Vitiligo-like Lesions Associated with CDK4/6 Inhibitors in Metastatic HR+/HER2– Breast Cancer: Multiple case reports from a Brazilian experience.

R. M. Borges[1], M. C. Gouveia[1], C. Giro[1], M. Aisen[1], L. C. Oliveira[1], N. J. Gomes[2], A. C. Ferrari[3], T. G. Rivelli[3], M. S. Neto[3], M. L. Brito[4], R. B. Sousa[5], K. P. Sacardo[6]; B. M. Zucchetti[1]

[1]Oncologia Clínica, Rede Américas, Hospital 9 de Julho, São Paulo, BRAZIL, [2]Oncologia Clínica, Hospital São Domingos, São Luís-MA, BRAZIL, [3]Oncologia Clínica, Rede Américas, Hospital Santa Paula, São Paulo, BRAZIL, [4]Oncologia Clínica, DASA Oncology - Clínica AMO, Salvador-BA, BRAZIL, [5]Oncologia Clínica, Brasília Hospital, Oncologia Américas, Brasilia, BRAZIL, [6]Oncologia Clínica, Rede Américas, Hospital Christóvão da Gama, Santo André - SP, BRAZIL.

Abstract

Vitiligo-like reactions associated with CDK4/6 inhibitors are rare. We describe eight women with HR+/HER2− metastatic breast cancer treated with ribociclib or abemaciclib in combination with endocrine therapy who developed well-demarcated hypopigmented lesions. None had prior autoimmune or dermatologic conditions. Skin changes appeared 6–24 months after treatment initiation, predominantly on the face, neck, and upper limbs. Biopsies in two cases revealed pigmentary incontinence and chronic perivascular inflammation, suggesting an immune-mediated mechanism. One patient achieved complete repigmentation after permanent drug discontinuation, while others showed partial improvement with topical corticosteroids. These findings underscore the rarity of CDK4/6 inhibitor–induced vitiligo-like reactions and the importance of further research into their pathophysiology and clinical relevance.

Case Series Description

A total of eight women with HR+/HER2− metastatic breast cancer receiving ribociclib (n=7) or abemaciclib (n=1), all in combination with endocrine therapy (aromatase inhibitor or fulvestrant), developed well-demarcated

Case Series Description

depigmented lesions consistent with vitiligo-like lesions. None had a prior history of autoimmune or dermatologic disease. Dermatologic evaluations and lesion photographs were obtained. In two cases, skin biopsies revealed pigmentary incontinence and chronic perivascular mononuclear infiltrate. Cutaneous changes developed within a median of 8 months (minimum 6 and maximum 24 months) after treatment initiation. The lesions were asymptomatic, hypopigmented, and primarily involved the face, neck, and upper limbs. No systemic symptoms were reported. Dermatological evaluation ruled out other differential diagnoses and suggested an immune-mediated mechanism. In one patient, treatment was permanently discontinued after two years due to cutaneous toxicity from vitiligo-like lesions, with sustained oncologic response; another patient had a temporary 3-month drug interruption due to lesion worsening, after which the skin changes stabilized. All patients were treated with topical corticosteroids, resulting in partial improvement. Complete lesion regression was observed in the patient who discontinued therapy; three patients had stable lesions while continuing medication; others showed partial regression after treatment change due to disease progression.

Discussion

The most common skin toxicities associated with ribociclib and abemaciclib include rashes and dermatitis (10–20%). Vitiligo-like reactions are rare. CDK4/6 inhibitors may affect the proliferation of keratinocyte precursors, compromising the secretion of melanocyte-supporting cytokines. Treatment-induced melanocyte apoptosis may contribute to depigmentation. Additionally, ultraviolet radiation-induced melanocyte damage may trigger immune responses, highlighting the importance of sun protection. However, the underlying pathophysiology remains unclear.



Fig. 1,2: Vitiligo-like lesions in two patients on the face, trunk and back.



Fig. 3, 4: Vitiligo-like lesions in two patients on the face and arms.

Conclusions

This case series highlights a potentially underrecognized cutaneous adverse event associated with CDK4/6 inhibitors (ribociclib and abemaciclib). Oncologists should be aware of vitiligo-like reactions as part of the toxicity spectrum of these agents. It is important to point out that this is not a life-threatening condition but it can affect appearance, specially of the face, causing burden for patients. Early recognition and collaborative management with dermatology can allow continuation of cancer therapy without compromising treatment outcomes or quality of life. Further studies are needed to better understand this phenomenon.

Contact

Bruna M. Zucchetti
Rede Américas Oncologia – Hospital 9 de Julho, São Paulo, Brazil
Email: brunamzucchetti@gmail.com

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