Ribociclib-induced Vitiligo in Advanced Stage Breast Cancer: Two Case Reports

Pemika Panathara MD, Sinee Weschawalit MD.

Division of Dermatology, Department of Internal Medicine, Faculty of Medicine, Thammasat University, Thailand.

ABSTRACT:

Cyclin-dependent kinase 4/6 (CDK4/6) inhibitors, including ribociclib, have markedly improved therapeutic outcomes for patients with hormone receptor-positive advanced breast cancer. While generally well-tolerated, these agents can cause various adverse effects, some of which are infrequent and may be underrecognized. Vitiligo is a rare but potentially distressing cutaneous side effect of CDK4/6 inhibitors. We present two cases of vitiligo occurring in patients receiving ribociclib therapy for advanced breast cancer. The first case involves a 68-year-old woman who developed depigmented macules on her face and extremities after 22 months of treatment. Ribociclib was discontinued due to disease progression, but the depigmented lesions worsen. The second case features a 55-year-old woman who developed similar lesions six months after beginning ribociclib therapy.

Key words: Vitiligo, Cutaneous Adverse Event, Ribociclib, Cyclin-dependent Kinase 4/6 Inhibitors

Introduction

Cyclin-dependent kinases (CDKs) are pivotal regulators of the cell cycle, particularly facilitating the G1-to-S phase transition, which is crucial for DNA replication and cellular proliferation[1,2]. Beyond their established role in cell cycle control, CDK4/6 also significantly influence immune cell function by modulating their development, differentiation, and activation[2]. In breast cancer, dysregulated CDK4/6 activation promotes unchecked tumor proliferation and contributes to resistance to hormone therapy, emphasizing the therapeutic relevance of targeting this pathway.

Palbociclib, ribociclib, and abemaciclib are three FDA-approved CDK4/6 inhibitors indicated for hormone receptor-positive advanced breast cancer. These small-molecule inhibitors, typically co-administered with hormonal therapy such as tamoxifen or letrozole, have demonstrated substantial clinical efficacy by delaying disease progression and improving progression-free survival, thus establishing them as a standard of care for this patient population[1].

Despite their clinical benefits, CDK4/6 inhibitors can cause adverse events that necessitate vigilant monitoring. Common toxicities include QTc prolongation, hematologic abnormalities such as neutropenia, anemia, and thrombocytopenia, hepatotoxicity, and early-onset diarrhea. Dermatologic adverse events, reported in up to 15% of patients, are also clinically significant. These cutaneous manifestations often present as maculopapular eruptions, pruritus, or alopecia and are generally mild to moderate, rarely requiring dose adjustments or treatment discontinuation[3].

Interestingly, many dermatologic toxicities appear to be a class effect of CDK4/6 inhibitors. However, abemaciclib, which preferentially inhibits CDK4 over CDK6, has been associated with a lower incidence of cutaneous reactions[1,3]. Among these dermatologic adverse effects, vitiligo is an uncommon but noteworthy complication, most frequently reported with ribociclib, with an estimated incidence of up to 1.4%[4].

Correspondence Author: Sinee Weschawalit MD., Email: sineewes@gmail.com

Received: 10 February 2025 Revised: 20 June 2025 Accepted: 14 October 2025

Vitiligo-like depigmentation has also been observed in PD-1 inhibitors (e.g., pembrolizumab), BRAF/MEK inhibitors (e.g., dabrafenib, trametinib), and tyrosine kinase inhibitors (e.g., imatinib)[5].

Here, we present two cases of patients who developed depigmented lesions while undergoing ribociclib therapy, highlighting the importance of early recognition and clinical monitoring of this adverse event.

Case Reports

Case 1

A 68-year-old woman with a 15-year history of right breast cancer underwent a right modified radical mastectomy, followed by hormonal therapy. Two years ago, her disease progressed with metastatic involvement of the pleura, lungs, and liver. She was subsequently started on systemic therapy with ribociclib (400 mg daily) in combination with letrozole, an aromatase inhibitor.

After 22 months of continuous ribociclib therapy, she developed well-demarcated depigmented patches on her face and extremities (Figure 1). Laboratory investigations, including thyroid function tests, were within normal limits. She was prescribed 0.1% topical tacrolimus, applied twice daily.

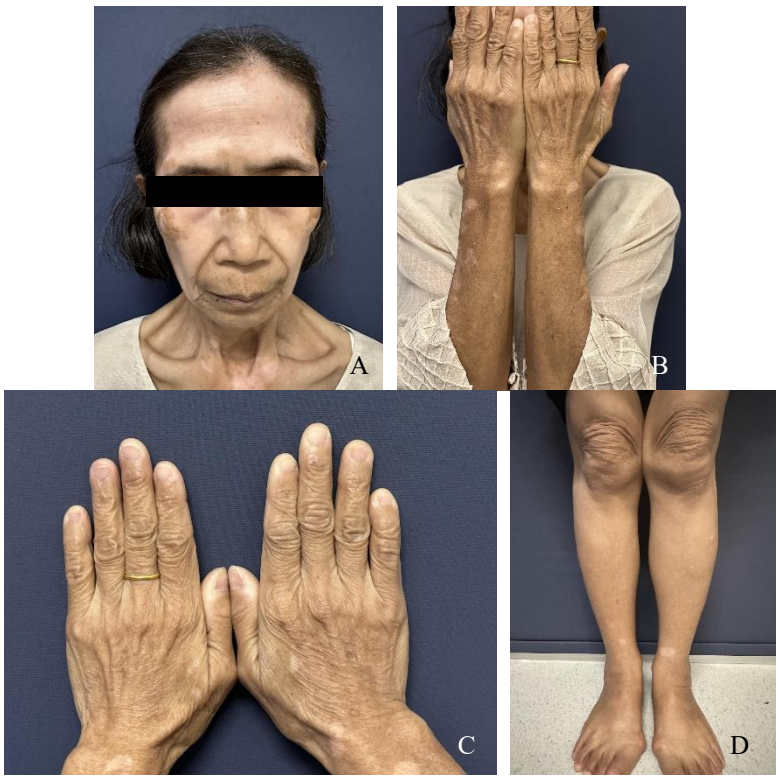

Figure 1 Well-demarcated depigmented patches on the face (A), forearms (B), hands (C), and legs (D) of the first patient following ribociclib therapy

Case 2

A 55-year-old woman with a one-year history of breast cancer presented with advanced disease involving multiple metastases. As part of her initial management, she underwent a left modified radical

mastectomy and was started on ribociclib and letrozole for systemic therapy. Follow-up imaging demonstrated a substantial reduction in liver metastases, confirming a strong therapeutic response.

Six months into ribociclib therapy, she developed well-circumscribed depigmented patches on her face and extremities (Figure 2). Laboratory workup was unremarkable.

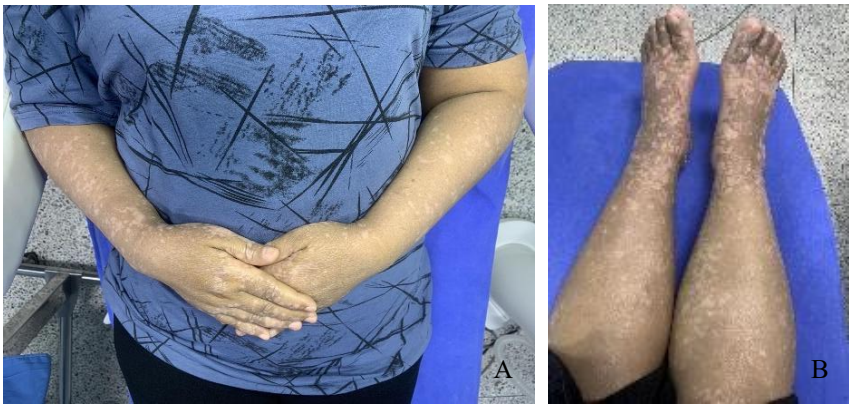

Figure 2 Well-demarcated depigmented macules observed on the forearms and hands (A) and legs (B) of the second patient during ribociclib therapy.

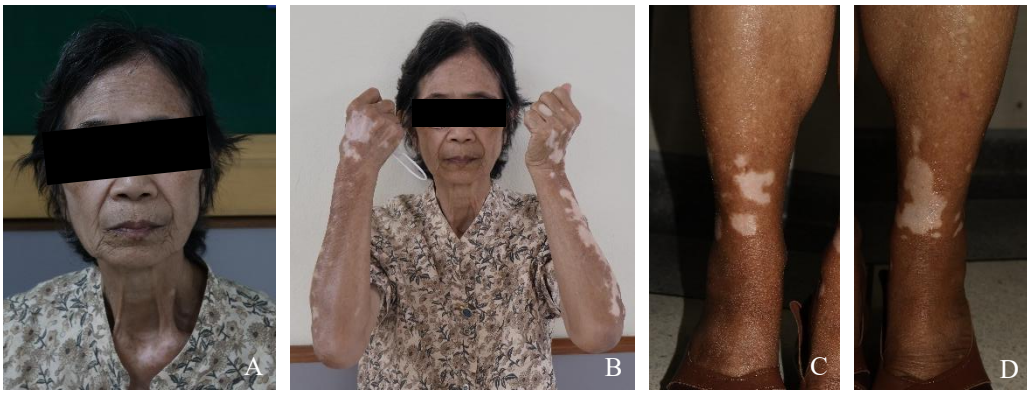

Figure 3 Progression of depigmented patches in the first patient one year after discontinuation of ribociclib, showing increased lesion size and distribution on the face (A), forearms (B), right leg (C), and left leg (D).

In both cases, ribociclib therapy was continued alongside vitiligo management. In the first patient, ribociclib was ultimately discontinued due to disease progression, and one year after discontinuation, the depigmented lesions had worsened (Figure 3). The second patient was lost to follow-up, preventing further assessment.

Discussion

CDK4/6 inhibitors have transformed the therapeutic landscape of hormone receptor-positive advanced breast cancer by improving disease control and progression-free survival. While generally well tolerated, these agents have increasingly been associated with dermatologic adverse events, including the rare occurrence of vitiligo[3]. CDK4/6 inhibitor-associated vitiligo is characterized by sharply demarcated depigmented or hypopigmented lesions, predominantly affecting sun-exposed regions[4]. This condition is often preceded by inflammatory symptoms such as erythema or pruritus[4,6].

The median onset of vitiligo following CDK4/6 inhibitor therapy is approximately nine months, with reported cases ranging from one to twenty-eight months[4,6,7]. Notably, among patients receiving abemaciclib, the mean onset is approximately 14 months, which is longer than that observed with palbociclib or ribociclib[7]. Histopathological and immunohistochemical analyses reveal findings indistinguishable from idiopathic vitiligo, further complicating differentiation[4,8,9].

The precise pathogenesis of CDK4/6 inhibitor-induced vitiligo remains incompletely understood. Proposed mechanisms include direct melanocyte injury mediated by increased oxidative stress, dysregulation of small ubiquitin-like modifiers, and altered Forkhead box protein M1 (FOXM1) phosphorylation. Additionally, these inhibitors may enhance T-cell–mediated cytotoxicity through nuclear factor of activated T-cells (NFAT) regulation, contributing to autoimmune destruction of melanocytes[8]. There is also speculation that shared tumor-associated antigens between breast cancer cells and melanocytes could provoke a cross-reactive immune response, leading to depigmentation and possibly reflecting an underlying antitumor immune activity[9].

In both of our cases, lesions were predominantly distributed on sun-exposed areas, supporting the theory that ultraviolet radiation may exacerbate or precipitate depigmentation in the setting of CDK4/6 inhibitor-induced immune dysregulation.

Currently, there are no standardized guidelines for managing CDK4/6 inhibitors-induced vitiligo. Treatment strategies are typically adapted from idiopathic vitiligo management and include topical corticosteroids, calcineurin inhibitors (e.g., tacrolimus), Janus Kinase (JAK) inhibitors (e.g., ruxolitinib), and narrow-band UVB phototherapy. Despite these interventions, treatment response remains variable, with some patients experiencing lesion stabilization while others continue to exhibit progressive depigmentation[4,6,7]. In certain cases, discontinuation of CDK4/6 inhibitors has been associated with further lesion expansion[9].

Table 1 Summary of published case reports of ribociclib-induced vitiligo in breast cancer patients

Case report	N	Age	Time to onset (months)	Location	Treatment	Outcome	Reference
1	14	40-79 (mean=62)	4-16 (mean=9)	Face, chest, trunk, extremities	TCI, TCS, UVB, oral corticosteroids	Partial response	[4]
2	1	51	10	Face, neck, forearms	TCI, TCS	Partial response	[6]
3	4	50, 51, 61, 73	1, 1, 13, 28	Face, trunk, extremities	TCI, TCS, home UVB	Persistent depigmentation	[7]
4	1	71	7	Face, chest, abdomen, extremities	TCS + oral antihistamine	Partial response	[8]
5	2	46, 80	3, 12	Face, trunk, legs, arms	TCS + oral antihistamine	Not response	[9]
Our case (Case 1)		68	22	Face and extremities	TCI	Worsened	
Our case (Case 2)		55	6	Face and extremities	None	Lost to follow up	

Abbreviations: TCI=topical calcineurin inhibitors, TCS=topical corticosteroids, UVB=ultraviolet B

While dermatologic adverse events, such as vitiligo can occur during CDK4/6 inhibitor therapy, these agents remain integral to the treatment of hormone receptor-positive advanced breast cancer. Interestingly, emerging evidence suggests a potential association between the presence of cutaneous adverse effects and improved progression-free survival[7,10]. Therefore, vitiligo should generally not necessitate treatment discontinuation unless symptoms become intolerable[7].

The clinical characteristics of previously reported cases of ribociclib-induced vitiligo are summarized in Table 1.

Conclusion

Vitiligo is a rare but clinically significant dermatologic adverse event associated with ribociclib therapy in advanced breast cancer. Although its precise pathogenesis remains elusive, it may represent a class-specific immune-mediated effect of CDK4/6 inhibition. Increased awareness of this potential toxicity is essential for early recognition, patient counseling, and appropriate management.

References

1. Johnston S, Emde A, Barrios C, et al. Cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitors: existing and emerging differences. JNCI Cancer Spectr 2023;7:pkad045.
2. Petroni G, Formenti SC, Chen-Kiang S, Galluzzi L. Immunomodulation by anticancer cell cycle inhibitors. Nat Rev Immunol 2020;20:669-79.
3. Sibaud V, Sollena P. Dermatologic toxicities to inhibitors of cyclin-dependent kinases CDK 4 and 6: An updated review for clinical practice. Ann Dermatol Venereol 2023;150:208-12.
4. Sollena P, Nikolaou V, Soupos N, et al. Vitiligo-like lesions in patients with advanced breast cancer treated with cycline-dependent kinases 4 and 6 inhibitors. Breast Cancer Res Treat 2021;185:247-53.
5. Ma J, Chen K, Luan C. Cutaneous adverse events under new clinical therapies: drug-induced vitiligo-like depigmentation. Int J Dermatol Venereol 2024.
6. Kothari R, Darling HS, Bhatnagar A, Janney M, Mohan S, Kumar R. Ribociclib induced vitiligo-like lesions. Indian J Dermatol Venereol Leprol 2024;91:396-7.
7. Bang AS, Fay CJ, LeBoeuf NR, et al. Multi-center retrospective review of vitiligo-like lesions in breast cancer patients treated with cyclin-dependent kinase 4 and 6 inhibitors. Breast Cancer Res Treat 2024;204:643-7.
8. Anjaneyan G, Keechilat P, Duraisamy P, Eapen M. Ribociclib-induced extensive vitiligo-like lesions: possible pathomechanisms with clinical, dermoscopic and histological correlation. BMJ Case Rep 2022;15:e248782.
9. Pasqualoni M, Orlandi A, Palazzo A, et al. Case report: Vitiligo-like toxicity due to ribociclib during first-line treatment of metastatic breast cancer: two cases of premature interruption of therapy and exceptional response. Front Oncol. 2023;13:1067264.
10. Borroni RG, Bartolini M, Gaudio M, et al. Ribociclib-Induced Cutaneous Adverse Events in Metastatic HR+/HER2- Breast Cancer: Incidence, Multidisciplinary Management, and Prognostic Implication. Oncologist. 2024;29:484-92.