SWEET-LIKE SYNDROME IN A PATIENT WITH ACUTE MYELOID LEUKAEMIA

M R Norhaya, S K Cheong, N H Hamidah, O Ainoon

ABSTRACT

A 45-year-old Malay lady developed brisk vesicular, plaque-like reaction to a Mantoux test concomitant with a diagnosis of acute myeloid leukaemia (AML). The lesion resolved one month after chemotherapy. Similar lesions developed later after she was bitten by mosquitoes on the forearms. She also had the lesions over her cheek. A skin biopsy showed infiltration of the dermis with neutrophils and some monocytoid cells. The lesion resolved one week after prednisolone therapy.

Keywords: *acute myeloid leukaemia, skin infiltrate*

SINGAPORE MED J 1996; Vol 37: 320-322

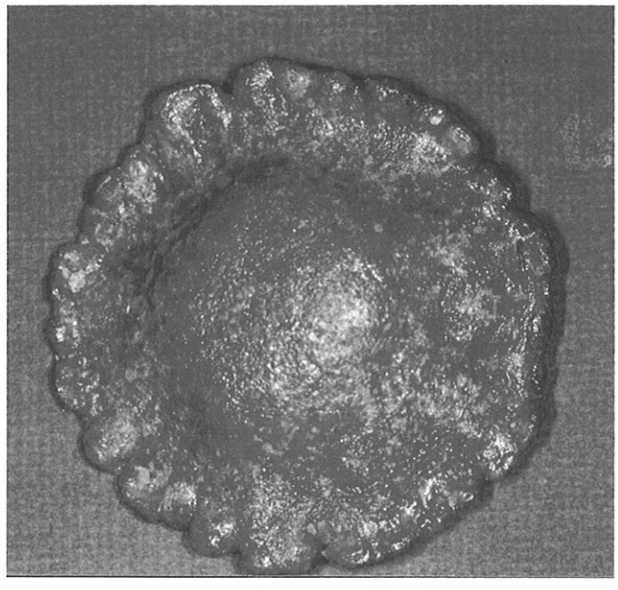
INTRODUCTION

Robert Douglas Sweet first described Sweet syndrome (SS) in 1964[1] which consists of 4 cardinal features: fever; neutrophil polymorphonuclear leucocytosis in the blood; raised, painful plaques on the limbs, face and neck; and dense dermal infiltrate with mature neutrophils seen histologically. As upper respiratory tract infection is the most common preceding illness, leukaemias and other malignancies are associated with SS. Lesions of SS may follow the leukaemia, may be manifestation of a leukaemic recurrence, or may herald in the onset of leukaemia in a patient not previously known to have this disease[2]. Acute myeloid leukaemia is the most common neoplasm associated with Sweet syndrome[3]. Up to 1993[4] there were 38 reported cases of SS associated with acute myeloid leukaemia. We report yet another case in which a patient developed SS coincident with the diagnosis of AML and recurrence of the lesions one month later. An interesting observation is that the lesions resembled a Malaysian delicacy 'kuih cucur' (Fig 1) which is a cake made of glutinous flour and sugar.

CASE REPORT

A 45-year-old Malay lady was hospitalised in January 1995 with low grade intermittent fever, loss of appetite and non-productive cough with occasional haemoptysis of three weeks' duration. The patient's temperature was 37.3°C; she was pale and there was gum hypertrophy. She had a concomitant right divergent squint. There was hepatomegaly with a liver span of 14cm. The Traub's space was dull. The rest of the physical examination was normal. Full blood count revealed a haemoglobin of 8.4g/L, total white count of 80.3 x 10^9/L (80% blasts) and a platelet count of 50 x 10^9. Her erythrocyte sedimentation rate (ESR) was 145mm/hr. Bone marrow aspirate morphology, cytochemistry and immunophenotyping results were consistent with AML (FAB M4). Septic workup including a Mantoux test was done on admission. The Mantoux reaction was 18mm and was reported as 'strongly positive' with a warm indurated, erythematous plaque surrounded by vesicles. She was started on chemotherapy consisting of intravenous epirubicin 80mg for four days and intravenous cytosine arabinoside 75mg twelve hourly for one week. Cultures from the blood and sputum were negative for bacteria and fungus. Widal Weil Felix test, blood film for malaria parasite and sputum for acid fast bacilli were also negative. However, her urine grew *Klebsiella species*. The 'Mantoux reaction' increased in size to 6cm in diameter within six days. It was exquisitely tender, there was surrounding erythema. The left forearm was warm, tender and inflamed. The patient received about three weeks of antibiotics including cloxacillin, ceftazidine, piperacillin, netromycin and tienam. She also received a course of anti-fungal treatment with fluconazole 100mg daily for 2 weeks. Her temperature settled two weeks after initiation of chemotherapy. During the week that she has received chemotherapy, there was marked improvement of the skin lesion, and by one month after diagnosis and treatment of AML, there

Fig 1 – The "Kuih Cucur"



Department of Medicine
Faculty of Medicine
Universiti Kebangsaan Malaysia (UKM)
Jalan Raja Muda Abdul Aziz
50300 Kuala Lumpur
Malaysia

M R Norhaya, MBBS
Medical Officer

Haematology Unit
Department of Pathology
Faculty of Medicine
Universiti Kebangsaan Malaysia

S K Cheong, MBBS, MRCP (UK), DCP (Lond), AM (M'sia), FRCP (Glas), FRCP (Edin), FRCPA (Aust)
Professor

N H Hamidah, MBBCh
Lecturer

O Ainoon, MBBS, DCP
Associate Professor

Correspondence to: Prof S K Cheong

was a complete resolution of the skin lesion. Review of her peripheral blood film showed that she was not in remission with persistence of blasts cells. She was scheduled for another course of chemotherapy the following month.

Three days before her second admission, she was bitten by mosquitoes on two sites over the right forearm (Fig 2). She developed severe 'reaction' to the mosquito bites with tender swelling and induration surrounded by erythematous raised papular edges. Her husband commented that the lesions resembled 'kuih cucur'.

Fig 2a - Lesions over the forearm (before prednisolone)

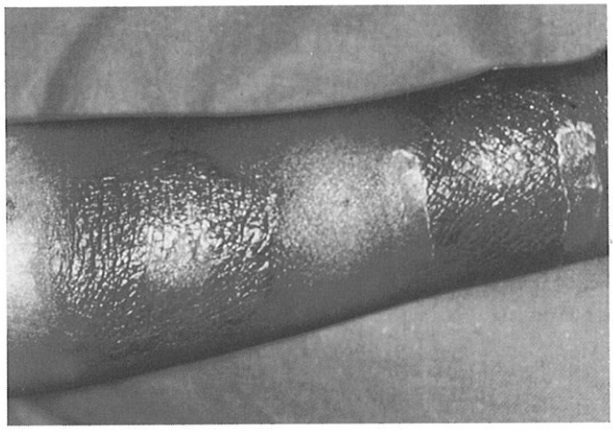
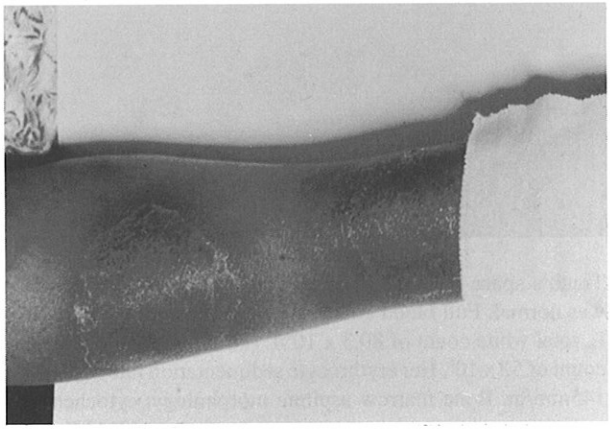


Fig 2b - One day after prednisolone



She was also noted to have similar but smaller lesions over the left cheek (Fig 3) and the left side of her neck. She developed low grade fever in the ward which settled after two days. She did not have upper respiratory tract or chest symptoms. She had myalgia, and while in the ward, developed bilateral wrist arthritis.

Cultures from blood, urine and throat were negative. Chest radiograph was normal. Her ESR was 120mm/hr. Biopsy of the new lesion showed dense dermal neutrophil infiltrates (Fig 4). Some monocytoid cells were also noted.

Urine for albumin was negative. Screening for collagen disease ie LE cells, rheumatoid factor, anti-nuclear factor were negative. The values of C_3 and C_4 were normal. She remained afebrile and another course of epirubicin and cytosar was initiated. Meanwhile, she was started on prednisolone 40 mg daily twelve days later and there was improvement of the lesions which resolved within one week. However, she did not respond to the second course of chemotherapy.

Fig 3a - Lesions over the cheek (before prednisolone)

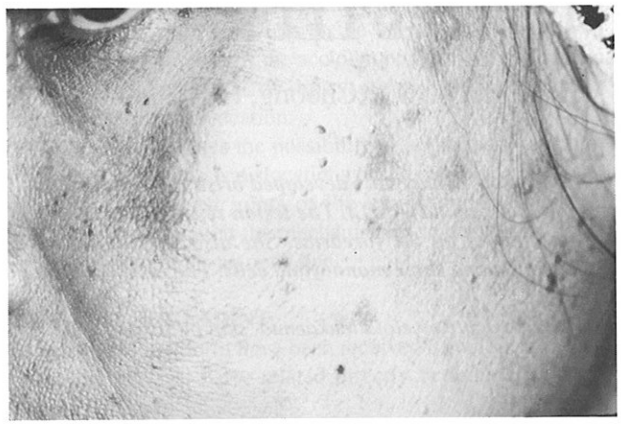


Fig 3b - One day after prednisolone

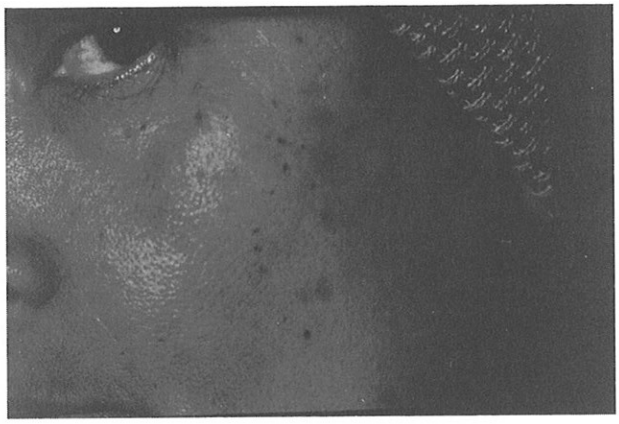
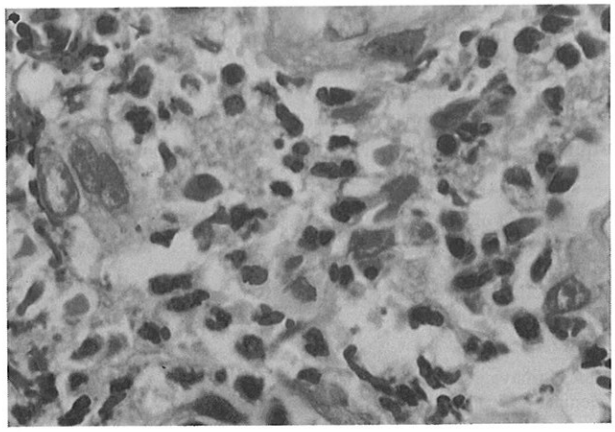


Fig 4 - Histology of the skin lesion showing dense dermal neutrophil infiltrates and some monocytoid cells



DISCUSSION

Sweet syndrome is an eponym for an acute neutrophilic leukocytosis. As the name implies, the syndrome consists of abrupt onset of red, tender cutaneous plaques on the face, extremities and upper trunk, accompanied by fever, malaise and neutrophilic leukocytosis. The plaque shows dense, dermal infiltrates of neutrophils histologically and the syndrome responds dramatically to steroids[5]. Cooper et al[5] compared the SS in patients having leukaemia and pre-leukaemia with those who are healthy. They found that there is no consistent difference

between both groups with regards to cutaneous symptoms, signs, histologic findings and response to therapy. Matta et al[6] was the first to describe SS in 2 patients who later developed acute leukaemia. Subsequently, other workers have reported the association of SS with myeloproliferative disorders.

The most common associations are with acute monocytic and acute myelomonocytic leukaemia[3]. In 1978[7], Raimer et al stated that SS may be a non-specific reaction to the underlying AML. The exact aetiology of SS is unknown, however, indirect evidence to support hypersensitivity-immunologic basis are preceding upper respiratory tract infection, arthropathy, nephropathy and curative response of steroid treatment. It has also been described with other autoimmune disorders such as interstitial inflammatory diseases and subacute thyroiditis[8]. Intradermal injections of bacterial antigens *((Streptococcus viridans)*[9] and fungal antigens *(Candida albicans)*[10] have reproduced similar lesions suggesting a limited Arthus' reaction. Our patient's lesions were both preceded by an antigen ie the first episode was by intradermal Mantoux. The brisk reaction followed by development of tender vesicles in retrospect was actually the Sweet-like syndrome induced by the antigen. These cutaneous lesions coincided with the diagnosis of acute myeloid leukaemia M4 as confirmed by bone marrow biopsy and immunophenotyping studies. Cellulitis is sometimes the first clinical impression in patients presenting with SS[2].

As the diagnosis of Sweet/SLS syndrome was not made at that time, she was not started on steroids. However, when the lesions recurred a month later, after she was bitten by mosquitoes, SS/SLS was suspected. This was confirmed by a skin biopsy which showed typical dense dermal infiltrate. As there were some monocytoid cells seen in the dermis, we decided to call the syndrome 'sweet-like'. There was dramatic response to prednisolone despite delay in treatment (12 days). A review of 15 patients with leukaemia associated SS (Cooper et al)[5] showed that considerable improvement occurred 24 to 48 hours after steroid therapy with reduction or disappearance of malaise, pain and tenderness and a drop in temperature. Complete resolution of skin lesion was typically achieved within one to four weeks.

Our patient was not in remission despite 2 courses of chemotherapy. Two of Cooper's[5] patients with AML died at 3 weeks and 3 months after diagnosis respectively; one patient described by Klock et al[11] relapsed after 10 months and died a month later. Another patient treated by Gyrd et al[12] as SS earlier on died of subdural haemorrhage when a diagnosis of AML was made. Does this mean that AML with SS or SLS is associated with a poorer prognosis? SS or SLS should be regarded as a cutaneous marker of a haematological malignancy. It is recommended that a full workup for haematological malignancy be done for all patients with SS or SLS.

References

1. Sweet RD. An acute febrile neutrophilic dermatosis. Br J Dermatol 1964; 76: 349.
2. Strorer JS, Nesbitt LT, Galen WK, Deleo VA. Sweet's syndrome. Int J Derm 1983; 22: 8-12.
3. Dereure O, Guillot B, Burneon G, et al. Dermatoses aigues febriles a neutrophiles et hemopathies malignes. Ann Derm Ven 1988; 115: 689-701.
4. Yokoyama K, Kojima M, Komatsumoto S, Nara M, Ohyashiki K, Ikeda Y, et al. Acute megakaryoblastic leukemia associated with Sweet's syndrome. Finsho-Ketsueki 1993; 34 (3): 341-7.
5. Cooper PH, Innes DJ, Greer KE. Acute febrile neutrophilic dermatosis (Sweet's Syndrome) and myeloproliferative disorders. Cancer 1982; 51: 1518-26.
6. Matta M, Malak J, Tabet E, et al. Sweet's syndrome: Systemic associations. Cutis 1973; 12: 561-5.
7. Raimer SS, Duncan WC. Febrile neutrophilic dermatosis in acute myelogenous leukaemia. Arch Dermatol 1978; 114: 413-4.
8. Driesch VP, Schlegel R, Kieswetter F, et al. Sweet's syndrome: Clinical spectrum and associated conditions. Cutis 1989; 44: 193-200.
9. Petrizzu HW, et al. Sweet's Syndrome: Unique local response to streptococcal antigen. Cutis 1976; 17: 267.
10. Itami S. Sweet's syndrome in infancy. Br J Dermatol 1980; 103: 449.
11. Klock JC, Oken RL. Febrile neutrophilic dermatosis in acute myelogenous leukaemia. Cancer 1976; 37: 922-7.
12. Gyrd T, Kassis V, Thomsen HK, Jensen G. Acute febrile neutrophilic dermatosis and abnormal bone marrow chromosomes as a marker for preleukemia. Arch Dermatol Venerol 1987; 65.