

Skin lesions caused by bortezomib targeted therapy of multiple myeloma

Zmiany skórne wywołane bortezomibem stosowanym w terapii szpiczaka mnogiego

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Inhibition of proteasomes (proteolytic complexes responsible for the degeneration of ubiquitinated proteins) is a promising option in the therapy of hematologic malignancies. Bortezomib is the first-in-class proteasome inhibitor, which has been used in the treatment of multiple myeloma, mantle cell lymphoma and non-Hodgkin lymphoma. Despite the fact that cutaneous adverse reactions caused by bortezomib are quite frequent, they are poorly described in the medical literature [1, 2]. To our knowledge, this is the first report in Poland on an adverse cutaneous reaction caused by bortezomib.

A 62-year-old woman was diagnosed with stage I-A IgGκ multiple myeloma. The patient was treated with combined chemotherapy (cyclophosphamide, thalidomide and dexamethasone), but remission was not achieved. Therefore, intravenous therapy with bortezomib (1.3 mg/m²) was administered. After the second cycle of bortezomib chemotherapy,

symptoms of polyneuropathy occurred, classified as grade 2 according to Common Terminology Criteria for Adverse Events 4.0 (CTCAE). Therapy was continued with a lower dose of the drug (1 mg/m²). After the third chemotherapy cycle, symmetrical, erythematous lesions with mild scaling and pruritus on the palms and axillary regions (grade 1 according to CTCAE) appeared (Figures 1 A, B). The cutaneous lesions resolved completely after topical treatment with mid-strength glucocorticosteroids and emollients. Similar lesions reappeared again after the fourth cycle of bortezomib chemotherapy, and again topical treatment proved to be successful. Bortezomib was discontinued due to the lack of clinical response of multiple myeloma.

The most common side effects of bortezomib are gastrointestinal symptoms, thrombocytopenia, neutropenia, fatigue and peripheral neuropathy [3]. Adverse cutaneous reactions during the therapy are



Figure 1. Erythematous lesions with mild scaling in axillary (A) and palmar (B) areas

Rycina 1. Rumieniowe wykwity z delikatnym złuszczeniem w okolicy pachowej (A) oraz na powierzchni dłoniowej rąk (B)

observed in 8–24% of patients [1, 2]. They are characterized by diversity of the clinical and histopathological presentation. The clinical spectrum of skin lesions described so far includes: different forms of rash (maculopapular, papulonodular, nodular, vasculitic, acneiform, purpuric, “folliculitis-like”), small vessel vasculitis, Sweet syndrome, Sweet-like syndrome, and lupus tumidus. Histopathological features of skin lesions generally show various vasculitis reactions [2, 4, 5]. The response to topical or systemic glucocorticosteroid treatment is usually quick and rewarding. Glucocorticosteroids may also be recommended in between the bortezomib cycles as a prophylaxis of adverse skin reactions.

The pathogenesis of skin involvement is probably related to the increased release of proinflammatory cytokines and the generation of a cell-mediated immune response. Some authors state that development of a rash during bortezomib therapy is correlated with better response to the treatment [6].

In conclusion, bortezomib has considerable potential to induce adverse cutaneous reactions, but the risk of serious or systemic involvement is very low. Most of them are rather mild skin reactions that can be easily managed and do not require withdrawal of the drug. The rise in the use of proteasome inhibitors will probably lead to more frequent cutaneous adverse reactions.

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