

Case Report

Acute onset of fever and rash in a patient with acute myeloid leukaemia: a case of Sweet's syndrome

一名急性骨髓性白血病患者的急性發熱及皮疹：史維特氏症候群一例

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A young man with underlying acute myeloid leukaemia presented with acute onset of fever and erythematous papules and plaques with pustules on the face and limbs. The clinical and histological findings were compatible with a diagnosis of Sweet's syndrome. He was treated with topical steroid and topical antibiotics with complete resolution of the skin lesions. In this article, the condition of Sweet's syndrome will be reviewed.

一名本身有急性骨髓性白血病的年輕男患者出現急性發熱及皮疹，在臉部和四肢長出紅色的丘疹和斑塊，並伴有膿疱。其臨床和組織學結果與史維特氏症候群的診斷吻合。他的皮損在使用外用類固醇及外用抗生素治療後，完全消退。本文將會回顧史維特氏症候群的情況。

Keywords: Acute febrile neutrophilic dermatosis, Sweet's syndrome

關鍵詞：急性發燒嗜中性白血球增多皮膚症、史維特氏症候群

Introduction

Sweet's syndrome (also known as acute febrile neutrophilic dermatosis) is characterised by acute onset of tender, non-pruritic, erythematous papules and plaques associated with systemic upset, in particular fever and leucocytosis. It often

presents in patients with underlying systemic conditions such as malignancies, infections, autoimmune diseases or drug use. The condition shows good response to treatment with systemic steroid and the prognosis is generally favourable although recurrences are known to occur especially if the underlying systemic condition has not been adequately treated.

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Case report

A 37-year-old man was admitted for treatment of newly diagnosed acute myeloid leukaemia. He developed acute onset of fever and rash seven days after the administration of chemotherapy.

The rash was non-pruritic but slightly tender. It started on both cheeks and progressed to both hands, forearms and pretibial regions. He subsequently developed pustules on both cheeks.

Physical examination showed erythematous papules and plaques with small pustules on both cheeks, the dorsa of the hands, the forearms and pretibial areas (Figures 1-3). There was no mucosal involvement and there were no vesicles or blisters. Complete blood picture showed normal neutrophil count, however it must be taken into consideration that this patient was recently given chemotherapy. Liver and renal function tests were normal.

The differential diagnosis included infective causes such as folliculitis, dermatophytic infection and disseminated herpes zoster. Other differential diagnoses included neoplastic conditions such as leukaemia cutis, other neutrophilic dermatosis such as neutrophilic eccrine hidradenitis, acute generalised exanthematous pustulosis, monomorphic acneiform eruption and cutaneous vasculitis such as leucocytoclastic vasculitis.

An incisional skin biopsy was performed over the forearm of this patient. Histology showed a dense infiltrate of mature neutrophils in the upper half of the dermis with the presence of leucocytoclasia. No true vasculitis or fibrinoid necrosis was present. Few eosinophils were present. No infectious pathogens were identified with special stains including PASD, Gram stain, Grocott, Ziehl-Neelsen, Wade-Fite or mucicarmine stain. Immunofluorescence studies were negative (Figures 4 & 5).

Both the clinical and histological findings were compatible with a diagnosis of Sweet's syndrome. The patient was treated with topical steroid (mometasone furoate) and erythromycin solution. He subsequently developed neutropaenia due to the effect of chemotherapy and the rash resolved without the need for systemic steroid.



Figure 1. Right cheek showing erythematous papules and pustules.



Figure 2. Left cheek showing erythematous plaques and pustules.

Discussion

Sweet's syndrome was first described by Robert Douglas Sweet in 1964.¹ He reviewed eight female patients who presented with fever, acute tender erythematous plaques, leucocytosis and infiltration of the dermis with neutrophils. He coined the term "acute febrile neutrophilic dermatosis." In 1968 Whittle et al reported a similar case and named it "Sweet's syndrome".²

Sweet's syndrome is an uncommon condition with a worldwide distribution although the condition seems to be more common in Japan. There is a female predominance of 4 to 1. The average age of onset is 30-60 years.³



Figure 3. Right forearm showing erythematous nodules and plaques.

Sweet's syndrome is classified into three major categories according to the underlying clinical setting; classic or idiopathic Sweet's syndrome, malignancy-associated Sweet's syndrome and drug-induced Sweet's syndrome.⁴ Classic Sweet's syndrome occurs in women aged 30-60 and is usually preceded by upper respiratory tract infection, streptococcal infection, pregnancy or autoimmune diseases. Malignancy-related Sweet's

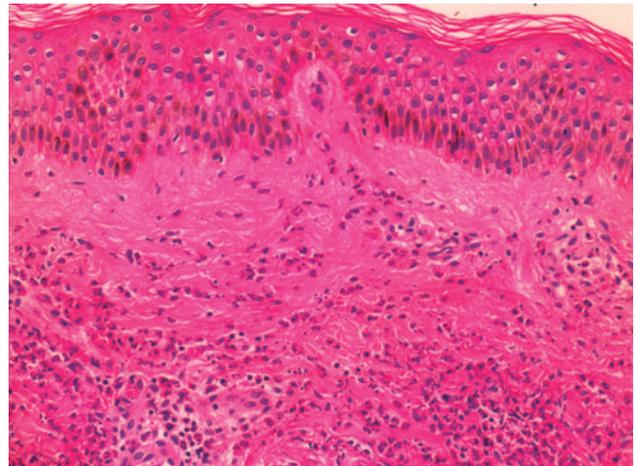


Figure 4. H&E at low power showing dense infiltrate of mature neutrophils in the upper half of the dermis with presence of leukocytoclasia (x40 magnification).

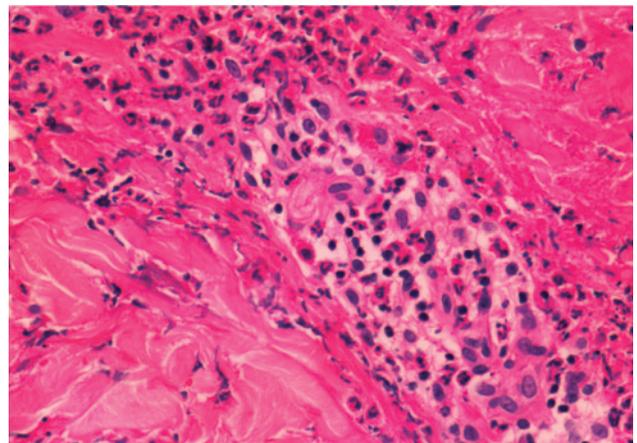


Figure 5. H&E at high power showing dense perivascular and interstitial dermal neutrophil infiltrate with minor element of leukocytoclasia consistent with Sweet's syndrome (x100 magnification).

syndrome is most commonly associated with underlying haematological malignancies. Twenty-one percent of all patients with Sweet's syndrome have an underlying malignancy, the majority being haematological malignancies.⁵ Solid organ tumours such as carcinoma of breast, genitourinary or gastrointestinal tract have also been reported to be associated with Sweet's syndrome. Drug induced Sweet's syndrome is commonly caused by the use of granulocyte-colony stimulating factor (G-CSF), granulocyte-myelocyte colony stimulating factor (GM-CSF), antibiotics such as septrin and clindamycin and non-steroidal anti-inflammatory drugs. Sweet's syndrome can also be associated with inflammatory bowel diseases and pregnancy.

After making a diagnosis of Sweet's syndrome, it is imperative to look for any underlying causes and associated conditions as treatment of the underlying cause is essential to the treatment of the condition. There are two subtypes of Sweet's syndrome known as histiocytoid Sweet's syndrome and neutrophilic dermatosis of the dorsal hands. Histiocytoid Sweet's syndrome presents with typical clinical features of Sweet's syndrome, however biopsy specimens show predominance of histiocytoid mononuclear cells in the infiltrate compared with the classical polymorphonuclear infiltrate. It is also characterised by intense myeloperoxidase activity and CD68 positive staining.⁶ Neutrophilic dermatosis of the dorsal hands is characterised by typical clinical lesions of Sweet's syndrome but the distribution is limited to the dorsa of both hands.⁷

The clinical features are characterised by acute onset of tender, non-pruritic erythematous papules and plaques. Due to the marked dermal papillary oedema, these lesions often have a pseudovesicular and pseudopustular appearance. The lesions are typically firm on palpation and may progress to vesiculation, bullae or pustules within the plaques. Lesions are typically located in the head, neck and upper extremities including the dorsal surface of the hands but can occur anywhere.

Sweet's syndrome is often associated with systemic manifestations. The commonest systemic features are fever and leucocytosis often occurring in around fifty percent of patients. Less common manifestations (20-50%) include arthralgia, arthritis, myalgias and ocular involvement (conjunctivitis, episcleritis, limbal nodules and iridocyclitis). Uncommonly, Sweet's syndrome may be associated with pulmonary involvement in the form of neutrophilic alveolitis, bone involvement with multifocal sterile osteomyelitis and renal involvement in the form of mesangial glomerulonephritis. Rare associations include hepatitis, aseptic meningitis, encephalitis and pancreatitis.³

Skin biopsy is often necessary to establish the diagnosis. The hallmark pathological feature of Sweet's syndrome is the dense and diffuse nodular and perivascular neutrophilic infiltrate with marked papillary dermal oedema. There is typically no evidence of vasculitis although leucocytoclasia with endothelial swelling but without fibrinoid necrosis may be present.³ The dermal infiltrate may uncommonly extend into the subcutis creating a septal or even lobular panniculitis. This condition is referred to as Sweet's panniculitis.⁸ Other investigations relevant to Sweet's syndrome include simple blood tests which demonstrate leucocytosis with neutrophilia and elevated inflammatory markers like erythrocyte sedimentation rate and C-reactive protein.

The pathogenesis of Sweet's syndrome is not known. It is postulated to be secondary to a local or systemic dysregulation of cytokine secretion including interleukin-1, granulocyte colony-stimulating factor and granulocyte-macrophage colony stimulating factor.⁹

The diagnostic criteria for Sweet's syndrome was devised by Su and Liu in 1986 (Table 1). Two major and two minor criteria are needed for a diagnosis of Sweet's syndrome to be made.⁴

In the treatment of Sweet's syndrome, it is important to search for and identify any underlying

Table 1. Diagnostic criteria for Sweet's syndrome⁴

Major	Minor
1. Abrupt onset of painful, erythematous plaques or nodules occasionally with vesicles, pustules, or bullae.	1. Fever >38°C
2. Histological evidence of predominantly neutrophilic infiltration of the dermis without leucocytoclastic vasculitis.	2. Preceded by a non-specific respiratory or gastrointestinal infection or vaccination, or associated with: <ul style="list-style-type: none"> - Pregnancy - Inflammatory diseases such as autoimmune disease - Haematologic or visceral malignancy
	3. Abnormal laboratory values at presentation (3 out of 4): <ul style="list-style-type: none"> - Leukocytosis >8000/μL - >70% neutrophils in peripheral blood smear - Elevated C-reactive protein - Erythrocyte sedimentation rate >20 mm/hr
	4. Excellent response to treatment with systemic corticosteroids or potassium iodide.

causes such as drugs, infections or malignancies and treat the associated conditions accordingly. Both the cutaneous and extracutaneous manifestations are highly responsive to systemic corticosteroid therapy. The starting dose of prednisolone is 0.5-1 mg/kg/day until resolution of the skin lesions. The dose of steroid should then be gradually tapered. The average duration of treatment ranges from four to six weeks.¹⁰ For treatment of localised lesions, superpotent topical steroid or intralesional corticosteroids may be helpful. Other treatment options reported to be useful include potassium iodide, colchicine, indomethacin, dapsone and cyclosporin.³

In conclusion, Sweet's syndrome is characterised by acute onset of tender erythematous papules and plaques associated with fever, leucocytosis and elevated serum inflammatory markers. Histologically, there is characteristic dense perivascular neutrophilic infiltrate and oedema. It is strongly associated with underlying malignancy, infections, autoimmune diseases and drug use. The diagnosis of Sweet's syndrome should prompt the search of underlying associated conditions. The condition responds well to the use of systemic steroid and has a good overall prognosis.

References

1. Sweet RD. An acute febrile neutrophilic dermatosis. *Br J Dermatol* 1964;76:349-56.
2. Whittle CH, Beck GA, Champion RH. Recurrent neutrophilic dermatosis of the face – a variant of Sweet's syndrome. *Br J Dermatol* 1968;80:806-10.
3. Moschella SL, Davis MD. Neutrophilic Dermatitis. In Bologna JL, Jorizzo JL, & Schaffer JV eds. *Dermatology*, 3rd ed. Elsevier 2012:423-8.
4. Fazili T, Duncan D, Wani L. Sweet's syndrome. *Am J Med* 2010;123:694-9.
5. Buck T, Gonzalez LM, Lambert WC, Schwartz RA. Sweet's syndrome and haematological disorders, a review and reappraisal. *Int J Dermatol* 2008;47:775-82.
6. Requena L, Kutzner H, Palmedo G, Pascual M, Fernandez-Herrera J, Fraga J, et al. Histiocytoid Sweet's syndrome: a dermal infiltration of immature neutrophilic granulocytes. *Arch Dermatol* 2005;141:834-42.
7. Abbas O, Kibbi AG, Rubeiz N. Sweet's syndrome: a retrospective study of clinical and histologic features of 44 cases from a tertiary center. *Int J Dermatol* 2010; 49:1244-9.
8. Tabanlıoğlu D, Boztepe G, Erkin G, Gokoz O, Karaduman A. Sweet's syndrome and erythema nodosum: a companionship or a spectrum? – a case report and review of the literature. *Int J Dermatol* 2010; 49:62-6.
9. Uhara H, Saida T, Nakazawa H, Ito T. Neutrophilic dermatosis with acute myeloid leukemia associated with an increase of serum colony stimulating factor. *J Am Acad Dermatol* 2008;59:S10-2.
10. Dabade TS, Davis MD. Diagnosis and treatment of the neutrophilic dermatoses (pyoderma gangrenosum, Sweet's syndrome). *Dermatol Ther* 2011;24:273-84.