IJMPR 2024, 8(10), 57-59

International Journal of Modern Pharmaceutical Research
www.ijmpronline.com

ISSN: 2319-5878
IJMPR
Case Report
SJIF Impact Factor: 6.669

UNRAVELING ABEMACICLIB-INDUCED CUTANEOUS CHALLENGES IN THE ADJUVANT BREAST CANCER SETTING

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Article Received on: 01/09/2024
Article Revised on: 20/09/2024
Article Accepted on: 01/10/2024

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ABSTRACT

Cyclin-dependent kinase 4 and 6 inhibitors have emerged as pivotal targeted therapies for hormone receptor-positive breast cancer. While bone marrow suppression and gastrointestinal toxicities are well-documented adverse effects, cutaneous reactions remain underreported. This case report presents a 64-year-old patient with breast cancer who developed cutaneous rashes upon initiating abemaciclib, confirmed through a skin biopsy revealing eosinophilic infiltration, indicative of a probable drug-induced etiology. Despite the rarity of such events, their impact on patient quality of life and treatment discontinuation warrants attention. The case contributes to the limited literature on skin-related adverse events associated with CDK 4/6 inhibitors, emphasizing the importance of recognizing and managing these less common yet impactful reactions. As targeted anticancer therapies become more prevalent, comprehensive monitoring and early intervention are crucial for optimizing patient outcomes. This report aims to raise awareness within the medical community and enhance proactive management strategies for cutaneous manifestations linked to abemaciclib.

INTRODUCTION

With the recent advancements in the treatment of breast cancer, cyclin-dependent kinase 4 and 6 inhibitors represent one such group of targeted anticancer therapies in patients with HR-positive breast cancer. As the use of these drugs becomes more prevalent, novel adverse reactions are being unveiled and recognized.[1] Although bone marrow suppression with palbociclib, ribociclib and gastrointestinal toxicities with abemaciclib are the most common side effects reported and there are very minimal case reports on cutaneous adverse events associated with CDK 4/6 inhibitors. The product monograph of abemaciclib also includes skin and subcutaneous tissue side effects such as pruritus, rash, dry skin, dermatitis, acneiform and nail ridging.[2]

Here we report a case of cutaneous rashes associated with the use of abemaciclib in a patient with breast cancer in the adjuvant setting, where the diagnosis was confirmed with a skin biopsy revealing eosinophilic infiltration, suggesting probable drug-induced etiology. We hope that this case report will add to the literature raising awareness of cutaneous rashes as a possible side effect associated with abemaciclib use.

CASE DESCRIPTION

A 64-year-old female with a known case of hypothyroidism and diabetes, currently on medication, was diagnosed with Carcinoma of the Right Breast. She underwent breast conservation surgery, for Invasive Breast Carcinoma NST, Grade 2, pT1c(m)N3a, ER/PR-positive, Her2 neu-negative, and ki-67 at 15%. After completing three cycles of epirubicin and cyclophosphamide, it was discontinued due to mild left ventricular systolic dysfunction (EF 48%), and the cardiologist recommended further withholding anthracyclines. She completed adjuvant chemotherapy with 12 weeks of liposomal paclitaxel lipid suspension (pacliaqualip). Hormonal therapy with Anastrazole was started.

The patient was scheduled to begin adjuvant Abemaciclib for 2 years post-radiotherapy. She received a total dose of 40 Gy in 15 fractions, along with 12.5 Gy in 5 fractions, using the 3DCRT technique for the right breast site and lumpectomy cavity boost. Post-radiotherapy, the patient experienced hyperpigmentation and desquamation at the inframammary site. The initiation of Abemaciclib at 150mg 1-0-1 resulted in loose stools, abdominal pain from Day 3, and skin rashes with redness and itching from one week. (figure 1-3)

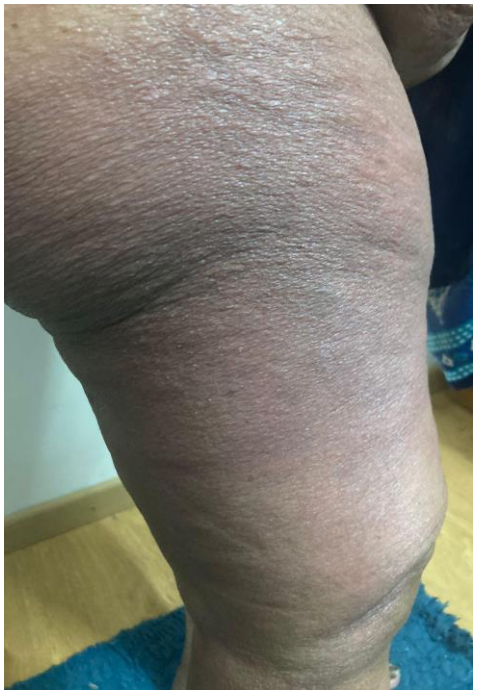

Figure 1.

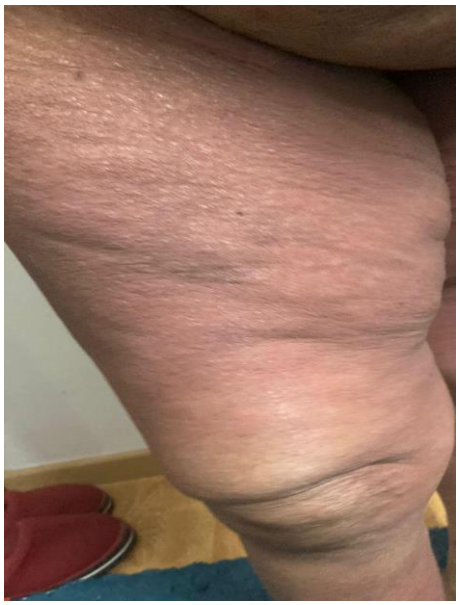

Figure 2.

Figure 3.

Skin reactions persisted, accompanied by generalised lymphedema, diffuse skin redness, and thickening. A dermatologist's opinion was sought, and subsequently, the patient underwent a punch biopsy of the rash, revealing spongiosis with eosinophilic infiltration, indicating drug-induced effects. The patient was prescribed steroids and antihistamines and advised to discontinue Abemaciclib. As a result, the generalised edema reduced, and erythema improved.

The causality assessment of ADR using the Naranjo adverse drug reaction probability scale revealed a Score of 5, implying probable ADR with abemaciclib.

After the skin lesions completely subsided, which took 14 days with the use of capped steroid courses, abemaciclib was reintroduced at a lower dose of 100mg 1–0-1, initially overlapped with antihistamines. The patient is continued abemaciclib, and there have been no additional reports of rashes.

DISCUSSION

The treatment of breast cancer has been significantly improved with the introduction of CDK 4/6 inhibitors particularly in patients with HR positive, HER 2 negative cancers. Since CDK 4/6 are the important regulators of cell proliferation, migration, and angiogenesis, inhibition these will lead to overall inhibition of cell cycle progression. Bone marrow suppression benign the most common adverse events reported with their use, cutaneous adverse events have also been reported.[1]

Skin toxicity being an important issue as it can significantly affect the patient’s quality of life and can lead to discontinuation of treatment, it is important to recognize these and manage these events that are associated with use of these drugs.

MONARCH is an open-label, phase III trial that investigated abemaciclib in participants with high-risk, node-positive, early-stage, hormone receptor-positive (HR+), human epidermal receptor 2 negative (HER2-), breast cancer, showed improved invasive disease-free survival (IDFS) compared to endocrine therapy alone. This trial reported diarrhea, neutropenia, and fatigue to be the most common adverse events with abemaciclib, there were no reports of any skin-related adverse events reported in this trial.[3]

A systematic review which included 41 articles by Martina Silvestri et.al reported 13 skin-related adverse events with the use of CDK 4/6 inhibitors which included alopecia, bullous skin rash, Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis(TEN), radiation recall and radiation dermatitis, Henoch–Schonlein purpura, cutaneous leukocytoclastic vasculitis, subacute and chronic cutaneous lupus erythematosus, histiocytoid Sweet syndrome, vitiligo-like lesions, and erythema dyschromicum perstans. Most of them where

with the use of palbociclib and ribociclib compared to abemaciclib.[4]

Pietro Sollena et.al performed a multicentric retrospective study described a spectrum of cutaneous adverse reactions with CDK inhibitors use with one patient developing Pruritus and one having alopecia and one having Lichenoid Reactions with abemaciclib. Vitiligo-like Lesions and Eczematous Lesions were also seen with other CDK 4/6 inhibitors, including palbociclib and ribociclib use.[5]

CONCLUSION

In conclusion, our case report highlights a rare dermatologic adverse event associated with the use of abemaciclib in a patient with breast cancer. The emergence of cutaneous rashes, confirmed through a skin biopsy revealing eosinophilic infiltration, underscores the importance of recognizing and managing skin-related adverse events linked to cyclin-dependent kinase 4/6 inhibitors. While the literature primarily focuses on bone marrow suppression and gastrointestinal toxicities, our case contributes to the growing awareness of less common but impactful cutaneous reactions.

This unique case serves as a reminder that as targeted anticancer therapies, such as CDK 4/6 inhibitors, become more prevalent, clinicians should remain vigilant for novel adverse reactions. Despite the general safety profile outlined in product monographs and clinical trials, our findings emphasize the need for comprehensive monitoring and prompt intervention when managing patients undergoing such treatments. By sharing our experience, we aim to enhance the medical community's awareness of cutaneous manifestations associated with abemaciclib, facilitating early recognition and proactive management to improve patient outcomes.

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