

Unusual Manifestation of Sweet's Syndrome in B-cell Lymphoma

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Sir,

Sweet's syndrome is a rare, acute skin disease, first described in 1964 (1). The acute febrile neutrophilic dermatosis is characterized by elevated erythematous plaques, fever, leucocytosis, general malaise and a dense dermal infiltrate of neutrophils with oedema of the papillary dermis (2). In general, there is no histological evidence for vasculitis, but leucocytoclasia is a prominent feature, as is endothelial cell swelling. Subcutaneous tissues are rarely involved (3).

Mostly idiopathic, Sweet's syndrome may occur in pregnancy or in association with infectious and autoimmune diseases. In 10–20% it is associated with malignancies, predominantly malignant haematological disorders (4–6). The association of Sweet's syndrome with non-Hodgkin's lymphoma is known, but bullous reaction of Sweet's syndrome associated with this disease has only been described in a few cases (4, 7).

We report on a patient with B-cell non-Hodgkin's lymphoma who showed clinical and histological features pointing to Sweet's syndrome and histological features which additionally showed deep and massive infiltration of eosinophils as well as leucocytoclastic vasculitis.

CASE REPORT

A 59-year-old female patient was first diagnosed for a B-cell non-Hodgkin lymphoma of low malignancy Rai stage II (8) in November 1996. Lymph nodes in the retroperitoneal area, in the region of the liver hilus and in the bone marrow were involved. Blood counts revealed leucocytosis of 100.0/nl (normal range 4.0–10.0/nl). Chemotherapy following the KNOSPE regimen (Chlorambucil 0.4 to 0.7 mg/kg, spread on day 1 to 3 p.o., prednisolone 75 mg on day 1, 50 mg on day 2, 25 mg on day 3 p.o.) applied from July 1998 until July 1999 and fludarabine from July until December 1999 had induced partial resolution. In August 1999, the patient was admitted to our outpatient clinic with erythematous plaques and vesicular and erosive lesions on the upper and lower extremities and trunk. Clinical examination revealed acute tonsillitis and fever up to 39°C. Blood counts were within the normal range, C-reactive protein was 14.6 mg/dl (normal range <5 mg/dl). Histopathological examination revealed a skin manifestation of the B-cell non-Hodgkin's lymphoma. The skin lesions cleared completely after topical treatment with glucocorticosteroids; the acute tonsillitis was treated with antibiotics.

Half a year later, in May 2000, the patient presented again with reddish plaques in distinct areas in comparison to the previous examination. The plaques were found on the face and extremities, developing firm bullae on inflamed skin (Fig. 1).

Blood counts revealed a leucocytosis of 67.26/nl, prolymphocytes and Gumbrecht's shadows. Immunoserological investigations were negative. Histopathological examination of a blister revealed a strong oedema of the papillary dermis with a bullous reaction and a perivascular and interstitial infiltrate consisting of lymphocytes, eosinophils and polymorphous neutrophils. Also, vascular changes with fibrinoid necrosis of the small vessels and nuclear dust were seen. Clinical symptoms as well as histopathological features of the skin lesions led to the diagnosis of Sweet's syndrome. Immunohistology did not show any features of bullous autoimmune diseases or vasculitis due to immunocomplexes (Fig. 2a).

The lesions cleared completely after 2 weeks of treatment with oral corticosteroids (60 mg methylprednisolone initially). During the course of the dermatological symptoms there was no activity of the B-cell lymphoma and therefore no necessity for specific treatment.

In June 2001, a relapse of the B-cell lymphoma occurred and the patient was treated with fludarabine and cyclophosphamid before the skin lesions reoccurred. In July 2001, the patient presented again with reddish, infiltrated plaques on the face and extremities in the same areas as previously. Blood counts revealed diminished leucocytes with 3.47/nl. Histopathologic features from a different lesion now revealed an eosinophilic dermatitis with superficial and deep perivascular, interstitial and periadnexal infiltrates of eosinophils. The histopathologic findings first suggested Wells syndrome, but no flame figures were found and peripheral blood did not show eosinophilia (Fig. 2b).

The patient was again treated with oral corticosteroids (60 mg methylprednisolone initially) and the lesions cleared within 2 weeks.



Fig. 1. Reddish patch with a firm bulla and peripheral vesicles as a manifestation of Sweet's syndrome.

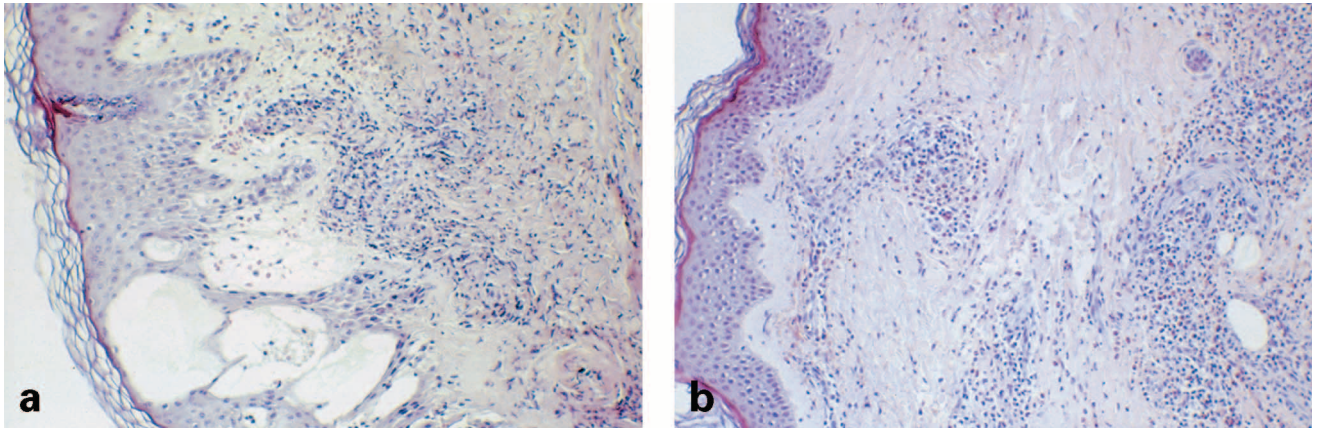


Fig. 2. Strong oedema of the papillary dermis with a bullous reaction, perivascular and interstitial infiltrate of lymphocytes, eosinophils and polymorphous neutrophils in Sweet's syndrome (a). Eosinophilic dermatitis with a superficial and deep perivascular and interstitial infiltrate of eosinophils frequently found in Wells' syndrome (b).

DISCUSSION

Sweet's syndrome is a disease with distinct clinical features, but the histological findings often vary. Nevertheless, the additional features of eosinophilic infiltration and leucocytoclastic vasculitis may require a new approach to this entity. The association of neoplasms and Sweet's syndrome has often been described in the literature (2, 4), and association with non-Hodgkin lymphoma was reported by Woodrow et al. in 1996 (7).

The biopsy taken in May 2000 showed a strong oedema of the papillary dermis and a perivascular and interstitial infiltrate of plasma cells, histiocytes, eosinophils and neutrophils. The histological features pointed to the diagnosis Sweet's syndrome. The numerous eosinophils in this biopsy were unusual for Sweet's syndrome, since a larger count of neutrophils might have been expected. Eosinophilic infiltration in Sweet's syndrome was reported by Masuda et al. (9) in up to 40% of the lesions, but also eosinophilia in peripheral blood. The histopathological features of leucocytoclastic vasculitis are not characteristic of Sweet's syndrome, although some reports show vasculitis up to 29%, due to noxious products released from neutrophils (10). In our patient, mostly eosinophils were seen. Nevertheless, clinical symptoms such as fever, leucocytosis and erythematous, indurated and sometimes bullous plaques pointed to the diagnosis Sweet's syndrome.

Later, in July 2001, histological findings showed a superficial and deep infiltrate of eosinophils. Although no flame figures were found in the lesion, the histopathology was compatible with Wells' syndrome but not with Sweet's syndrome. Flame figures in Wells' syndrome are characteristic, but not always seen in early stages of the lesion (11–13).

Bullous Sweet's syndrome in association with non-Hodgkin's B-cell lymphoma has only rarely been observed. In addition, this case showed clinical symptoms of Sweet's syndrome but at different times histopathological findings characteristic of Sweet's syndrome, some features of Wells' syndrome and leucocytoclastic vasculitis. The fact that histopathology changed successively might suggest the existence of an overlap between these three disorders. There is only one report on a similar phenomenon: In a retrospective study on nine patients with Wells' syndrome,

Cosigny et al. described a subsequent development of Wells' syndrome, Sweet's syndrome and a leucocytoclastic vasculitis in a patient who had developed a ganglioneuric lymphoma several months after the onset of Wells' syndrome (14).

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