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Case Report

Pomalidomide Related Pulmonary Toxicity: A Case Report

Arya Shaji Kumar[1], Raghuveer Prabhu Santhakumara[2], Lakshmi Ramachandran[1*]
[1]Department of Pharmacy Practice, Amrita School of Pharmacy, Amrita Vishwa Vidyapeetham, Kochi, Kerala, INDIA.
[2]Department of Medical Oncology and Hematology, Amrita Institute of Medical Sciences and Research Centre, Amrita Vishwa Vidyapeetham, Kochi, kerala, INDIA.

ABSTRACT

Pomalidomide, an analogue of thalidomide, developed as a third generation oral immunomodulatory antineoplastic agent used for the management of multiple myeloma refractory to both lenolidomide and bortezomib. It exerts a potential immunomodulatory effect in myeloma cells and T lymphocytes. We report a case of 67 year old male patient undergoing treatment for multiple myeloma presented with fever and cough. He was receiving pomalidomide 4 mg, once daily (OD). After taking pomalidomide he developed fever, cough, breathing difficulty and desaturation. He was tachycardiac and tachypenic, auscultation of chest revealed scattered crepts bilateral, ABG (arterial- blood gas) showed hypoxia and chest X-ray showed hilar opacities. MDCT (Multidetector computed tomography) pulmonology angiogram showed no pulmonary thromboembolism, consolidation involving both the lungs, bilateral minimal left pleural effusion and multiple collapsed thoracic vertebra with lytic lesions in all visualized bones. Most commonly reported hematological complaint was dose dependent bone marrow suppression presented by neutropenia, anemia and thrombocytopenia and most commonly reported non-hematological complaints were fatigue, weakness, constipation and back pain. The drug has been rarely known to cause pulmonary toxicity. We document a case report of pomalidomide related pulmonary toxicity in a patient with Multiple Myeloma and conclude that pulmonary toxicity is a potential adverse reaction of pomalidomide treatment and motivate physicians to remain aware of its clinical presentation.

Key words: Immunomodulatory effect, Multiple myeloma, Pomalidomide, Pulmonary toxicity.

Correspondence

Mrs. Lakshmi Ramachandran, Department of Pharmacy Practice, Amrita School of Pharmacy, Amrita Vishwa Vidyapeetham, Kochi, Kerala, INDIA.

Phone: +91-9400493114

Email: lakshmir@aims.amrita.edu

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INTRODUCTION

Pomalidomide, a third generation oral immunomodulatory antineoplastic agent used for the treatment of multiple myeloma.[1] It exerts a potential immunomodulatory effect via cereblon- dependent proteasomal degradation of IKZF1 (Ikaros) and IKZF3 (Aiolos) in myeloma cells and T lymphocytes.[2] Its pharmacological effects include: cell cycle arrest and apoptosis of myeloma cells, enhances T cells and natural killer (NK) cell-mediated cytotoxicity.[3] It inhibits production of proinflammatory cytokines tumor necrosis factor –α (TNF-α), interleukin-1 (IL-1), IL-6, IL-12 and inhibits angiogenesis.[4] Common adverse events of Pomalidomide include hematological effects, fatigue, weakness, constipation and back pain.[5]

CASE DESCRIPTION

Here, we report an interesting case of Pomalidomide induced pulmonary toxicity. A 67-year-old male patient undergoing treatment for multiple myeloma presented with fever and cough. His multiple myeloma was diagnosed five years back. Previous chemotherapy regimens had included cyclophosphamide, bortezomib, dexamethasone (CyBorD) for sixteen weeks and he underwent autologous stem cell transplantation. He received maintenance treatment with lenalidomide for two years. He had a relapse and his medication was changed to lenalidomide/ bortezomib/ dexamethasone. He then developed pneumonia requiring ventilatory support and was off multiple myeloma medications for two months. Positron emission tomography–computed tomography (PET CT) showed disease progression. He was then started on daratumumab/dexamethasone therapy, after 1st cycle of daratumumab, reassessment showed progression and added tablet pomalidomide. He received pomalidomide 4 mg OD (once daily). After taking medicines, he developed fever, cough, breathing difficulty and desaturation. He was tachycardiac and tachypenic, auscultation of chest revealed scattered crepts bilateral, ABG (arterial- blood gas) showed hypoxia, blood culture sterile, sputum culture showed moderate growth of non-fermenter (Presumptive Acinetobacter species) and chest X-ray showed hilar opacities. For further evaluation MDCT (Multidetector computed tomography) pulmonology angiogram was done and it showed no pulmonary thromboembolism, consolidation involving both the lungs, bilateral minimal left pleural effusion and multiple collapsed thoracic vertebra with lytic lesions in all visualized bones. He was treated with antibiotics (Inj. meropenem 1g TID for 14 days, Inj. polymixin B 5 lakhs units BID for 10 days, Inj. clarithromycin 500mg BID for 5 days, Inj. tigecycline 500mg BID for 10 days, neb collision 1Mu TID for 2 weeks) , antifungals (Inj. micafungin 100mg OD for 5 days), LMWH (low molecular weight heparin, Inj LMWH 40mg/0.4ml OD for 7 days) for thromboprophylaxis, other supportive measures (neb mesna 200mg/3ml for 3 days, Inj hydrocortisone 100mg OD for 7 days) and withheld Pomalidomide. He was improved symptomatically, chest showed better air entry, breathing difficulty and cough decreased, no fever and SPO2 (saturation) was 87% in room temperature.

DISCUSSION

An analogue of thalidomide, pomalidomide is a third generation oral immunomodulatory antineoplastic agent for the management of multiple myeloma.[6] Most commonly cited hematological complaint was dose dependent bone marrow suppression presented by neutropenia, anemia

and thrombocytopenia.[7] The most commonly reported non-hematological complaints were fatigue, weakness, constipation and back pain.[8]

Pomalidomide is extensively metabolized through various pathways, including CYP1A2 and CYP3A4 to a higher extent and to a lesser extent by CYP2C19 and CYP2D6. 73% of the pomalidomide dose was eliminated through urine and 15% excreted through feces, whereas 2% is excreted as an unchanged drug in the urine and 8% as an unchanged drug in feces.[9] In multiple myeloma patients, mean half-life (t1/2) of pomalidomide was approximately 7.5 h.

According to the literature and in terms of our findings, the most typical radiologic finding observed was hilar opacities.[10] The most common complaints, as in our case were fever, cough, breathing difficulty and desaturation.

The direct mechanism behind the pulmonary toxicity of immunomodulatory drugs remains unknown.[10] In general, symptoms of pulmonary toxicity with pomalidomide were similar to those resulting from an infectious disease and include fever, cough, breathing difficulty, sputum production, desaturation and hypoxia. Echocardiogram showed tachycardia. Chest X-ray showed hilar opacities and MDCT pulmonology angiogram showed consolidation involving both the lungs, bilateral minimal left pleural effusion and multiple collapsed thoracic vertebra with lytic lesions in all visualized bones. Laboratory data showed elevated levels of erythrocyte sedimentation rate and C-reactive protein.

Treatment with antibiotics and other supportive measures along with discontinuation of the medication was the most potent management for pomalidomide related pulmonary toxicity.

CONCLUSION

The clinicians must be aware about this potential toxicity of Pomalidomide in patients appearing with pulmonary complaints and no identifiable infectious source. Prompt withdrawal of the medication and other supportive measures leads to rapid resolution of symptoms without long-term sequelae.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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