

Histiocytoid sweet syndrome related to bortezomib: A mimicker of cutaneous infiltration by myeloma

Sir,
Histiocytoid Sweet syndrome presents with lesions mimicking classical Sweet syndrome but histopathologically is characterized by an inflammatory

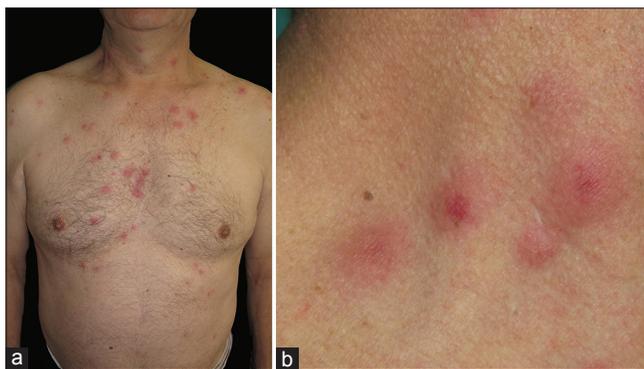


Figure 1: (a) Nonconfluent, erythematous, and edematous well-demarcated plaques, slightly infiltrated and without epidermal involvement. (b) Closer view of the lesions

infiltrate composed of monocytoid or histiocytoid cells positively stained with CD15, CD43, CD45, CD68, MAC-386, HAM56, myeloperoxidase, and lysozyme, which correspond with immature neutrophils.^[1] This pattern is independent of the length of time the lesion has been present and can be demonstrated in lesions of less than 24 h duration.^[1]

Several skin lesions associated with bortezomib have been described as skin rash which show histopathological findings of lymphocytic infiltrates, interphase dermatitis,^[2] vasculitis,^[3] and different neutrophilic diseases.^[4-11]

A 66-year-old male with an IgG lambda myeloma that progressed despite autologous peripheral blood stem cell transplantation was being treated with bortezomib (1.3 mg/m²) and melphalan (9 mg/m²) according to VISTA protocol (Velcade as Initial Standard Therapy in Multiple Myeloma). On the 8th day of the second chemotherapy cycle, he presented with asymptomatic lesions on the trunk that had appeared 5 days earlier on his chest and remained stable. No fever, malaise, or systemic symptoms were present. On physical examination, he had 15–20 well-demarcated erythematous, slightly infiltrated, edematous plaques [Figure 1]. Blood analysis showed neutropenia (2860/mm³ with 39.2% neutrophils). Erythrocyte sedimentation rate was 54 mm.

Skin biopsy revealed a perivascular, polymorphous, inflammatory infiltrate composed of lymphocytes and histiocyte-like cells [Figure 2]. Histiocyte-like cells were positive for myeloperoxidase and lysozyme. Karyorrhexis was observed although vasculitis was not seen. Skin biopsy culture was negative. He did not receive treatment with granulocyte-macrophage-colony stimulating factor or other drugs known to be associated with Sweet's

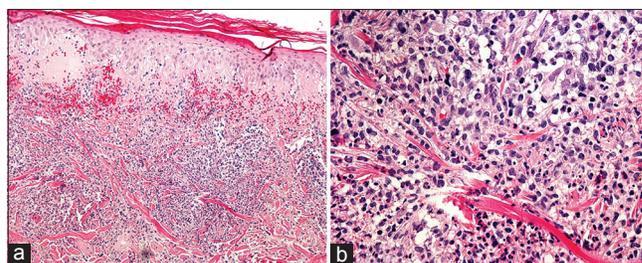


Figure 2: (a) Edema in papillary dermis. Polymorphous nodular infiltrates in reticular dermis and extravasation of erythrocytes (H and E, x100). (b) Lymphocytes without atypical nuclei, scattered mature neutrophils and many histiocyte-like cells (H and E, x200)

syndrome. We made a diagnosis of histiocytoid Sweet's syndrome related to bortezomib.

With intramuscular corticosteroid injection, the lesions disappeared but reappeared on the second day of the second part of the cycle. After this recurrence, he was treated with 20 mg prednisone for 4 days after every bortezomib treatment and did not develop any further recurrences.

Sweet's syndrome related to multiple myeloma is infrequent,^[9] but bortezomib-related neutrophilic diseases have been previously described with typical lesions that usually appear between the first and the third cycle.^[4-11] The presence of leucocytosis or fever may favor the diagnosis of myeloma associated-Sweet's syndrome, but both findings were not present in our case unlike some other cases.^[11] We were able to find only 2 previous cases of histiocytoid Sweet's syndrome related to bortezomib.^[4,12] The main differential diagnoses of histiocytoid Sweet's syndrome include interstitial granuloma annulare and interstitial granulomatous dermatitis, both showing a denser, "bottom-heavy," inflammatory infiltrate of histiocytes with large, pleomorphic nuclei that in some small foci are arranged in palisades surrounding degenerated basophilic collagen;^[1] methotrexate-induced rheumatoid papules, which appears only in methotrexate-treated patients; and leukemia cutis that shows nodular dermal infiltrates of medium-sized, round to oval mononuclear cells that express lysozyme, myeloperoxidase, CD43, CD45, and CD68. Specific myeloma infiltration should be ruled out when evaluating presumed lesions of histiocytoid Sweet's syndrome. A cytologic examination of peripheral blood should be performed and fluorescence *in situ* hybridization may be useful to detect underlying cytogenetic abnormalities in histiocytoid Sweet's syndrome when there is an identifiable chromosomal abnormality.^[13]

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REFERENCES

1. Requena L, Kutzner H, Palmedo G, Pascual M, Fernandez-Herrera J, Fraga J, *et al.* Histiocytoid Sweet syndrome: A dermal infiltration of immature neutrophilic granulocytes.

Arch Dermatol 2005;141:834-42.

2. Garcia-Navarro X, Puig L, Fernandez-Figueras MT, Dalmau J, Roe E, Alomar A. Bortezomib-associated cutaneous vasculitis. *Br J Dermatol* 2007;157:799-801.

3. Agterof MJ, Biesma DH. Images in clinical Medicine. Bortezomib-induced skin lesions. *N Engl J Med* 2005;352:2534.

4. Murase JE, Wu JJ, Theate I, Cole GW, Barr RJ, Dyson SW. Bortezomib-induced histiocytoid Sweet syndrome. *J Am Acad Dermatol* 2009;60:496-7.

5. Van Regenmortel N, Van de Voorde K, De Raeve H, Rombouts S, Van de Velde A, Lambert J, *et al.* Bortezomib-induced Sweet's syndrome. *Haematologica* 2005;90:43.

6. Liu CI, Hsiao CH, Wu JT, Tsai TF. Sweet syndrome with histiocytoid infiltrate and neutropenia: A rare combination. *J Am Acad Dermatol* 2009;61:882-4.

7. Knoops L, Jacquemain A, Tennstedt D, Theate I, Ferrant A, Van den Neste E. Bortezomib-induced Sweet syndrome. *Br J Haematol* 2005;131:142.

8. Paiva CM, Kurtis B, Mekki M, Newman MA, Singhal S, Lacouture ME. Neutrophilic dermatitis associated with bortezomib in a patient with multiple myeloma. *Ann Oncol* 2007;18:1744-5.

9. Tanguy-Schmidt A, Avenel-Audran M, Croue A, Lissandre S, Dib M, Zidane-Marinnes M, *et al.* Bortezomib-induced acute neutrophilic dermatosis. *Ann Dermatol Venereol* 2009;136:443-6.

10. Thomas M, Cavelier Balloy B, Andreoli A, Briere J, Petit A. Bortezomib-induced neutrophilic dermatosis with CD30+lymphocytic infiltration. *Ann Dermatol Venereol* 2009;136:438-42.

11. Thuillier D, Lenglet A, Chaby G, Royer R, Vaida I, Viseux V, *et al.* Bortezomib-induced eruption: Sweet syndrome? Two case reports. *Ann Dermatol Venereol* 2009;136:427-30.

12. Kim JS, Roh HS, Lee JW, Lee MW, Yu HJ. Distinct variant of Sweet's syndrome: Bortezomib-induced histiocytoid Sweet's syndrome in a patient with multiple myeloma. *Int J Dermatol* 2012;51:1491-3.

13. Chavan RN, Cappel MA, Ketterling RP, Wada DA, Rochet NM, Knudson R, *et al.* Histiocytoid Sweet syndrome may indicate leukemia cutis: A novel application of fluorescence *in situ* hybridization. *J Am Acad Dermatol* 2014;70:1021-7.

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