# Severe Pulmonary Arterial Hypertension Induced by Dasatinib in a Patient with Chronic Myeloid Leukemia: A Case Report

## Abstract

Pulmonary arterial hypertension (PAH) is a rare but recognized adverse effect of tyrosine kinase inhibitors, notably Dasatinib, prescribed in chronic myeloid leukemia (CML). Due to potential reversibility, prompt recognition and management are essential.  
  
We report a 60-year-old male receiving Dasatinib for CML who presented with NYHA class IV dyspnea. Echocardiography showed severe right ventricular dilation and elevated pulmonary pressures. Right heart catheterization confirmed precapillary PAH. Other causes were ruled out. Following discontinuation of Dasatinib and initiation of combination PAH-specific therapy (epoprostenol, bosentan, tadalafil), the patient demonstrated clinical and hemodynamic improvement.  
  
This case highlights the need for vigilance in patients on Dasatinib, especially when respiratory symptoms arise. Early intervention can improve outcomes in drug-induced PAH.

## Keywords

Pulmonary arterial hypertension, Dasatinib, Chronic myeloid leukemia, Tyrosine kinase inhibitors, Right heart catheterization

## Introduction

Pulmonary arterial hypertension (PAH) is a progressive and potentially fatal condition characterized by elevated pulmonary vascular resistance leading to right ventricular failure. While idiopathic forms are the most common, drug-induced PAH represents a growing subset of secondary cases. Among chemotherapeutic agents, Dasatinib—a second-generation tyrosine kinase inhibitor (TKI) primarily targeting BCR-ABL and SRC family kinases—has emerged as a well-documented cause. First identified as a risk in 2009, Dasatinib-induced PAH (D-PAH) remains rare but can be severe and sometimes irreversible. The pathophysiology is believed to involve direct endothelial injury, reduced nitric oxide availability, mitochondrial dysfunction, and vascular remodeling.  
  
The European Medicines Agency and FDA have both issued warnings regarding this potential adverse effect. Importantly, D-PAH is potentially reversible if identified early and managed appropriately, typically through drug discontinuation and pulmonary vasodilator therapy. Despite this, many cases are diagnosed late due to nonspecific respiratory symptoms and low clinical suspicion.  
  
Herein, we present a severe case of D-PAH in a patient with chronic myeloid leukemia (CML), highlighting the need for clinical vigilance and the benefits of early, targeted therapeutic intervention.

## Case Presentation

A 60-year-old male with a history of chronic phase CML diagnosed in January 2023 was initially treated with Imatinib. The treatment was discontinued after three weeks due to a generalized allergic reaction with urticaria and facial swelling. The patient was subsequently switched to Dasatinib at a dose of 100 mg daily, which was well tolerated and led to complete hematologic remission within two months.  
  
By December 2024, the patient began to experience progressive dyspnea on exertion, orthopnea, and profound fatigue, ultimately classified as NYHA class IV. He denied chest pain, hemoptysis, or syncope. Physical examination revealed jugular venous distention, a right parasternal heave, loud P2, and a grade 3/6 tricuspid regurgitant murmur. Peripheral oxygen saturation was 89% on room air.  
  
Laboratory investigations showed normal thyroid function, negative HIV and hepatitis serologies, normal NT-proBNP, and no signs of infection or anemia. Electrocardiogram revealed right axis deviation and signs of right ventricular strain.  
  
Transthoracic echocardiography demonstrated marked right atrial and ventricular dilation, elevated systolic pulmonary artery pressure (105 mmHg), flattening of the interventricular septum, and a preserved left ventricular ejection fraction (67%). The tricuspid annular plane systolic excursion (TAPSE) was 42 mm, indicating preserved right ventricular systolic function initially.  
  
A thoracic CT angiogram excluded pulmonary embolism but confirmed significant right heart enlargement and septal inversion. Pulmonary function tests showed no evidence of restrictive or obstructive defects. Right heart catheterization demonstrated a mean pulmonary artery pressure (mPAP) of 51 mmHg, pulmonary capillary wedge pressure of 10 mmHg, pulmonary vascular resistance (PVR) of 12.6 Wood Units, and a cardiac index of 1.77 L/min/m²—consistent with precapillary PAH. Vasoreactivity testing using inhaled nitric oxide was negative.  
  
Given the exclusion of other causes and temporal association with Dasatinib, the diagnosis of D-PAH was established. After multidisciplinary discussion, Dasatinib and beta-interferon (Rebif) were discontinued immediately. The patient was admitted to the intensive care unit and started on intravenous epoprostenol, along with oral bosentan and tadalafil.  
  
Over the following three weeks, the patient showed significant symptomatic relief, improvement in 6-minute walk distance, and gradual normalization of right heart size on echocardiography. After stabilization, intravenous therapy was tapered and transitioned to an oral maintenance regimen.

## Discussion

Dasatinib is a potent second-generation TKI widely used for treating CML and Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL). Although it offers improved efficacy compared to first-generation agents like Imatinib, Dasatinib has been associated with a range of pulmonary adverse effects, including pleural effusions, interstitial lung disease, and pulmonary arterial hypertension (PAH). The incidence of Dasatinib-induced PAH (D-PAH) is low, estimated between 0.45% and 1% of treated patients. However, its clinical impact can be profound, with reported cases of irreversible PAH and right heart failure.  
  
The pathophysiological mechanisms of D-PAH are multifactorial. Preclinical studies suggest that Dasatinib induces endothelial dysfunction by disrupting mitochondrial function, inhibiting Src-family kinases in pulmonary endothelial cells, and increasing reactive oxygen species production. This results in impaired vasodilation, endothelial cell apoptosis, and progressive vascular remodeling. Additionally, Dasatinib has been shown to impair hypoxic pulmonary vasoconstriction and promote a pro-inflammatory vascular environment.  
  
In our patient, the diagnosis was established based on the combination of clinical signs, echocardiographic findings, and invasive hemodynamic data. Alternative causes of PAH, including connective tissue disease, HIV, congenital heart disease, portal hypertension, and chronic thromboembolic disease, were excluded. According to the ESC/ERS 2022 guidelines, drug-induced PAH falls under Group 1 PAH, with management principles similar to idiopathic PAH, including drug withdrawal and initiation of targeted pulmonary vasodilator therapy.  
  
Several studies support the use of combination therapy in severe PAH. The AMBITION trial demonstrated improved clinical outcomes with upfront dual oral therapy (ambrisentan and tadalafil). In patients with WHO Functional Class III/IV symptoms, parenteral prostacyclin analogues like epoprostenol offer rapid hemodynamic improvement. Our decision to initiate triple therapy was based on the severity of symptoms, right heart failure, and high pulmonary vascular resistance.  
  
Reversibility of D-PAH remains variable. Some patients improve following drug discontinuation alone, while others require prolonged therapy or develop persistent PAH. In a 2020 French registry study, approximately 65% of patients had partial or complete recovery, while 35% developed chronic PAH despite treatment. This underlines the importance of early recognition, regular cardiopulmonary monitoring, and collaborative management involving cardiology, hematology, and pulmonology teams.  
  
In our case, the patient's improvement after aggressive PAH therapy suggests timely intervention was critical. Long-term follow-up with periodic echocardiography, 6-minute walk testing, and NT-proBNP monitoring is planned. Given the high likelihood of recurrence with re-challenge, Dasatinib should be permanently avoided in such cases. Alternatives like Nilotinib or Bosutinib may be considered under close supervision.

## Conclusion

This case underscores the importance of early recognition of Dasatinib-induced PAH in patients presenting with unexplained dyspnea during TKI therapy. While rare, D-PAH can be life-threatening if not diagnosed and managed promptly. Discontinuation of Dasatinib, exclusion of alternative etiologies, and initiation of combination pulmonary vasodilator therapy are key components of management.  
  
Clinicians should maintain a high index of suspicion in symptomatic patients, and routine cardiopulmonary screening may be warranted in high-risk populations. Multidisciplinary collaboration is essential for optimizing outcomes. Further studies are needed to define predictors of reversibility and guide therapeutic decisions.

**Consent**

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

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## Figures

Figure 1. Chest X-ray showing cardiomegaly and prominent pulmonary arteries.



Figure 2. Echocardiography demonstrating right ventricular dilation and elevated pulmonary artery pressure.

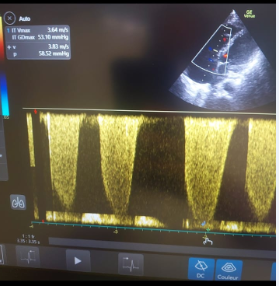


Figure 3. Thoracic CT scan revealing right heart dilation and septal inversion.

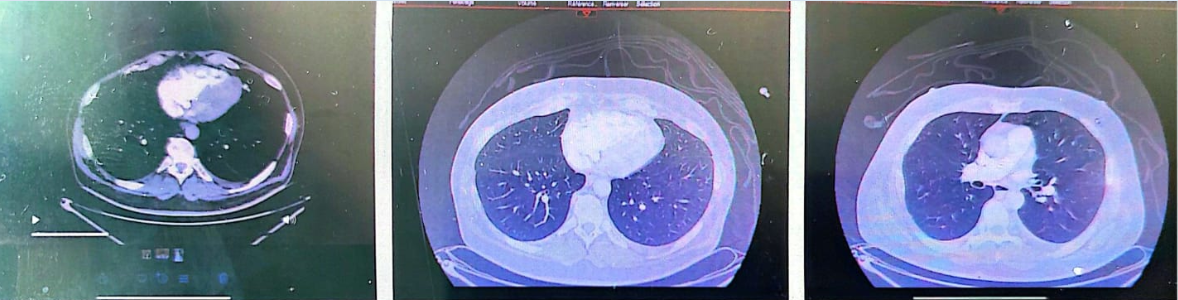


Figure 4. Right heart catheterization waveform showing precapillary pulmonary arterial hypertension.

