

CLINICAL VIGNETTE

Ribociclib-induced Vitiligo in a Patient with Metastatic Breast Cancer

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Case

A 61-year-old woman with metastatic breast cancer presented to Dermatology with two-months of rash on the chest, arms, and legs. The rash started after four months of treatment with ribociclib. Associated symptoms include intermittent redness, itching, burning, and skin tightness.

Her medical history was notable for both left-sided ductal carcinoma in situ and right-sided breast cancer (HR+/PR+/HER2-) treated with bilateral mastectomy, anastrozole, and exemestane. Nearly two years after diagnosis imaging detected metastatic disease to the liver and bones. She started fulvestrant and ribociclib therapy. The patient had no personal or family history of autoimmune disease.

Physical exam was notable for well-demarcated erythema and scaling affecting the mid-chest, arms, and lower legs (Figure 1). Skin punch biopsy of the left upper arm found lichenoid/interface dermatitis with papillary dermal pigment incontinence and associated histiocytes. The clinical and histologic findings supported the diagnosis of a drug-related eruption, likely secondary to ribociclib. She was started on clobetasol 0.05% ointment and daily antihistamine treatment.

At her one-month follow-up visit, the patient's initial lichenoid drug reaction rash had resolved. However, dermatological examination revealed several well-demarcated, hypopigmented macules and patches on the hands as well as bilateral upper and lower extremities, which progressed to fully depigmented macules and patches (Figure 2A and 2B). These were confirmed on Wood's light examination.

The examination was consistent with vitiligo-like lesions. The patient was initially started on phototherapy NB-UVB three times per week and clobetasol 0.05% ointment. After two months of treatment, the patient still had depigmentation. Phototherapy was continued, and her topical regimen was adjusted to clobetasol ointment on weekends only with weekday triamcinolone 0.1% ointment. At return examination two months later, she reported slight improvement of extremity pigmentation, with new vitiligo-like forehead lesions. Hydrocortisone 2.5% ointment was prescribed for new forehead lesions. She reported only slow improvement and was subsequently tapered off all topical steroids and phototherapy and started topical ruxolitinib 1.5% cream with continued improvement and faster re-pigmentation. The patient discontinued

ribociclib recently after significant improvement due to worsening gastrointestinal side effects.

Discussion

The use of CDK 4/6 cyclin inhibitors in combination with hormonal therapy—in this case, ribociclib and fulvestrant—is a standard treatment option for women with hormone receptor-positive, human epidermal growth factor receptor 2-negative (HR+/HER2-) advanced or metastatic breast cancer. The MONALEESA-7 clinical trial assessed the clinical efficacy of ribociclib plus endocrine therapy. The most common adverse events reported were neutropenia, leukopenia, fatigue, nausea, alopecia, diarrhea, and headache.¹ There was no report of vitiligo-like lesions as an adverse event. However, an increasing number of case reports have reported vitiligo-like adverse events.²⁻⁷ Similarly, another CDK 4/6 cyclin inhibitor, palbociclib, has also been associated with vitiligo-like lesions in case reports.^{2,8-11}

Some studies have evaluated cutaneous adverse events associated with CDK 4/6 cyclin inhibitors. A recent single-center retrospective study of 12 patients reported five of the 12 patients (41.7%) experienced a rosaceiform face rash, four reported an eczematous rash, and three reported vitiligo. However, more severe cutaneous adverse events have been reported, including Stevens-Johnson syndrome, toxic epidermal necrolysis, radiation recall dermatitis, histiocytoid sweet syndrome, bullous skin rash, and ashy dermatosis.¹²

The exact pathophysiological mechanism leading to vitiligo-like lesions in the context of ribociclib therapy remains unclear. Reported theories include immune-mediated destruction of melanocytes induced by UV radiation⁴ and disruption in the retinoblastoma ubiquitination process of keratinocytes leading to neighboring melanocyte dysfunction.¹³ Interestingly, vitiligo-like lesions have been associated with favorable outcomes with melanoma.¹⁵ This case report also contributes to the current body of data that these lesions tend to occur on sun-exposed areas of the body.^{2,4,11,15}

Management of vitiligo-like lesions poses a clinical challenge, as discontinuation of an effective cancer therapy like ribociclib for dermatologic side effects must be carefully weighed against the benefits of ongoing treatment for metastatic breast cancer. In this case, various treatment modalities were tried, including

antihistamines, topical steroids, and phototherapy, with ruxolitinib ultimately demonstrating good clinical improvement. One study has presented ruxolitinib cream as a potential treatment for vitiligo-like lesions induced by CDK 4/6 cyclin inhibitors, and this case supports its use.¹¹

In conclusion, this case demonstrates the importance of vigilance for cutaneous adverse events in patients undergoing targeted CDK 4/6 cyclin inhibitor cancer therapies such as ribociclib. While rare, the development of vitiligo-like lesions supports the need for close interdisciplinary collaboration and individualized treatment approaches to optimize therapeutic outcomes.

Figures



Figure 1. Well-demarcated erythematous and photo-distributed rash on the left upper extremity.



Figure 2A. Multiple well-demarcated hypopigmented macules and patches on the left upper extremity.



Figure 2B. Progression to fully depigmented macules and patches on the left upper extremity.

REFERENCES

1. **Parati MC, Pedersini R, Perego G, Reduzzi R, Savio T, Cabiddu M, Borgonovo K, Ghilardi M, Luciani A, Petrelli F.** Ribociclib in the Treatment of Hormone-Receptor Positive/HER2-Negative Advanced and Early Breast Cancer: Overview of Clinical Data and Patients Selection. *Breast Cancer (Dove Med Press)*. 2022 Apr 12;14:101-111. doi: 10.2147/BCTT.S341857. PMID: 35440873; PMCID: PMC9013420.
2. **Sollena P, Nikolaou V, Soupos N, Kotteas E, Voudouri D, Stratigos AJ, Fattore D, Annunziata MC, Orlandi A, Di Nardo L, Apalla Z, Deilhes F, Romano MC, Fabbrocini G, Sibaud V, Peris K; European Network for Cutaneous ADverse event of Oncologic drugs (ENCADO) group.** Vitiligo-like lesions in patients with advanced breast cancer treated with cyclin-dependent kinases 4 and 6 inhibitors. *Breast Cancer Res Treat*. 2021 Jan;185(1):247-253. doi: 10.1007/s10549-020-05914-w. Epub 2020 Sep 10. PMID: 32914354.
3. **Sharaf B, AlMasri R, Abdel-Razeq N, Salama O, Hamad I, Abunasser M, Abdel-Razeq H.** Vitiligo-Like Lesions in a Patient with Metastatic Breast Cancer Treated with Cyclin-Dependent Kinase (CDK) 4/6 Inhibitor: A Case Report and Literature Review. *Clin Cosmet Investig Dermatol*. 2022 Jan 5;15:5-10. doi: 10.2147/CCID.S344867. PMID: 35023941; PMCID: PMC8743357.
4. **Chan OB, Su JC, Yazdabadi A, Chan A.** Drug induced vitiligo-like depigmentation from a CDK 4/6 inhibitor. *Asia Pac J Clin Oncol*. 2022 Apr;18(2):e154-e156. doi: 10.1111/ajco.13585. Epub 2021 Jun 28. PMID: 34180575.
5. **Silvestre Torner N, Aguilar Martínez A, Echarri González MJ, Tabbara Carrascosa S, Román Sainz J, Gruber Velasco F.** Ribociclib-induced Vitiligo: a Case Report. *Dermatol Pract Concept*. 2022 Apr 1;12(2):e2022045. doi: 10.5826/dpc.1202a45. PMID: 35646430; PMCID: PMC9116537.
6. **Türkel A, Karaçin C, Öner İ, Şeyran E, Öksüzoğlu B.** Vitiligo-like lesions associated with ribociclib in a woman with metastatic breast cancer. *J Oncol Pharm Pract*. 2023 Feb 9:10781552231156521. doi: 10.1177/10781552231156521. Epub ahead of print. PMID: 36760158.
7. **Pasqualoni M, Orlandi A, Palazzo A, Garufi G, Cannizzaro MC, Pontolillo L, Pannunzio S, Cutigni C, Sollena P, Federico F, Bria E, Tortora G.** 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 Mar 9;13:1067264. doi: 10.3389/fonc.2023.1067264. PMID: 36969030; PMCID: PMC10034067.
8. **Gao S, Wei G, Hao Y.** Vitiligo-like lesions induced by cyclin-dependent kinase 4/6 inhibitor Palbociclib: a case report and literature review. *Pathol Oncol Res*. 2023 Jul 6;29:1611115. doi: 10.3389/pore.2023.1611115. PMID: 37483648; PMCID: PMC10358287.
9. **Starace M, Rapparini L, Cedirian S, Evangelista V, Pampaloni F, Bruni F, Misciali C, Rubino D, Zamagni C, Pileri A, Piraccini BM.** Management of cutaneous adverse events caused by antineoplastic therapies: a single-center experience. *Support Care Cancer*. 2024 Feb 29;32(3):200. doi: 10.1007/s00520-024-08407-4. PMID: 38421520.
10. **Pérez NB, Millán PI, Menéndez AD, Domínguez Auñón JD.** Vitiligo-like depigmentation affecting sun-exposed areas caused by palbociclib. *Photodermatol Photoimmunol Photomed*. 2024 Jan;40(1):e12923. doi: 10.1111/phpp.12923. Epub 2023 Nov 6. PMID: 37929877.
11. **Bang AS, Fay CJ, LeBoeuf NR, Etaee F, Leventhal JS, Sibaud V, Arbesman J, Wang JY, Kwong BY.** 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 Apr;204(3):643-647. doi: 10.1007/s10549-023-07217-2. Epub 2024 Jan 15. PMID: 38224427.
12. **Silvestri M, Cristaudo A, Morrone A, Messina C, Bernardo L, Nisticò SP, Mariano M, Cameli N.** Emerging Skin Toxicities in Patients with Breast Cancer Treated with New Cyclin-Dependent Kinase 4/6 Inhibitors: A Systematic Review. *Drug Saf*. 2021 Jul;44(7):725-732. doi: 10.1007/s40264-021-01071-1. Epub 2021 May 6. PMID: 33959899.
13. **Zhou M, Lin F, Xu W, Jin R, Xu A.** Decreased SUMOylation of the retinoblastoma protein in keratinocytes during the pathogenesis of vitiligo. *Mol Med Rep*. 2018 Sep;18(3):3469-3475. doi: 10.3892/mmr.2018.9299. Epub 2018 Jul 19. PMID: 30066925.
14. **Teulings HE, Limpens J, Jansen SN, Zwinderman AH, Reitsma JB, Spuls PI, Luiten RM.** Vitiligo-like depigmentation in patients with stage III-IV melanoma receiving immunotherapy and its association with survival: a systematic review and meta-analysis. *J Clin Oncol*. 2015 Mar 1;33(7):773-81. doi: 10.1200/JCO.2014.57.4756. Epub 2015 Jan 20. PMID: 25605840.
15. **Romagnuolo M, Alberti Violetti S, Riva D, Barberi F, Moltrasio C.** Vitiligo-like lesions induced by cyclin-dependent kinase 4/6 inhibitor palbociclib. *Int J Dermatol*. 2023 Feb;62(2):e98-e100. doi: 10.1111/ijd.16356. Epub 2022 Jul 3. PMID: 35781265.