

Sweet's Syndrome Associated with *Mycobacterium chelonae* and Herpes Simplex Virus Infections: A Case Report

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Abstract

Introduction: We report a case of Sweet's syndrome associated with *Mycobacterium chelonae* and herpes simplex virus infection. **Clinical Picture:** A 56-year-old Chinese woman presented with a granulomatous subglottic mass and right lung nodules, which responded to a 9-month course of anti-tuberculous treatment. Subsequently, she developed genital herpes simplex virus infection, which was followed by a cutaneous eruption with vesicular plaques associated with fever, bilateral cervical lymph nodes and neutrophilia. *Mycobacterium chelonae* was isolated from lymph node cultures. The cutaneous presentation of Sweet's syndrome was confirmed on skin biopsy. There was no evidence of underlying immunosuppression, malignancy or connective tissue disease. **Treatment:** She was treated with rifampicin, clarithromycin and oral prednisolone. **Outcome:** There was complete resolution of her cutaneous lesions and cervical lymphadenopathy. **Conclusion:** The association between Sweet's syndrome and *Mycobacterium chelonae* as well as herpes simplex virus, though rare, should be considered in all patients presenting with Sweet's syndrome.

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Key words: Atypical mycobacterium, Herpes genitalis, Neutrophilic dermatosis

Introduction

Sweet's syndrome is an acute febrile neutrophilic dermatosis. An association with malignancy is well recognised. Nonetheless, it is believed to be a result of hypersensitivity to a variety of conditions, including bacterial, fungal and viral infections.

The rare association with atypical mycobacteria infection has been reported. Here, we report a patient with Sweet's syndrome associated with *Mycobacterium chelonae* cervical lymphadenitis and herpes genitalis.

Case Report

A 56-year-old Chinese woman presented with a subglottic mass which was causing her throat discomfort. Excision biopsy showed granulation tissue with ulceration. Computed tomographic (CT) scan of the thorax showed two nodules in the apex of the right lung.

Two weeks later, she presented with stridor and dyspnoea due to recurrence of the subglottic mass. She underwent a tracheostomy and resection of the subglottic tumour. Histology showed granulomatous inflammation with presence of acid-fast bacilli. Cultures for *Mycobacterium tuberculosis* and atypical mycobacteria were negative. CT

scan of the thorax showed two nodules in the apex of the right lung. The clinical impression was that of *Mycobacterium tuberculosis* infection and she completed a 9-month empiric treatment of rifampicin, isoniazid and ethambutol, with complete radiological clearance on follow-up.

Six months after completion of her anti-tuberculous treatment, she presented with a 4-month history of painful vulval ulcerations. She is married with a stable monogamous relationship. On examination, there were 2 tender erosions, 3 cm and 0.5 cm in diameter, over the right labia minora. Biopsy showed an eroded lesion with epidermal hyperplasia, a moderately dense infiltrate of lymphocytes and plasma cells in the dermis. The epidermis also showed a mild degree of dysplasia with no features of giant cells or inclusion bodies. The histology was interpreted as showing inflammatory dysplasia. Culture was positive for herpes simplex virus type II.

Shortly thereafter, she presented with a sudden blistering, erythema multiforme-like eruption associated with fever and a 1-month history of painful neck lumps. She had tense blisters on the face, neck and limbs, with bilateral firm cervical lymph nodes. Her white cell count was raised at

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26.0 x 10⁹/L, with 80% neutrophils. The rest of her biochemistry was unremarkable. Her CD4 and CD8 counts were normal, as was her chest X-ray (CXR). She refused human immunodeficiency virus (HIV) serological testing. Based on initial clinical impression of bullous erythema multiforme secondary to herpes simplex virus infection, she was given oral acyclovir 200 mg 5 times a day for a week, followed by maintenance therapy of 400 mg bd to which there was clearance of vulval and skin lesions. However, biopsy of the cutaneous lesion showed dense diffuse dermal infiltrates of neutrophils. There were no features of interface dermatitis and acid-fast bacilli and fungal organisms were not demonstrated. She was then diagnosed as Sweet's syndrome, based on histological features and clinical presentation of fever and neutrophilia. The direct immunofluorescence was negative. Biopsy of a cervical lymph node showed reactive lymphadenopathy and was negative for acid-fast bacilli.

One month later, she presented to the clinic with a 4-day history of blistering eruption, involving the palms, face and neck with swelling of her knees and hands. On examination, she was afebrile and had multiple oedematous tender red plaques over the face, neck, upper limbs, back and knees (Figs. 1 & 2). There were effusions over both knees and swelling of the finger joints and dusky erythematous patches over both shins which were warm and tender. She had multiple bilateral enlarged cervical lymph nodes. *Mycobacterium chelonae* was isolated from her previous lymph node culture.

Investigations done showed increased total white cell count of 30.9 x 10⁹/dL with 80% polymorphs and ESR was 108 mm/h. Her CD4 and CD8 counts were normal and the ratio was not reversed. She was investigated to rule out connective tissue disease and underlying immunodeficiency. ANA, dsDNA, anti-Ro, anti-La and rheumatoid factor were negative. Myeloma screen was negative and nitroblue tetrazolium (NBT) test was normal. A repeat biopsy showed similar features of dense diffuse infiltrates of neutrophils throughout the dermis, mixed with few histiocytes, lymphocytes and eosinophils, consistent with Sweet's syndrome (Figs. 3 & 4).

The final diagnosis was then Sweet's syndrome associated with *Mycobacterium chelonae* infection and reactive arthritis. The patient was started on clarithromycin and ethambutol, and in view of progressive skin lesions, prednisolone 30 mg/day was also added. Her skin lesions, cervical lymphadenopathy and arthritis responded dramatically to the treatment. She was subsequently discharged with prednisolone alone. The dose of prednisolone was tapered over 3 months and the patient was continued on ethambutol and clarithromycin for a total of 6 months. On last review 4 months after discontinuation

of prednisolone, the patient was well. Her skin lesions and cervical lymphadenopathy had completely resolved, and there was no recurrence of the lesions at the time of writing this report.

Discussion

Sweet's syndrome is an acute febrile neutrophilic dermatosis which was first described in 1964.¹ Su and Liu² in 1986 proposed a revised diagnostic criteria for Sweet's syndrome, which comprises 2 major and 4 minor criteria. Sweet's syndrome classically presents as tender oedematous plaques and nodules, and may be accompanied by fever, arthralgia and conjunctivitis. There have been many reports of association with underlying malignancy, particularly haematological malignancies³⁻⁵ and to a lesser extent, solid organ malignancies⁶ and infection. The infections reported in association with Sweet's syndrome include *Chlamydia pneumoniae*,⁷ *Helicobacter pylori*,⁸ *Salmonella typhimurium*,⁹ hepatitis B¹⁰ and HIV infections.¹¹

Our patient presented with a bullous eruption and genital herpes. The initial clinical impression was that of bullous erythema multiforme associated with genital herpes, as this is a more common association. Sweet's syndrome was diagnosed later on review of the histological findings. The association between Sweet's syndrome and herpes simplex virus infections is rare but has been reported.¹² The initial improvement of her skin condition may have been a result of the use of acyclovir. There have also been previous reports of spontaneous resolution of Sweet's syndrome without treatment^{13,14} and the improvement in our patient may have been the natural progression of her disease at that time.

She presented again with tender oedematous plaques, arthritis and leukocytosis. Based on the constellation of clinical and histological features, our patient thus fulfilled all the proposed major and minor criteria of Sweet's syndrome.

The culture from her cervical lymph node biopsy grew *Mycobacterium chelonae*. It is possible that her previous subglottic mass and lung nodule were a result of *Mycobacterium chelonae* infection which may also respond to anti-tuberculosis treatment. Presence of cervical lymphadenitis and positive culture of *Mycobacterium chelonae* from the cervical lymph nodes may be an indication of recurrence of infection.

In view of her susceptibility to atypical mycobacterial infection, we had investigated the patient for underlying immunosuppression and connective tissue disease which were negative. Her total white and lymphocyte counts were normal and her CD4 to CD8 ratio was not reversed, making HIV infection highly unlikely, though not excluded unequivocally as she had refused HIV serological testing.

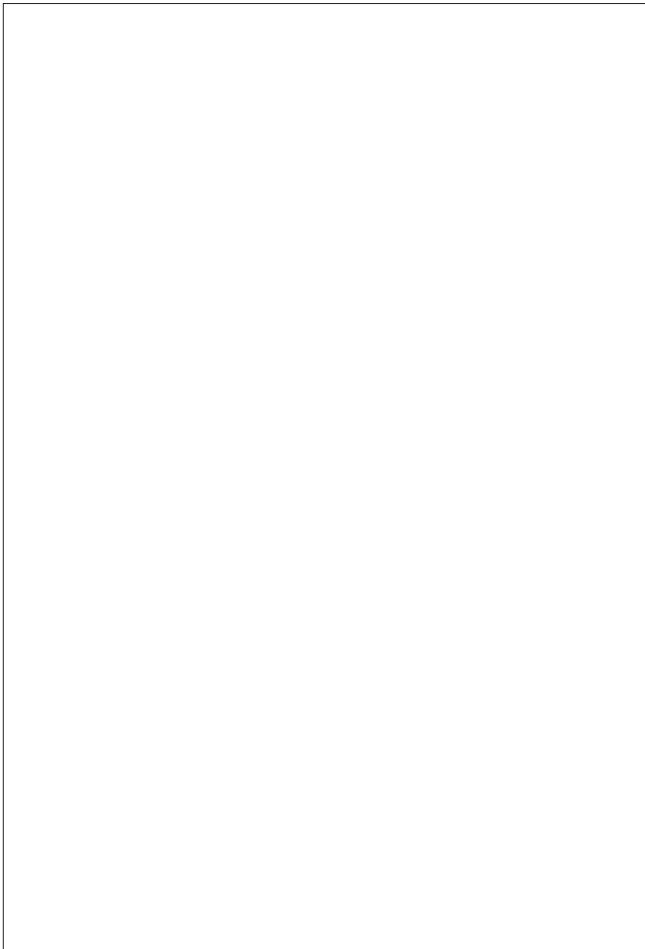


Fig. 1. Nodules and plaques studded with pustules on the face.

There were 3 previous reports of the rare association of Sweet's syndrome and atypical mycobacterial infection. In 1992, Kramers et al¹⁵ reported a case of Sweet's syndrome as the presenting symptom of hairy cell leukaemia in a patient with concomitant *Mycobacterium kansasii*. In 1995, Hsiao and Chiu¹⁶ reported a case of Sweet's syndrome in a patient with cervical lymphadenitis caused by *Mycobacterium fortuitum*. Choonhakarn et al¹⁷ reported 5 cases of Sweet's syndrome associated with non-tuberculous mycobacteria infection in 1998. In this series, 3 cases were associated with *Mycobacterium chelonae*, one with *Mycobacterium avium intracellulare* and one with *Mycobacterium scrofulaceum*. All cases were treated with prednisolone with improvement. The simultaneous resolution of cervical lymphadenitis and the bullous tumid skin lesions in our patient seems to suggest *Mycobacterium chelonae* as a cause of Sweet's syndrome.

A hypersensitive response to infections has been postulated as a possible cause of Sweet's syndrome. This case report lends further credence to this hypothesis. In the search for an underlying cause of Sweet's syndrome,

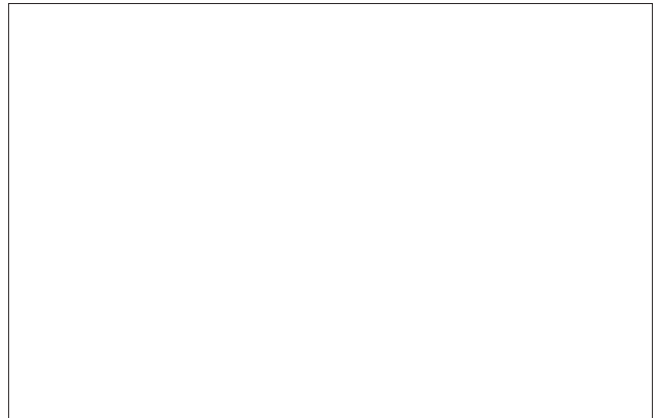


Fig. 2. Erythematous-indurated plaques on the right forearm.

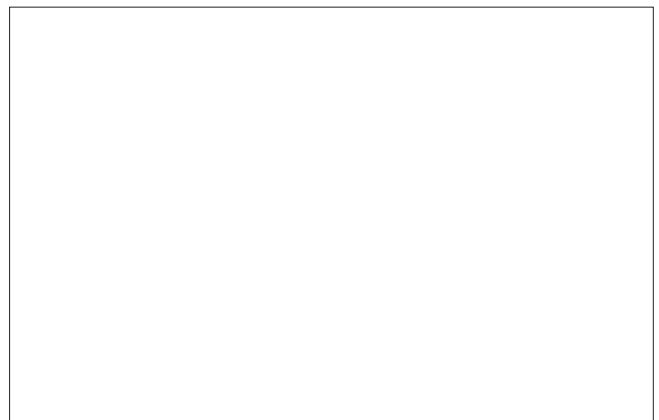


Fig. 3. Papillary dermal oedema with dense neutrophilic infiltrate (H&E, x10).

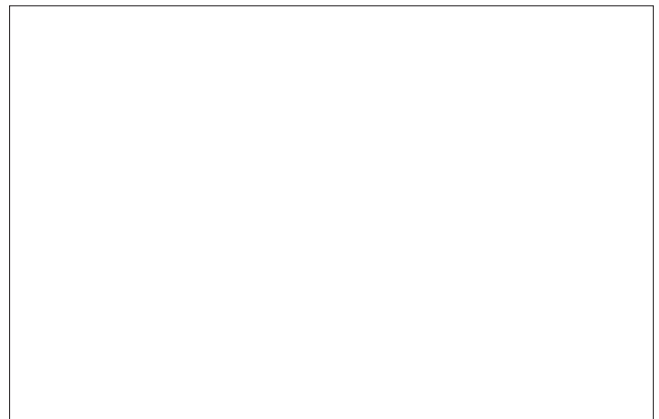


Fig. 4. Dense dermal neutrophilic infiltrate (H&E, x40).

infections including non-tuberculous mycobacterial infections and herpes simplex virus infections should be looked for, in addition to internal malignancies.

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