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Palbociclib-Induced Pneumonitis: A Reported Case and Review of the Literature

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Abstract **Case Report**

The treatment of metastatic breast cancer has undergone significant changes in recent years. Palbociclib, a selective cyclin-dependent kinase 4/6 (CDK4/6) inhibitor, has become a cornerstone in the treatment of hormone receptor-positive, HER2-negative advanced breast cancer, in addition to endocrine therapy. While palbociclib is generally well-tolerated, pneumonitis has emerged as a rare but serious adverse effect. This article presents a case of palbociclib-induced pneumonitis leading to death, followed by a comprehensive review of the literature to outline the clinical features, diagnosis, and management strategies for this condition.

Keywords: HR+/HER2− breast cancer, palbociclib, cyclin-dependent kinase, interstitial lung disease, pneumonitis.

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INTRODUCTION

Palbociclib is a selective cyclin-dependent kinase CDK4 and CKD6 inhibitor to treat hormone receptor-positive metastatic breast cancer in combination with Letrozole (Aromatase Inhibitor).

Palbociclib has revolutionized the treatment landscape of metastatic breast cancer by halting cancer cell proliferation through CDK4/6 inhibition. It is commonly combined with endocrine therapy to significantly extend progression-free survival. However, as its use increases, so does the recognition of its adverse effects, one of which is drug-induced pneumonitis. Although infrequent, palbociclib-induced pneumonitis (PIP) can lead to severe respiratory impairment, necessitating early diagnosis and prompt intervention. In this article, we describe a rare case of PIP in a patient with metastatic HR+/HER2- breast cancer, leading to death. We also review the current literature for pneumonitis associated with palbociclib therapy to provide insights into the clinical presentation, diagnostic workup, and management of this adverse event.

CASE REPORT

Patient Presentation:

A 50-year-old menopausal female with hormone receptor-positive, HER2-negative metastatic breast cancer was started on a regimen of palbociclib and letrozole. After two months of therapy, the patient developed persistent dry cough and exertional dyspnea. She had no history of chronic lung disease or other respiratory conditions. Physical examination revealed reduced breath sounds in both lungs, with no signs of infection.

Upon presentation, she was noted to have hypoxia requiring four liters of oxygen via nasal cannula. On examination, she was in severe respiratory distress and had bilateral crackles on lung auscultation.

Diagnostic Evaluation

Initial laboratory investigations, including complete blood count and inflammatory markers, were unremarkable. A chest X-ray showed bilateral interstitial infiltrates. Computed tomography (CT) of the chest revealed ground-glass opacities predominantly in the peripheral regions of both lungs, without evidence of infection or tumor progression. Pulmonary function tests demonstrated a restrictive pattern with decreased diffusion capacity. Based on clinical and radiological findings, a diagnosis of drug-induced pneumonitis was suspected.

CT chest with contrast revealed no pulmonary embolism and bilateral patchy interstitial opacities. Her lab work showed neutropenia and anemia. She had a thorough evaluation, heart failure, and autoimmune

disorders, which were negative. Bronchoscopy she declined the procedure. She continued to have worsening hypoxemia and required a high flow nasal cannula (FiO2 70% and 50 liters of flow) for moderate ARDS, which was presumed to be secondary to drug-induced pneumonitis. A pleural biopsy was performed with study of the pleural puncture fluid, in favour of an inflammatory cytology with no signs of malignancy or atypical cells. Argument in favor of palbociclib-induced interstitial pneumopathy.

Management and Outcome

Palbociclib was immediately discontinued, and the patient was started on corticosteroids with a tapering regimen. Over the following weeks, the patient's respiratory symptoms improved, and follow-up imaging showed resolution of the ground-glass opacities. She did not experience a recurrence of pneumonitis upon switching to an alternative CDK4/6 inhibitor.

She was managed conservatively with discontinuation of Palbociclib, and IV steroids were initiated (20 mg dexamethasone daily). Over 14 days during the hospital stay, the patient's respiratory symptoms worsened, leading to her death.

DISCUSSION

Incidence and Risk Factors

While pneumonitis is a known adverse effect of various cancer therapies, PIP is relatively rare. The exact incidence is not well-defined, but post-marketing surveillance and clinical trials report rates ranging from 1-3% of patients treated with palbociclib. Risk factors for developing PIP include advanced age, pre-existing lung disease, and prolonged therapy with CDK4/6 inhibitors.

Clinical Presentation

The presentation of PIP can be insidious, with patients developing nonspecific respiratory symptoms such as cough, dyspnea, and low-grade fever. Symptoms may resemble respiratory infections or other pulmonary conditions, making diagnosis challenging. In some cases, PIP can progress to life-threatening acute respiratory distress syndrome (ARDS), highlighting the need for early detection.

Diagnostic Challenges

The diagnosis of PIP is primarily clinical, supported by imaging and the exclusion of other causes such as infection, pulmonary embolism, or disease progression. High-resolution CT scans typically reveal bilateral ground-glass opacities, often without significant consolidation. Bronchoscopy and lung biopsy are rarely required but can be considered if the diagnosis is unclear. Inflammatory markers such as C-reactive protein may be elevated but are not specific for PIP.

Management

Early discontinuation of palbociclib is the cornerstone of PIP management. Mild cases may resolve with supportive care, but moderate to severe pneumonitis typically requires corticosteroid therapy. The dosage and duration of steroids depend on the severity of the pneumonitis, with tapering protocols recommended to prevent recurrence. In patients who respond well, rechallenging with a lower dose of palbociclib or switching to an alternative CDK4/6 inhibitor, such as ribociclib or abemaciclib, can be considered under close monitoring.

Literature Review

A review of published case reports and clinical studies reveals a growing number of PIP cases, particularly as palbociclib use becomes more widespread. Most patients presented with respiratory symptoms within the first six months of therapy, though late-onset cases have also been documented. Radiological findings were consistent across cases, with ground-glass opacities and interstitial changes being the predominant features. In nearly all cases, discontinuation of palbociclib and initiation of corticosteroids led to symptom resolution. Fatal outcomes, although rare, have been reported, underscoring the importance of prompt diagnosis.

CONCLUSION

Palbociclib-induced pneumonitis is a rare but serious adverse effect that clinicians should be aware of, especially in patients presenting with new respiratory symptoms during treatment. Timely recognition, discontinuation of therapy, and appropriate management with corticosteroids can lead to a favorable outcome. As more cases are reported, further research is needed to better understand the mechanisms underlying PIP and to establish standardized guidelines for its management.

Additional Information: Disclosures Human subjects: Consent was obtained by all participants in this study.

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