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CASE REPORT

Lenalidomide-Induced Interstitial Pneumonitis in a Patient with Multiple Myeloma: A Case Report

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Abstract

Lenalidomide, a second-generation immunomodulatory agent used in the treatment of multiple myeloma (MM), is generally well tolerated. Pulmonary toxicity, though rare, can present as interstitial pneumonitis, leading to diagnostic challenges. We describe a case of a 67-year-old man with relapsed MM who developed progressive dyspnea and cough after initiation of lenalidomide. High-resolution chest CT revealed bilateral ground-glass opacities suggestive of interstitial lung disease. Infectious, autoimmune, and cardiogenic causes were excluded. Symptoms and imaging abnormalities resolved upon discontinuation of lenalidomide and initiation of corticosteroids. This case illustrates the need for awareness of lenalidomide-induced pneumonitis as a potential but reversible adverse event in MM patients, emphasizing early recognition and drug withdrawal.

1. Introduction

Lenalidomide is a widely used immunomodulatory derivative of thalidomide, approved for treatment of various hematological malignancies, particularly multiple myeloma (MM) (Kumar and Rajkumar, 2006). It functions by modulating the cereblon E3 ubiquitin ligase complex, thereby enhancing immune activity and promoting tumor cell apoptosis (Zhou and Xu, 2022). Despite its efficacy, lenalidomide can cause several adverse effects, including hematologic toxicity, thromboembolic events, and gastrointestinal disturbances (Rodríguez, 2011).

Pulmonary toxicity, particularly interstitial pneumonitis, remains a rare but serious complication of lenalidomide (O'Meara et al., 2024). The nonspecific respiratory symptoms and overlap with infections or cardiopulmonary diseases make diagnosis challenging. Drug-induced interstitial lung disease (ILD) accounts for a small percentage of adverse drug reactions but can lead to significant morbidity if unrecognized. Here, we report a case of lenalidomide-induced interstitial pneumonitis in a patient with relapsed MM, which resolved after cessation of the drug and administration of corticosteroids.

2. Case Report

A 67-year-old man with a 2-year history of IgG kappa multiple myeloma presented to the emergency department with worsening shortness of breath, dry cough, and low-grade fever for 7 days. He was recently started on lenalidomide (25 mg/day for 21 days of a 28-day cycle) in combination with dexamethasone (40 mg weekly) for relapsed disease. This was his second cycle of lenalidomide-based therapy (Table 1).

Prior treatments included bortezomib-dexamethasone and autologous stem cell transplantation, after which he remained in partial remission for 18 months.

On examination, the patient had a respiratory rate of 24 breaths per minute, oxygen saturation of 89% on room air, and bilateral fine inspiratory crackles. There was no peripheral edema or jugular venous distension.

Extensive microbiologic work-up including sputum and blood cultures, testing for COVID-19, influenza, pneumocystis jirovecii (PCR), and fungal markers were negative. Autoimmune serologies (ANA, ANCA, RF) and echocardiography were normal.

Given the temporal correlation with lenalidomide

Table 1: Initial Clinical and Laboratory Data

Parameter	Value	Reference Range	Interpretation
Temperature	37.8°C	<37.5°C	Low-grade fever
SpO_2 (room air)	89%	>95%	Hypoxia
WBC count	7.4 ×10^3/μL	4–11 ×10^3/μL	Normal
CRP	32 mg/L	<5 mg/L	Elevated
NT-proBNP	168 pg/mL	<300 pg/mL	Normal
Chest X-ray	Bilateral haziness	—	Suggestive of infiltrates
High-Resolution CT	Ground-glass opacities	—	Interstitial pneumonitis

initiation, absence of other causes, and typical radiologic findings, a diagnosis of lenalidomide-induced interstitial pneumonitis was made.

Lenalidomide was discontinued, and the patient was initiated on oral prednisone 1 mg/kg/day. Oxygen supplementation was continued for 72 hours, after which saturation improved to 96% on room air.

3. Discussion

Lenalidomide-induced interstitial pneumonitis is an underrecognized but increasingly reported complication (Iino, 2012). The pathogenesis is not well established but may involve immune activation and cytokine release triggered by cereblon modulation, resulting in alveolar inflammation and fibrosis.

The latency period varies from a few days to several weeks after drug initiation (Abelson et al., 2006; Behrens et al., 1999). Symptoms typically include dyspnea, cough, and fever often mimicking infection or heart failure. Imaging findings such as bilateral ground-glass opacities or diffuse infiltrates support the diagnosis but are nonspecific.

Drug-induced interstitial lung disease (DILD) is a diagnosis of exclusion (Matsuno, 2012). In our case, thorough investigations ruled out infectious, autoimmune, and cardiogenic causes. The rapid improvement following drug withdrawal and corticosteroid initiation further supports the diagnosis.

It is important to note that no dose-dependent pattern is consistently observed, and re-exposure should be avoided. Clinicians must maintain a high index of suspicion in patients presenting with respiratory symptoms on lenalidomide, particularly after the first few cycles.

4. Conclusion

Lenalidomide-induced interstitial pneumonitis, though rare, should be considered in the differential diagnosis of new-onset dyspnea in patients receiving lenalidomide for MM. Early recognition, prompt withdrawal of the offending agent, and corticosteroid therapy can lead to complete recovery. Regular respiratory assessment and patient education on symptom recognition are key to preventing morbidity.

Declarations

Ethics approval statement

No ethical approval was required for the current study as it did not deal with any human or animal samples.

Consent to participate

Not applicable

Consent to publish

Not applicable

Data Availability Statement

The data are available from the corresponding author upon reasonable request

Competing Interests

The authors declare that they have no conflict of interest

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Author contribution

Conceptualization, Data curation, Investigation, Formal analysis: D.N. Writing—review and editing: A.M.M.A.T. All authors have read and agreed to the published version of the manuscript

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Reference

1. Abelson, J., Treloar, C., Crawford, J., Kippax, S., Van Beek, I., Howard, J., 2006. Some characteristics of early-onset injection drug users prior to and at the time of their first injection. Addiction 101, 548–555. https://doi.org/10.1111/j.1360-0443.2006.01379.x
2. Behrens, D.A., Caulkins, J.P., Tragler, G., Haunschmied, J.L., Feichtinger, G., 1999. A dynamic model of drug initiation: implications for treatment and drug control. Math. Biosci. 159, 1–20. https://doi.org/10.1016/S0025-5564(99)00016-4
3. Iino, M., 2012. Interstitial pneumonitis associated with the immunomodulatory drugs thalidomide and lenalidomide. Int. J. Hematol. 95, 223–224. https://doi.org/10.1007/s12185-011-0997-2
4. Kumar, S., Rajkumar, S.V., 2006. Thalidomide and lenalidomide in the treatment of multiple myeloma. Eur. J. Cancer 42, 1612–

1622. https://doi.org/10.1016/j.ejca.2006.04.004

5. Matsuno, O., 2012. Drug-induced interstitial lung disease: mechanisms and best diagnostic approaches. Respir. Res. 13, 39. https://doi.org/10.1186/1465-9921-13-39
6. O'Meara, K.T., Fansiwala, K., Kathuria-Prakash, N., El-Masry, M., Oh, S., 2024. Acute hypoxic respiratory failure due to Lenalidomide-induced interstitial pneumonitis in a patient with multiple myeloma. BMC Pulm. Med. 24, 321. https://doi.org/10.1186/s12890-024-03129-z
7. Rodríguez, A.P.G., 2011. Management of the adverse effects of lenalidomide in multiple myeloma. Adv. Ther. 28, 1–10. https://doi.org/10.1007/s12325-010-0104-8
8. Zhou, L., Xu, G., 2022. The Ubiquitination-Dependent and -Independent Functions of Cereblon in Cancer and Neurological Diseases. J. Mol. Biol. 434, 167457. https://doi.org/10.1016/j.jmb.2022.167457