CASE REPORT

Sweet's syndrome in a patient with chronic lymphocytic leukaemia

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SUMMARY

Bullous Sweet's syndrome is a rare variant of the inflammatory neutrophilic dermatosis characterised by painful bullous skin lesions, fever, leukocytosis and a neutrophilic infiltrate of the dermis. The condition may be classified according to aetiology into classical (idiopathic), malignancy-associated and drug-induced. Neutrophilic infiltration occurs in response to a systemic insult. A punch biopsy for histology and culture is necessary due to its close resemblance to infection. Characteristic histology features a dense infiltration of neutrophils in the upper and mid dermis, oedema in the superficial dermis and endothelial swelling. Treatment with systemic glucocorticosteroids typically results in a dramatic clinical response. This case report illustrates a rare case of bullous Sweet syndrome associated with chronic lymphocytic leukaemia in a 53-year-old man.

BACKGROUND

Sweet's syndrome (SS) is a rare inflammatory neutrophilic dermatosis that is characterised by the acute eruption of painful, oedematous lesions on the skin, associated with fever and leukocytosis. The syndrome was first described by Sweet in 1964, who identified eight women with the cutaneous manifestation, several in association with prior infection.¹ SS has since been associated with a range of conditions, leading to a classification system based on aetiology. There are three major subtypes of SS: classical, malignancy-associated and drug-induced. Classical, or idiopathic, SS forms the majority of cases, however malignancy-associated SS constitutes a significant proportion, and of those the condition is more likely to occur in association with haematological malignancies rather than solid

tumours.² Atypical presentations of the condition include subcutaneous SS, where the site of neutrophilic infiltration is in the subcutaneous fat rather than the dermis, resulting in the development of deep erythematous nodules, and in bullous SS, whereby vesicles and bullae are seen, often along with ulceration resembling pyoderma gangrenosum.^{3,4} This rare manifestation of SS is described in the following case report, in association with chronic lymphocytic leukaemia (CLL).

CASE PRESENTATION

A 53-year-old man presented to the Medical Assessment Unit following the development of painful haemorrhagic bullous lesions on the dorsum and in the first web spaces of both hands (see [figure 1](#)). He was afebrile and systemically well. The patient had no medical history and had worked as a stone-mason for several years. A review of systems was unremarkable, notably there was no history of weight loss or fever. Full skin examination was otherwise normal.

INVESTIGATIONS

A full blood count revealed a white cell count of 27.7 and lymphocyte count of 19.7. Blood film showed a reactive lymphocytosis with evidence of smear cells. An incisional biopsy was taken for histology and immunofluorescence, and a punch biopsy was sent for culture. Histology showed marked spongiosis and oedema within the papillary dermis and a dermal infiltrate predominantly composed of neutrophils exhibiting leukocytoclasia consistent with a localised variant of SS (see [figures 2 and 3](#)). Further peripheral blood results confirmed a persistent lymphocytosis and immunophenotyping was consistent with CLL. The lack of B symptoms and normal bone marrow function indicated stage A (early CLL).

DIFFERENTIAL DIAGNOSIS

Differential diagnosis included bullous pyoderma gangrenosum, epidermolysis bullosa acquisita and viral and bacterial infection.

TREATMENT

Initial treatment with topical clobetasol propionate 0.05%, neomycin sulfate 0.5% and nystatin 100 000 U/g was commenced. Thereafter, joint care between dermatology and haematology ensued and the patient was started on 40 mg of prednisolone,

Figure 1 Haemorrhagic bullous lesions on the dorsum and in the first web spaces of both hands.

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Figure 2 Acral skin showing marked spongiosis and oedema within papillary dermis and a dermal infiltrate predominantly composed of neutrophils exhibiting leukocytoclasia (4×).

reducing by 10 mg /week. Specific treatment for CLL was not required.

OUTCOME AND FOLLOW-UP

Subsequently, skin lesions have improved, appearing as erythematous warty plaques on most recent review. He continues to be regularly reviewed in both haematology and dermatology outpatient clinics.

DISCUSSION

Bullous SS is a rare variant of the dermatological condition, characterised by the formation of vesicles and, often flaccid, bullae with underlying erythematous or violaceous plaques.⁵ Lesions typically present as tender papules, plaques or nodules that progress into the characteristic lesions. Ulceration, often resembling pyoderma gangrenosum, may occur, usually in association with haematological malignancy.⁴ Acute myeloid leukaemia is the most common haematological malignancy to be associated with SS. CLL, as presented in this case, is a much less common association.²

The pathophysiology of SS is characterised by an immunological process of neutrophilic infiltration, in response to a systemic insult such as malignancy, infection, inflammation or drug

Figure 3 High-power view of inflammatory infiltrate (20×).

Major criteria

- Abrupt onset of painful erythematous plaques or nodules
- Histopathologic evidence of a dense neutrophilic infiltrate without evidence of leukocytoclastic vasculitis

Minor criteria

- Pyrexia > 38
- Association with an underlying haematologic or visceral malignancy, inflammatory disease, or pregnancy, OR preceded by an upper respiratory of gastrointestinal infection or vaccination
- Excellent response to treatment with systemic corticosteroids or potassium iodide
- Abnormal laboratory values at presentation (three of four): erythrocyte sedimentation rate >20mm/hr; CRP elevated; >8000 leukocytes; >70% neutrophils

The presence of both major criteria and two of the four minor criteria is required

Figure 4 Diagnostic criteria for classical and malignancy-associated Sweet's syndrome. CRP, C reactive protein.

exposure. Exogenous granulocyte colony-stimulating factor is a common cause of drug-induced SS, due to its role in increasing the number of circulating neutrophils.⁶ Diagnosis relies on both clinical and laboratory findings based on criteria outlined in 1986 (see figure 4).⁷ Both major criteria plus two of the four minor criteria are required to establish a diagnosis. Clinical assessment should include a complete physical examination not limited to the skin surface. In addition to the typical cutaneous manifestations of SS, extracutaneous manifestations and involvement of other systems such as the musculoskeletal system may occur. Ocular involvement is a common manifestation, particularly in the classical variant of SS resulting from neutrophilic infiltration of the eye. This may present as conjunctivitis, episcleritis, scleritis, keratitis or glaucoma among other pathologies.^{2,8} Laboratory tests including skin biopsy and serology are required to make the diagnosis. A punch biopsy for histology and culture should be performed due to the condition's close resemblance to infection. Characteristic histological features of SS include dense infiltration of neutrophils in the upper and mid dermis (sparing the epidermis), oedema in the superficial dermis, leukocytoclasia and endothelial swelling. Vasculitis is not a feature.⁹ A leukocytosis (neutrophilia) on serology is consistent with SS. Additional laboratory tests are useful in identifying extracutaneous involvement or associated conditions and workup for underlying malignancy should be performed.¹⁰

Infection is one of the key differential diagnoses to exclude in a patient presenting with fever, leukocytosis and neutrophilic infiltrative cutaneous lesions. Other differential diagnoses largely depend on the morphology of the presenting lesions. Bullous lesions such as those in the reported case may represent other bullous conditions of the autoimmune, infective or vasculitic variety, such as pemphigoid, or bullous systemic lupus erythematosus. Other neutrophilic dermatoses should be considered, for example, pyoderma gangrenosum and Behçet's syndrome.¹¹

First-line treatment with systemic glucocorticoid therapy usually results in a dramatic clinical response in all variants of SS. In drug-induced SS, an improvement is often seen within several weeks of withdrawing the offending medication however acceleration of response with pharmacological intervention warrants its use.¹² Statistics relating to the resolution of SS in response to treatment of associated malignancy are lacking, thus treatment with systemic glucocorticoid is typically initiated without delay.¹³ Systemic treatment is usually required, though patients

who present with localised lesions of <5% body surface area and no systemic symptoms may be successfully treated with local corticosteroid therapy. Alternative therapies include colchicine, dapsone, and potassium iodide. For severe SS or disease that fails to respond to other therapies, pulse intravenous glucocorticoid therapy may be effective.¹²

Learning points

- ▶ Sweet's syndrome (SS) is rare in patients with chronic lymphocytic leukaemia (CLL) however investigating for an underlying cause, particularly malignancy, is imperative.
- ▶ Underlying infection and drug causes must also be actively sought.
- ▶ It should be borne in mind that malignancy-associated SS can accompany both solid tumours and haematological malignancies, and cannot be managed easily as an idiopathic form.
- ▶ In the context of CLL, despite lymphocytic infiltration of the bone marrow, neutrophilia remains a part of the diagnostic criteria.

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REFERENCES

- 1 Sweet RD. An acute febrile neutrophilic dermatosis. *Br J Dermatol* 1964;76:349–56.
- 2 Cohen PR. Sweet's syndrome—a comprehensive review of an acute febrile neutrophilic dermatosis. *Orphanet J Rare Dis* 2007;2:34.
- 3 Cohen PR. Subcutaneous Sweet's syndrome: a variant of acute febrile neutrophilic dermatosis that is included in the histopathologic differential diagnosis of neutrophilic panniculitis. *J Am Acad Dermatol* 2005;52:927–8.
- 4 Tacke J, Diepgen TL, Albrecht HP, et al. [Idiopathic pustular and bullous variants of sweet syndrome]. *Hautarzt* 1994;45:184–7.
- 5 Voelter-Mahlknecht S, Bauer J, Metzler G, et al. Bullous variant of Sweet's syndrome. *Int J Dermatol* 2005;44:946–7.
- 6 White JM, Mufti GJ, Salisbury JR, et al. Cutaneous manifestations of granulocyte colony-stimulating factor. *Clin Exp Dermatol* 2006;31:206–7.
- 7 Su WP, Liu HN. Diagnostic criteria for Sweet's syndrome. *Cutis* 1986;37:167.
- 8 Cohen PR, Hongsmann H, Kurzrock R et al. Acute febrile neutrophilic dermatosis (Sweet syndrome). In: Goldsmith LA, Katz SI, Gilchrist BA, eds. *Fitzpatrick's Dermatology in General Medicine*. 8th ed. McGraw Hill, 2012;1:362.
- 9 Weedon D. The vasculopathic reaction pattern. In: *Weedon's Skin Pathology*. 3rd ed. Elsevier Limited, 2010:195.
- 10 Cohen PR, Kurzrock R. Sweet's syndrome and cancer. *Clin Dermatol* 1993;11:149.
- 11 Dabade TS, Davis MD. Diagnosis and treatment of the neutrophilic dermatoses (pyoderma gangrenosum, Sweet's syndrome). *Dermatol Ther* 2011;24:273–84.
- 12 Cohen PR, Kurzrock R. Sweet's syndrome: a review of current treatment options. *Am J Clin Dermatol* 2002;3:117.
- 13 Cohen PR, Talpaz M, Kurzrock R. Malignancy-associated Sweet's syndrome: review of the world literature. *J Clin Oncol* 1988;6:1887–97.

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