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Lenalidomide and Bortezomib-Induced Interstitial Lung Disease in a Patient with Multiple Myeloma: A Case Report

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Abstract

We report a rare case of interstitial lung disease (ILD) in a 74-year-old Australian woman with multiple myeloma (MM) treated with RVd (lenalidomide, bortezomib, dexamethasone) induction followed by lenalidomide and dexamethasone maintenance. She developed progressive dyspnoea and imaging revealed bilateral ground-glass opacities with a 37.4% reduction in diffusing capacity for carbon monoxide (DLCO). Cardiac, autoimmune, and infectious causes were excluded. Her symptoms worsened during second-line DVd (daratumumab, bortezomib, dexamethasone) therapy. Marked improvement occurred following discontinuation of therapy and initiation of oral corticosteroids (prednisone). However, residual fibrotic changes persisted, suggesting irreversible pulmonary damage from cumulative drug exposure. This case, the first reported in Australia implicating both lenalidomide and bortezomib in ILD, emphasizes the importance of early recognition of respiratory toxicity in patients with MM on combination therapy.

Keywords: Lenalidomide; Bortezomib; Interstitial lung disease; Multiple myeloma; Drug-induced pneumonitis

Introduction

Multiple myeloma (MM) is a plasma cell malignancy treated with immunomodulatory agents (IMiDs) such as lenalidomide and proteasome inhibitors like bortezomib. These therapies have improved survival outcomes but may lead to rare yet serious pulmonary complications, including interstitial lung disease (ILD). ILD associated with anti-myeloma therapy can present as dyspnoea, dry cough, or hypoxia, and radiologically manifest with ground-glass opacities, reticular changes, or fibrosis. Lenalidomide-induced ILD is rare, with a reported incidence of approximately 0.76%, while bortezomib has a post-market pulmonary toxicity rate of approximately 3.77%, particularly noted in East Asian cohorts. Combination regimens may heighten pulmonary risk due to synergistic toxicity. Early diagnosis is essential to prevent irreversible fibrosis. We present an Australian case of ILD attributed to sequential lenalidomide and bortezomib use, highlighting diagnostic challenges and the value of corticosteroid intervention.

Case Presentation

A 74-year-old Australian woman was diagnosed with IgA kappa MM in August 2021, presenting with anaemia (Hb 85 g/L), hypercalcaemia (corrected calcium 2.8 mmol/L), and widespread osteolytic lesions. Initial staging was ISS stage II. She had no smoking history, no known environmental exposures, and no prior lung disease. She commenced six cycles of RVd chemotherapy: lenalidomide 25 mg (days 1–21), bortezomib 1.3 mg/m² (days 1, 4, 8, 11), and dexamethasone 40 mg weekly. She achieved complete remission by Cycle 6 (undetectable paraprotein, normal bone marrow). From Cycle 3 onwards, she developed mild exertional dyspnoea, initially attributed to anemia and deconditioning. Echocardiography showed normal left ventricular function and mild pulmonary hypertension (RVSP ~30 mmHg). Due to poor stem cell mobilization, she was

ineligible for autologous transplantation and transitioned to lenalidomide maintenance (10 mg days 1–21) with weekly dexamethasone (20 mg). Over 32 cycles (30 months), she remained in hematologic remission but experienced insidious worsening of dyspnoea. By mid-2024, she had MMRC Grade 3 dyspnoea, requiring rest after minimal exertion.

In September 2024, she developed new back pain and biochemical relapse (IgA 8 g/L; kappa free light chain 66.5 mg/L). Second-line DVd was initiated (daratumumab 16 mg/kg weekly, bortezomib 1.3 mg/m² weekly, and dexamethasone 20 mg weekly). Gastrointestinal side effects improved, but her dyspnoea progressed rapidly over three cycles to Grade 3–4. She could walk only a few steps without breathlessness. On days following dexamethasone administration, she experienced transient improvement. A CT pulmonary angiogram (January 2025) showed bilateral ground-glass opacities and reticular changes, predominantly in the lower lobes. Pulmonary function testing revealed a 37.4% reduction in DLCO (from 6.7 to 4.2 mmol/min/kPa), with preserved FVC (2.8 L, 92% predicted). ABG demonstrated respiratory alkalosis (pH 7.48, pCO_2 32 mmHg). Transthoracic echocardiography showed no change. Autoimmune serologies (ANA, ENA, ANCA, RF) were negative. Bronchoscopy with bronchoalveolar lavage (BAL) ruled out infection or malignancy, with a lymphocytic inflammatory pattern noted. A clinical diagnosis of drug-induced ILD was made. The DVd regimen was discontinued after three cycles in May 2025. She was concurrently commenced on oral prednisone 25 mg daily, with a planned taper over six weeks. Her respiratory symptoms improved markedly within two weeks. By June 2025, she resumed her daily activities with only mild exertional dyspnoea (Grade 1). A follow-up HRCT demonstrated partial resolution of ground-glass opacities but persistent bilateral fibrotic changes.

Discussion

This case demonstrates a delayed but progressive presentation of drug-induced ILD following long-term lenalidomide exposure, exacerbated by bortezomib during relapse therapy. The clinical and radiological course, improvement with corticosteroids, and exclusion of other causes strongly support a drug-related mechanism. Lenalidomide may induce ILD via inhibition of prostaglandin E_2 synthesis, leading to unchecked fibroblast activation, or via delayed hypersensitivity pneumonitis. Bortezomib's mechanism is less defined but may involve TNF-α and IL-6 mediated pulmonary inflammation or proteasomal interference in alveolar cell repair. In the literature, most lenalidomide-related ILD cases occurred within 3–5 months of therapy initiation. Our patient, however, developed symptoms insidiously over 30 months, which may have masked early pulmonary toxicity. Bortezomib reintroduction likely exacerbated the injury (Figures 1,2) (Table 1).

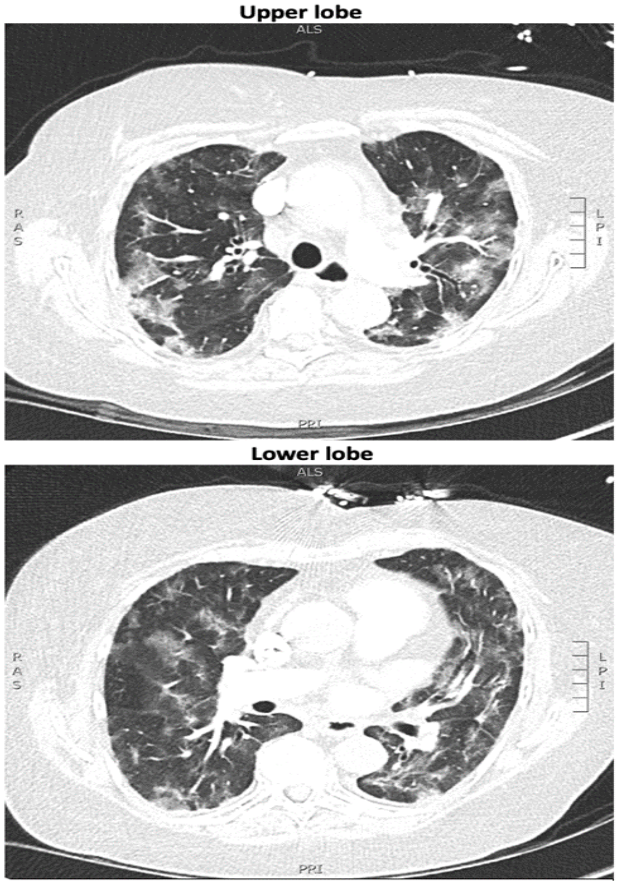

Figure 1: *CT pulmonary angiogram (January 2025) showing bilateral lower zone ground-glass opacities and reticular changes.*

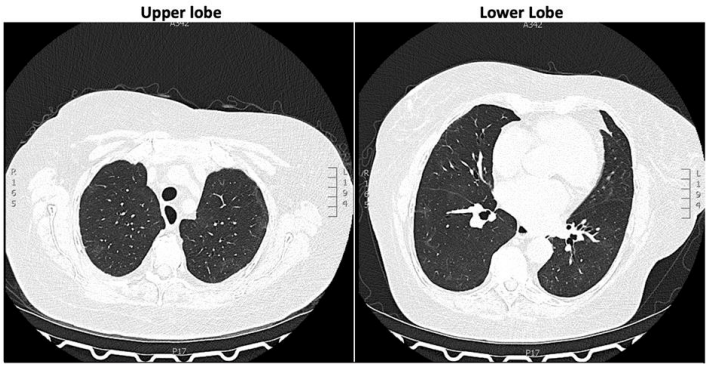

Figure 2: *High-resolution CT (May 2025) demonstrating persistent fibrotic changes despite partial resolution of acute infiltrates.*

Japanese post-marketing studies highlighted a higher incidence of bortezomib-associated ILD. The concurrent use of both agents, as in RVd and DVd regimens, likely increases pulmonary risk. Improvement in symptoms and radiology with corticosteroid therapy (prednisone 25 mg daily tapered) supports an inflammatory rather than fibrotic predominant process, though HRCT indicated residual fibrosis. Notably, lenalidomide

monographs in the Australian Medicines Handbook and eviQ do not currently list ILD as a major standalone adverse effect but do caution regarding pulmonary events in combination protocols. This case reinforces the need for vigilance and early diagnostic evaluation in MM patients with unexplained respiratory decline [1-15].

Table 1: *Pulmonary Function Tests (2021 vs. 2025).*

Year	DLCO (mmol/min/kPa)	FVC (L)	% Predicted FVC
2021	6.7	2.9	95%
2025	4.2 (↓37.4%)	2.8	92%

Conclusion

Lenalidomide- and bortezomib-associated ILD is rare but potentially irreversible if unrecognized. This case illustrates progressive respiratory decline during maintenance and relapse therapy in an MM patient, ultimately improving with cessation of the offending agents and corticosteroid therapy. Despite partial clinical recovery, persistent fibrotic changes were evident on follow-up imaging. Clinicians should maintain a high index of suspicion for ILD in MM patients receiving long-term or combination regimens and consider early intervention with imaging, lung function testing, and corticosteroids.

References

1. Palumbo A, Anderson K. Multiple myeloma. N Engl J Med. 2011; 364: 1046-1060.
2. Camus P, Kudoh S, Ebina M. Interstitial lung disease associated with drug therapy. Br J Cancer. 2004; 91: S18-S23.
3. Vahid B, Marik PE. Pulmonary complications of novel antineoplastic agents. Am J Med. 2008; 121: 93-97.
4. Skeoch S, Weatherley N, Swift AJ, Oldroyd A, Johns C, Hayton C, et al. Drug-induced interstitial lung disease: A systematic review. J Clin Med. 2018; 7: 356.
5. Celgene Corporation. Lenalidomide safety profile update. Drug Safety Communication. 2011.
6. Zagouri F, Roussou M, Kastritis E, et al. Lenalidomide-associated pneumonitis. Leuk Lymphoma. 2016; 57: 1698-1703.
7. Miyakoshi S, Kami M, Yuji K, Matsumura T, Takatoku M, Sasaki M, et al. Severe pulmonary complications in Japanese patients after bortezomib. Blood. 2006; 107: 3492-3494.
8. Dimopoulos MA, Richardson PG, Moreau P, Anderson KC. Treatment landscape for relapsed MM. Nat Rev Clin Oncol. 2015; 12: 42-54.
9. Chen Y, Huang X, Li J. Mechanisms of lenalidomide-induced pulmonary toxicity. J Clin Oncol. 2012; 30: e18001.
10. Sasaki M, Isobe Y, Miura Y. Lenalidomide-induced organizing pneumonia. Respir Med Case Rep. 2019; 28: 100876.
11. Chen R, Chen J, Zhang Q. Delayed diagnosis of lenalidomide-induced ILD. Clin Case Rep. 2020; 8: 349-352.
12. Kim YJ, Kim JG, Kim JH. Bortezomib-induced ILD. Acta Haematol. 2013; 130: 112-115.
13. Park HS, Lee SH, Kim JH. Bortezomib-associated pulmonary fibrosis. Int J Hematol. 2015; 102: 369-372.
14. Australian Medicines Handbook. Lenalidomide monograph. AMH Online. 2024.
15. eviQ Cancer Treatments Online. Lenalidomide combination adverse effects. eviQ. 2024.