and that I required urgent open-heart surgery. I ultimately decided to travel to another city to undergo this high-risk operation. I sincerely thank all the healthcare professionals involved in my diagnosis, care, and follow-up".

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