Pomalidomide Associated Pulmonary Toxicity: A Rare, Ravaging Reaction

Presenting Author	Jeremy Mark Hess, DO, Internal Medicine Resident PGY-2, Department of Medicine, New Hanover Regional Medical Center, Wilmington, NC
Co-authors	Michael Pietrangelo, DO, Internal Medicine Resident, NHRMC, Wilmington, NC; Obinna Ejimonyeugwo, MD, Internal Medicine Resident, NHRMC, Wilmington, NC
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Abstract

Introduction: Pomalidomide is an immunomodulatory imide drug (IMiD) used in the treatment of refractory multiple myeloma (MM). First approved for this indication by the FDA in 2013, when used alongside low-dose dexamethasone, for MM patients who have failed two previous therapies including lenalidomide and a protease inhibitor while exhibiting progression of their disease (1,2). This drug is a cell growth inhibitor and directly inhibits both myeloma cell expansion and angiogenesis (3). Given its powerful activity there is interest to investigate its potential effects on other cancers and it was approved for treatment of Kaposi sarcoma in May 2020 (4). The most common side effects of pomalidomide include fatigue, pancytopenia, peripheral edema, peripheral neuropathy, and gastrointestinal intolerance (5). However, less commonly but more seriously, pamolidomide has been associated with pulmonary toxicity. This case is only the seventh to ever be reported, per extensive literature review, and follows a similar pattern of restrictive lung disease and pulmonary fibrosis (6).

Case Report: A 73 year old African American male with a history of MM, stage 3a chronic kidney disease, chronic obstructive pulmonary disease, systolic heart failure, paroxysmal atrial fibrillation on warfarin, sick sinus syndrome status-post pacemaker, tobacco use disorder (20 pack-year history - stopped smoking 14 years ago), and peripheral vascular disease presented to the hospital with complaints of malaise for the past few days as well as dyspnea and a cough productive of yellow sputum. On exam the patient was elderly-appearing, cachectic with temporal wasting, a scaphoid abdomen, coarse breath sounds bilaterally, and 3+ pitting edema to bilateral lower legs. He was hypotensive, septic, and had a chest x-ray showing a small right pleural effusion and stable lung markings compared to a chest x-ray from the month prior. The patient was admitted to the intensive care unit, administered supplemental oxygen via high flow nasal cannula, and given appropriate antibiotics for what was later confirmed to be pseudomonal pneumonia. Upon more thorough review of the patient's chart, a chest CT from the prior month was found that showed substantial new fibrotic lung disease not seen on CT imaging from 4 months prior (figure 1). Interestingly, outpatient pulmonary function testing had also been completed around the same time as the abnormal chest CT the month prior which showed new restrictive lung disease: a very low diffusing capacity for carbon monoxide (DLCO) at 22% of predicted that did not correct and a reduced total lung capacity (TLC) of 62% (figure 2). Discussion with the patient's primary oncologist revealed that he had been on pomalidomide intermittently for approximately the last six years, the most recent cycle of which started 4 months ago – the same time as the stable chest CT without fibrosis. The patient's pamolidomide was stopped and high-dose prednisone was administered with mild clinical improvement, exhibited by gradually decreasing oxygen requirements in the following days. Unfortunately, after a prolonged hospital course the patient became increasingly encephalopathic and his family elected to pursue comfort care per the patient's wishes.

Final diagnosis: Pomalidomide associated restrictive lung disease with pulmonary fibrosis

Discussion: This patient's well-documented timeline of developing restrictive lung disease after starting a cycle of pamolidomide argues for the potential pulmonary toxicity of the drug even after years of previously uneventful use (figure 3). The pattern of restrictive disease with marked pulmonary fibrosis is a typical lung injury pattern with the other few reported cases (6). No other potential causes for the new-onset restrictive lung disease could be identified including a thorough medication review and interview regarding environmental exposures. There was marginal improvement in respiratory status upon drug cessation and administration of corticosteroids further supporting pamolidomide as the

offending agent. Sadly, this patient did not survive long enough to observe for potential reversal of lung injury. These findings suggest continued caution with the use of pamolidomide even in previously safe chronic use and the need to consider alternative treatment therapies if the development of new-onset of restrictive lung disease or pulmonary fibrosis are seen.

References and Resources

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Learning Objectives

-Discuss possible side effects of immunomodulatory imide drugs used in the treatment of multiple myeloma
-Interpret pulmonary function testing
-Implement a new strategy for patients receiving pomalidomide who develop worsening pulmonary function

Tables and/or Figures

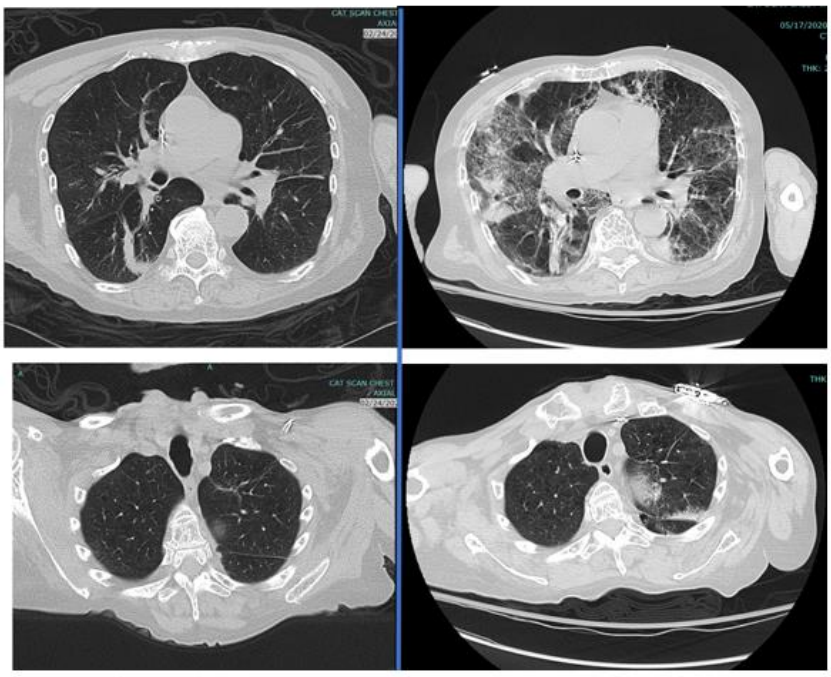

Figure 1. Side-by-side comparison of chest CT from 2/24/20 (left) and 5/17/20 (right). Mid-chest images on top. More apical views on bottom.