CASE REPORT

JIACM 2026; 27 (1): 69-71

Imatinib-Induced Interstitial Lung Disease Successfully Switched to Nilotinib

Kamran Chaudhary, Chandan Kumar***

Abstract

Imatinib mesylate (IM) is a tyrosine kinase inhibitor (TKI) approved for treating Philadelphia-positive chronic myeloid leukaemia (Ph+ CML). Although it is mostly well tolerated, IM-induced interstitial lung disease (ILD) is a rare phenomenon and consensus regarding its management is lacking. We describe a case of IM-induced ILD in a patient with CML, that demonstrated significant clinico-radiological resolution after discontinuation of IM, and switching to Nilotinib along with oral corticosteroid therapy.

Key words: Imatinib, Interstitial Lung disease, Nilotinib, CML.

Introduction

Imatinib mesylate (IM) was the first approved tyrosine-kinase inhibitor (TKI) that revolutionised the treatment of Philadelphia-positive, Ph+ chronic myeloid leukaemia (Ph+ CML). Imatinib competitively blocks the adenosine triphosphate (ATP) binding site of several tyrosine kinases that are responsible for clonal cell proliferation. It is also approved for the treatment of acute lymphoblastic leukaemia (Ph+ALL), Gastro-intestinal stromal tumour (GIST), myelodysplastic/myeloproliferative diseases, systemic mastocytosis and hypereosinophilic syndrome[1,2].

Imatinib is generally well tolerated. Pleural effusions have been reported in 1 - 6% of cases, with resolution after withdrawal of the drug[1]. Interstitial lung disease with Imatinib is considered rare. Although the mechanism of ILD with TKI is unclear, recent evidence suggests a role of T-helper cell-mediated hypersensitivity reaction and immune complex deposition[3]. Here we describe a patient with CML who developed imatinib-induced ILD, with significant clinico-radiological resolution after discontinuation of the drug, adding corticosteroids and switching to Nilotinib.

Case history

A 49-year-old male was diagnosed with Ph+ CML, in January 2022. He was commenced on Imatinib (IM) therapy at a dose of 400 mg daily. The patient tolerated the medication well and had achieved complete haematological remission at 6 months. He presented to the respiratory medicine outpatient clinic in October 2023 with gradually progressive breathlessness on exertion, modified medical research council (MMRC) grade three, dry cough for two months, with no history of fever. He did not have any other co-morbid condition. He was a former smoker of twenty pack years. On examination, his room air saturation was 94%, no clubbing, bibasal inspiratory crackles on auscultation. A chest X-ray showed bilateral diffuse reticular shadows (Fig. 1). A high-resolution computed tomography scan (HRCT) of the chest showed bilateral ground glass opacities, with interstitial septal thickening and traction bronchiectasis involving bilateral lower lobes with diffuse centriacinar and paraseptal emphysematous changes (Fig. 2).

His routine laboratory investigations including acute phase reactants were within normal limits. He was started on broad-spectrum antibiotics. His sputum culture, acid-fast bacilli (AFB) smear, sputum Gene Xpert, fungal stain and fungal culture reports were negative. Anti-nuclear antibody (ANA) and a complete autoimmune profile panel were also negative. Spirometry showed a forced expiratory volume in one second (FEV1) of 3.19 L (80% predicted), forced vital capacity (FVC) of 3.2 L (66% predicted) and reduced diffusion capacity of lungs for carbon monoxide (DLCO) of 4.1 mmol/min/Kpa (51% predicted). Thus, imatinib-induced interstitial lung disease was suspected on clinical and radiological grounds, after ruling-out infectious causes, and imatinib was stopped. Oral corticosteroids were started at 40 mg once daily and then slowly tapered over 3 months. Nilotinib was started as an alternative to Imatinib at a dosage of 400 mg twice daily, which was well tolerated and haematological remission was sustained at three months follow-up. The patient was also provided with bronchodilators for underlying emphysema. A repeat HRCT chest scan in December 2023 showed significant resolution of ground glass opacities and septal thickening (Fig. 3). The

Head, **Senior Resident, Department of Respiratory Medicine, Indira Gandhi Hospital (Government of NCT of Delhi), Dwarka, New Delhi - 110 077.

Corresponding Author: Dr Kamran Chaudhary, Head, Department of Respiratory Medicine, Indira Gandhi Hospital (Government of NCT of Delhi), Dwarka, New Delhi - 110 077. Tel: 9871022476, E-mail: kamran851@gmail.com

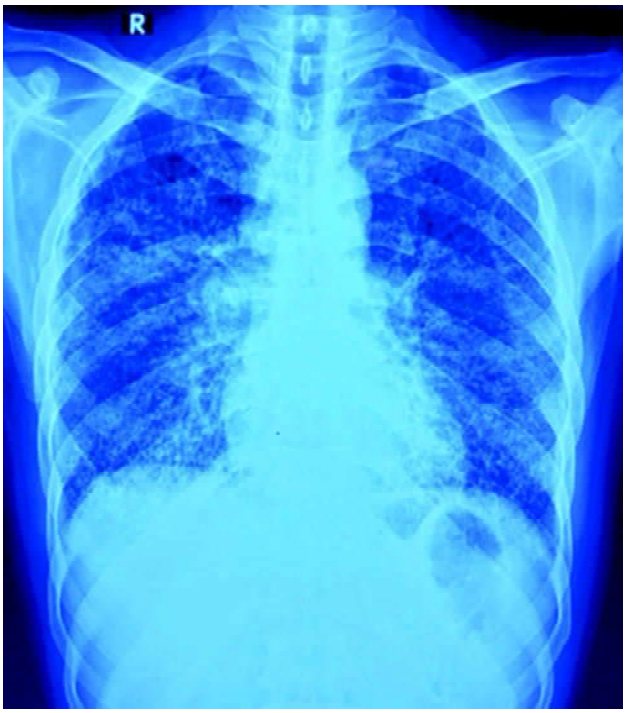

Fig. 1: *Chest X-ray on presentation showing bilateral diffuse reticular shadows.*

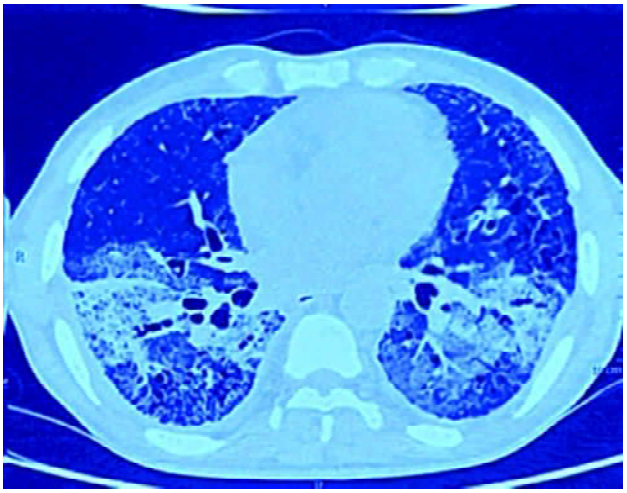

Fig. 2: *CT chest (October 2023) shows bilateral ground glass opacities, septal thickening and traction bronchiectasis.*

patient also reported improvement in dyspnoea with a room air saturation of 96%. Oral corticosteroids were tapered off at three months and Nilotinib was continued for CML.

Discussion

Imatinib is mostly well tolerated with mild adverse reactions including gastrointestinal disturbances, fluid retention and myalgias. IM-induced interstitial lung disease (ILD) is rare, with a median onset of 49 days (14 - 282 days). One study

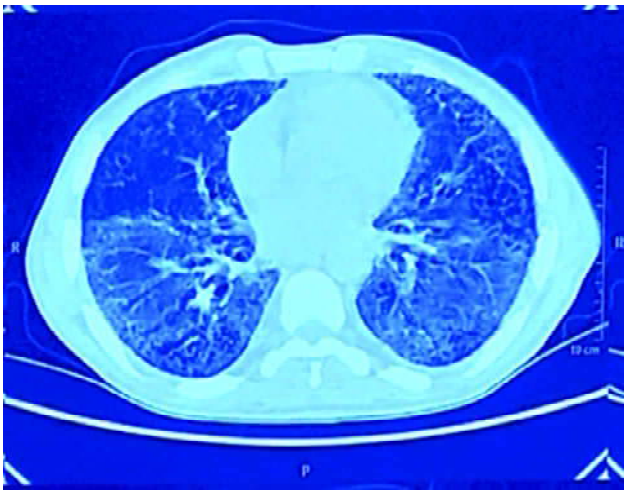

Fig. 3: *CT chest (December 2023) shows significant resolution of ground glass opacities.*

reported an onset of 2 weeks after discontinuation of IM, with clinico-radiological improvement after treatment with corticosteroids[1,3]. Commonly reported radiological features include bilateral nodular, interstitial or ground glass opacities or organising pneumonia[1]. In a large Japanese case series involving 27 cases of IM-induced ILD, 24 patients received corticosteroids. Most patients recovered, while five patients showed no improvement. A pre-existing lung disease was identified as a risk factor for the development of IM-induced lung disease[4]. In this case, emphysema was considered to be the pre-existing pulmonary disease predisposing to IM-induced ILD.

Nilotinib, a second-generation TKI, has a twenty-fold higher affinity for BCR-ABL kinases. It has been approved for the treatment of CML in patients with imatinib resistance or intolerance. There have been few reports of the development of pleural effusions and interstitial pneumonitis with Nilotinib[2]. However, many studies have shown substituting Nilotinib for imatinib to be favourable in the management of IM-induced interstitial lung disease in patients with CML. A study by Zhang *et al* reported worsening clinical symptoms after re-introducing imatinib in a patient with CML and IM-induced ILD one month after it had been stopped. The clinical symptoms subsided, lung functions improved and sustained remission was achieved after substitution with Nilotinib[5]. Another case of IM-induced ILD that had developed in a previously treated patient of pulmonary tuberculosis, was successfully switched to Nilotinib. The patient demonstrated sustained remission with lung function improvement and partial radiological resolution after 8 months of follow-up[6]. However, one study by Cho *et al* reported nilotinib-induced irreversible fibrotic ILD that responded to corticosteroids and a change of medication to ponatinib for CML treatment[7].

The mainstay of treatment involves discontinuation of Imatinib. Most studies have reported initiation of corticosteroids followed by gradual tapering over two to three months, resulting in clinical, radiological and lung function improvement. However, development of a fibrotic pattern of ILD, that is likely related to the duration of imatinib exposure, usually does not respond to corticosteroid treatment and is associated with poor outcomes[7]. Switching to Nilotinib or an alternate TKI can be considered in patients who develop ILD associated with Imatinib.

Conclusion

Imatinib-induced interstitial lung disease is an uncommon but serious condition with varied radiological patterns. Hence, it is important to monitor patients regularly for IM-induced ILD, especially those with underlying chronic lung disease. Discontinuation of Imatinib along with initiation of corticosteroids and switching to a different TKI has demonstrated favourable clinical and radiological outcomes.

Key Messages: *Imatinib-induced interstitial lung disease is an uncommon but serious condition. Patients on Imatinib therapy should be regularly monitored especially those with an underlying chronic lung disease. Withdrawal of the drug, switching to a different TKI along with corticosteroid therapy should be considered in patients developing ILD due to Imatinib.*

References

1. Yoneda KY, Cross CE. The Pulmonary Toxicity of Anticancer Agents, Comprehensive Toxicology (second edition). *Elsevier* 2010: 477-510.
2. Weatherald J, Bondeelle L, Chaumais M-C *et al*. Pulmonary Complications of Bcr-Abl Tyrosine Kinase Inhibitors. *Eur Respir J* 2020; in press (https://doi.org/10.1183/13993003.00279-2020)
3. Nakashima S, Kakugawa T, Motomura H *et al.* Development of imatinib mesylate-induced interstitial lung disease 2 weeks after discontinuation of the treatment: a case report. *Multidiscip Respir Med* 2012; 7: 48.
4. Ohnishi K, Sakai F, Kudoh S. Twenty-seven cases of drug-induced interstitial lung disease associated with imatinib mesylate. *Leukaemia* 2006; 20 (6): 1162-4.
5. Zhang P, Huang J, Jin F. Imatinib-induced irreversible interstitial lung disease: A case report. *Medicine (Baltimore)* 2019; 98 (8): e14402.
6. Luo ZB, Xu N, Huang XP. Imatinib-Induced Interstitial Pneumonitis Successfully Switched to Nilotinib in a Patient with Prior History of Mycobacterium tuberculosis Infection. *Turk J Haematol* 2017; 34 (4): 362-4.
7. Cho JY, Lee OJ, Kwon J. A case report of nilotinib-induced irreversible interstitial lung disease. *Medicine (Baltimore)* 2022; 101 (4): e28701.