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Case Report

Dasatinib-Induced Pulmonary Arterial Hypertension: A Case Report

Dr.Amit Kumar Pandey[*1], Dr.Krishan Kumar [2], Dr.Darshak Mehul Patel[3], Dr.Anubha Tiwari [4]

1. Senior Consultant Pulmonary and Critical Care medicine Midland healthcare and Research Centre.

2,3,4. DNB Respiratory Medicine,Midland healthcare and Research Centre.

Correspondence to: Dr.Amit Kumar Pandey , Senior Consultant Pulmonary and Critical Care medicine Midland healthcare and Research Centre.

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Abstract

Background: *Dasatinib, a second-generation tyrosine kinase inhibitor (TKI), is widely used in the treatment of chronic myeloid leukemia (CML). Although effective, it has been rarely associated with pulmonary arterial hypertension (PAH), a potentially reversible condition,but severe adverse effect.*

Case Presentation: *We describe a 34-year-old man with CML who presented with progressive exertional dyspnea and features of right heart failure while on long-term dasatinib therapy. Echocardiography demonstrated severe pulmonary hypertension (RVSP 96 mmHg) with marked right ventricular enlargement and compression of the left ventricle. Computed tomography excluded pulmonary thromboembolism. Dasatinib was discontinued, and treatment with tadalafil, ambrisentan, and conventional heart-failure therapy was initiated, followed by switch to nilotinib. The patient demonstrated progressive symptomatic and hemodynamic improvement over serial follow-up.*

Conclusion: *Dasatinib-induced PAH (DASA-PAH) is an uncommon but clinically significant complication. Prompt recognition and cessation of dasatinib, coupled with pulmonary vasodilator therapy, can lead to substantial or even complete recovery.*

Keywords: *Dasatinib, Tyrosine kinase inhibitor, Pulmonary arterial hypertension, Chronic myeloid leukemia, Reversible PAH.*

Introduction

Dasatinib, an oral second-generation TKI targeting BCR-ABL and SRC kinases, has become a first-line therapy for CML and Philadelphia chromosome–positive acute lymphoblastic leukemia. Although generally well tolerated, post-marketing data have revealed its association with pleural effusion and, rarely, pulmonary arterial hypertension (PAH).

Since the initial reports from European pharmacovigilance registries, more than a hundred cases of dasatinib-induced PAH (DASA-PAH) have been described, with varying degrees of reversibility after discontinuation. The exact pathophysiological mechanism remains unclear but likely involves endothelial injury, vascular remodeling, and immune-mediated processes.

We report a typical case of DASA-PAH presenting with severe right heart failure, which improved substantially following drug withdrawal and vasodilator therapy.

Case Presentation

A 34-year-old male presented with progressive shortness of breath on exertion, associated with intermittent cough, lower limb swelling, abdominal distension, and easy fatigability. His symptoms had been slowly progressive for a year, worsening in the preceding 15 days.

He had been diagnosed with CML at age 26 and was initially treated with 6-mercaptopurine and methotrexate, later transitioned to dasatinib 75 mg twice daily as first-line TKI therapy. After three years, cytopenias prompted step-wise dose reduction to 50 mg twice daily and subsequently 75 mg once daily.

At presentation, he had no history of connective-tissue disease, HIV infection, or congenital heart disease.

Clinical findings: On examination, jugular venous distension, hepatomegaly, ascites, and severe bilateral pitting pedal edema were present. Cardiac auscultation revealed a loud P2 and systolic murmur along the left sternal border

Investigations:

• **Electrocardiogram:** Right axis deviation with tall R waves in V1 (R/S > 1).

• **Echocardiography:** Dilated right atrium and ventricle with markedly elevated right ventricular systolic pressure (RVSP ≈ 96 mmHg), flattening of the interventricular septum, and compressed left ventricle.

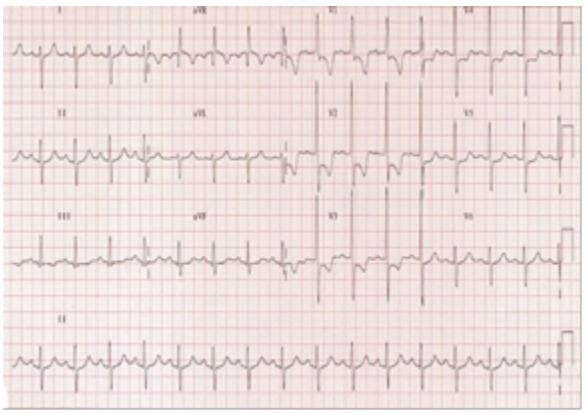
• **Laboratory:** NT-proBNP markedly elevated (1086 pg/mL).

• **Chest X-ray / CT thorax**: Bilateral pleural effusions (right > left).

• **CT pulmonary angiography:** No filling defects; pulmonary embolism excluded.

• **Abdominal ultrasonography:** Gross ascites without portal hypertension.

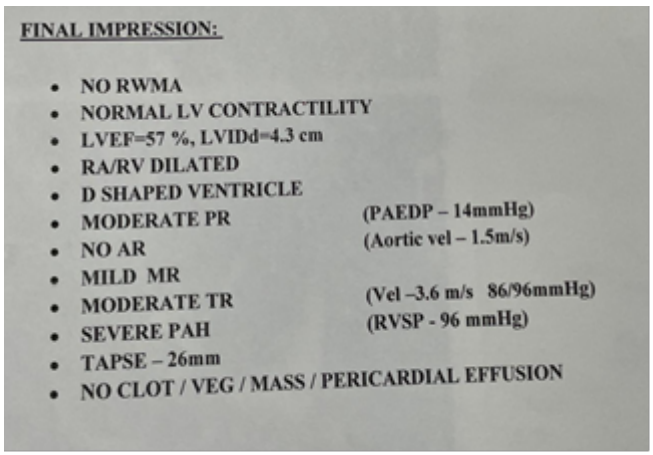
ELECTROCARDIOGRAPHY



ECG shows Right Axis deviation, R/S > 1 in V1

Figure. 1

ECHOCARDIOGRAPHY



TRANSTHORACIC ECHOCARDIOGRAPHY at the time of admission showing dilated RA & RV, RVSP – 96 mmhg

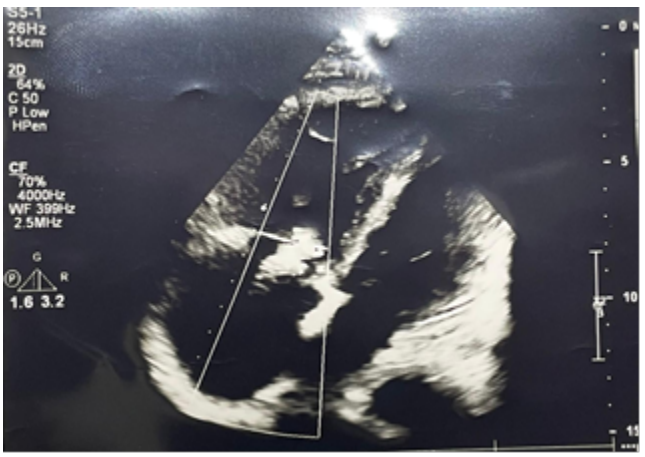


Figure 2

FINAL IMPRESSIONS:

- NO RWMA
- NORMAL LV CONTRACTILITY
- LVEF =64%, LVIDD = 5.6CM
- NO MR / AR (Aortic vel - 1.0 m/s)
- MILD TR (velocity = 3.2 m/s /42/47mmHg)
- MILD PAH (RVSP=47mmHg)
- ALL CHAMBERS ARE NORMAL

CT SCAN

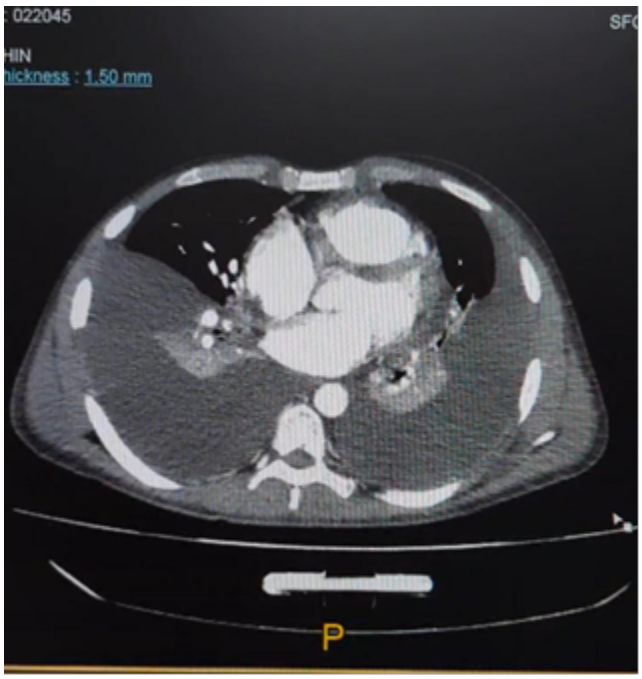


Figure 3. CT SCAN mediastinal window showing bilateral pleural effusion (right > left).

CT PULMONARYANGIOGRAPHY

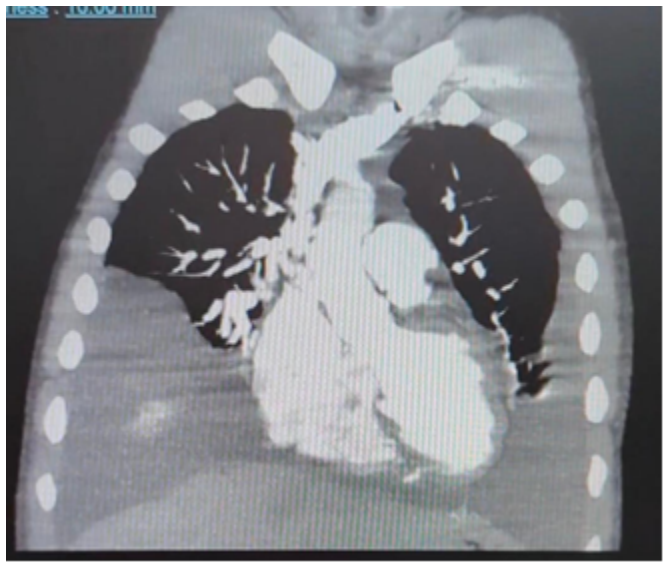


Figure 4. CTPA SHOWING NO EVIDENCE OF THROMBOEMBOLISM WITH BILATERAL PLEURAL EFFUSION (RT > LT)

USG WHOLE ABDOMEN

Electrocardiography (Figure 1) and TTE (Figure 2A) on admission indicated severe right ventricular pressure overload. Physical examination showed jugular vein dilatation. Right lung percussion dulled. Left lung respiratory sound decreased and right lung respiratory sound disappeared. No obvious crepetations were heard. Cardiac auscultation revealed P2 hyperactivity and a systolic murmur on the left sternum 4–5 intercostal. Gross ascites and Severe pitting edema of both lower extremities was found. Laboratory data showed markedly elevated N-terminal of the prohormone brain natriuretic peptide (NT-proBNP) (1086.0 pg/mL; normal reference value, <100 pg/mL). X-ray and chest computed tomography (CT) scan showed large pleural effusion on the right chest (around 1100 ml) and small on the left (around 850 ml). (Figure 3). No evidence of pulmonary embolism showed by CT Pulmonary Angiography (Figure 4). Abdominal ultrasonography showed gross ascites and no evidence of portal hypertension (Figure 5). Initially tadalafil (10 mg once daily) and ambrisentan (5 mg once daily) was added to the treatment.

The amount of tadalafil, ambrisentan was gradually increased during follow-up, tadalafil (20 mg o.d.) and ambrisentan (10 mg o.d.). Nilotinib (300 mg qd8) was added on discharge and advised to follow up after 8 days. The patient's activity tolerance gradually restored during follow-up. The patient was followed up every three months in our Pulmonary Department, and rechecked for echocardiography every 3 monthly.

Management:

Dasatinib was immediately withdrawn. Tadalafil (10 mg → 20 mg once daily) and ambrisentan (5 mg → 10 mg once daily) were initiated for pulmonary vasodilatation, along with standard diuretic-based anti-heart-failure therapy. Nilotinib (300 mg once daily) was introduced as an alternative TKI prior to discharge.

Follow-up:

Over the ensuing three months, the patient experienced marked improvement in functional status and exercise tolerance. Repeated echocardiography at three-month intervals showed gradual reduction in pulmonary pressures and right ventricular size.

Discussion

Dasatinib exerts broad kinase inhibition, including the SRC family, which may contribute to endothelial dysfunction and pulmonary vascular remodeling. Unlike imatinib or nilotinib, dasatinib uniquely predisposes to pulmonary vascular injury.

Pathophysiology:

Experimental studies suggest a "two-hit" hypothesis—dasatinib-induced endothelial sensitization followed by a secondary insult (e.g., hypoxia, infection, or autoimmune activation) precipitating PAH. In a rat model, pre-exposure to dasatinib enhanced monocrotaline-induced pulmonary vascular remodeling, whereas dasatinib alone did not significantly increase PAPs (Guignabert et al., 2016).

Clinical data:

A multicenter registry (Shah et al., 2015) identified 41 right-heart-catheterization-confirmed cases of DASA-PAH. Ninety-four percent improved after drug cessation, though complete resolution occurred in only 58%. Similarly, Weatherald et al. (2017) reported variable reversibility and emphasized early recognition.

Diagnosis:

DASA-PAH should be suspected in any patient on dasatinib who develops unexplained dyspnea, pleural effusion, or signs of right heart failure. Diagnostic work-up includes echocardiography, right heart catheterization (if available), and exclusion of secondary causes of PAH.

Management:

The cornerstone of management is immediate discontinuation of dasatinib. Pulmonary vasodilators such as phosphodiesterase-5 inhibitors (tadalafil, sildenafil) and endothelin-receptor antagonists (ambrisentan, bosentan) are effective adjuncts. Conventional heart-failure measures (diuretics, salt restriction) aid symptom control.

Rechallenge with dasatinib is contraindicated; alternative TKIs such as nilotinib or bosutinib may be considered under hematologic supervision.

Prognosis and follow-up:

While the majority demonstrate improvement within weeks to months, residual pulmonary hypertension may persist in some, necessitating long-term vasodilator therapy. Serial echocardiography every 3–6 months is recommended. Withdrawal of pulmonary vasodilators can be cautiously attempted after sustained hemodynamic normalization for at least one year, though evidence remains limited.

Preventive considerations:

Given the rarity but seriousness of this toxicity, baseline and periodic cardiopulmonary screening—comprising ECG and echocardiography—is advisable for all patients on long-term dasatinib. Awareness of early respiratory symptoms facilitates timely intervention and improved outcomes.

Conclusion

Dasatinib-induced pulmonary arterial hypertension represents a rare yet potentially reversible complication of CML therapy. Early identification, prompt discontinuation of dasatinib, and appropriate initiation of pulmonary vasodilator and heart-failure therapy can achieve substantial clinical recovery. Comprehensive cardiopulmonary monitoring should be integral to the management of all patients receiving dasatinib to enable early detection and intervention.

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