Concurrent Sweet's syndrome and erythema nodosum: two manifestations of the same disease or the same spectrum?

Zahra Hallaji, MD
Alireza Ghanadan, MD
Maryam Akhyani, MD
Nafiseh Esmaili, MD
Somayeh Khezri, MD
Mehdi Mirzaeipour, MD

Department of Dermatology, Razi Skin Hospital, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran

Corresponding Author:
Somayeh Khezri, MD
Department of Dermatology, Razi Skin Hospital, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran
Email: khezri@razi.tums.ac.ir

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Sweet's syndrome and erythema nodosum are rarely seen together. Herein, we report a case of concurrent Sweet's syndrome and erythema nodosum and review previous cases.

Keywords: erythema nodosum, neutrophil dermatosis, Sweet's syndrome

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INTRODUCTION

Although Sweet's syndrome and erythema nodosum (EN) concurrence is considered rare [1,2], there are increasingly recognized association reports [3-9]. Here, we report another case of Sweet's syndrome and EN which is, to our knowledge, the first report from Iran.

CASE REPORT

A 50-year-old female was referred to the dermatology outpatient clinic of Razi Hospital, Tehran, Iran, in January 2010, complaining of a 2-month history of tender erythematous lesions on her shins and dorsal aspect of hands in association with malaise and arthralgia in both knees and wrists (Figure 1). She had an upper respiratory tract infection with low-grade fever prior to this presentation. Her past medical and drug histories were unremarkable. Her husband had hepatitis B.

On examination, there were tender erythematous nodules over the shins and tender, red-violet and targetoid plaques on her hands. Dermatologic examinations were otherwise normal. The results of laboratory tests are listed below:

White blood cell count: 7600 (neutrophils 67%); anti-streptolysin O titre: more than 200 units/ml (positive ASLO titer); Erythrocyte sedimentation rate (1hr): 20 mm/h; C-reactive protein (CRP): negative; Serological tests for various viral diseases, *tuberculin* test, antinuclear antibodies and anti-neutrophil cytoplasmic antibodies (ANCAs) were negative; urinalysis, biochemical parameters, thyroid and liver function tests were within normal limits. Chest X-ray and electrocardiogram were normal. Two skin biopsy specimens taken from upper and lower extremities respectively showed:

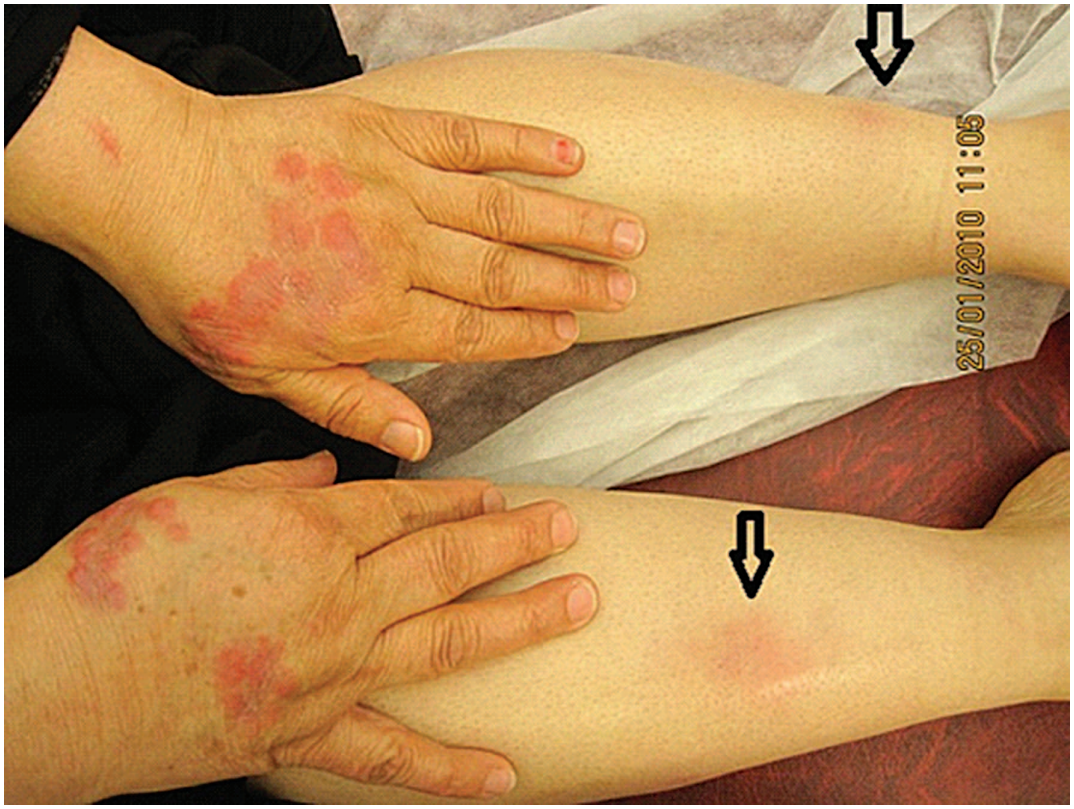

Figure 1. Erythematous lesions on the shins and dorsal aspect of hands.

- Compact hyperkeratosis and marked acanthosis associated with edema of the upper dermis, patchy infiltration of neutrophils and intermixed lymphocytes around the vessels of the upper dermis with no vasculitis (Figure 2).
- Normal appearing epidermis and deep perivascular lymphocytic inflammation without

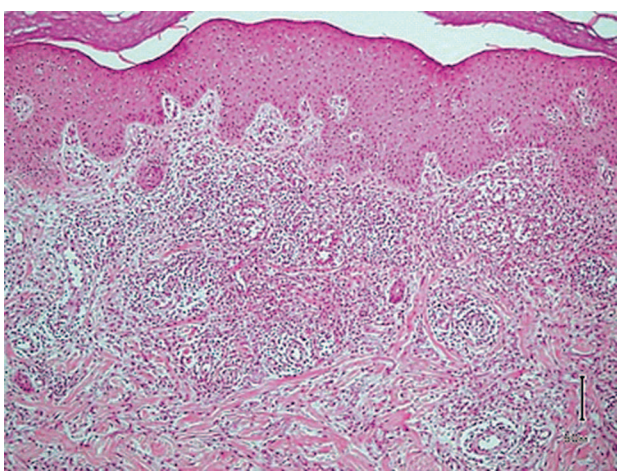

Figure 2. Upper dermal edema and patchy infiltration of neutrophils around the vessels of upper dermis without vasculitis (H&E* ×10).

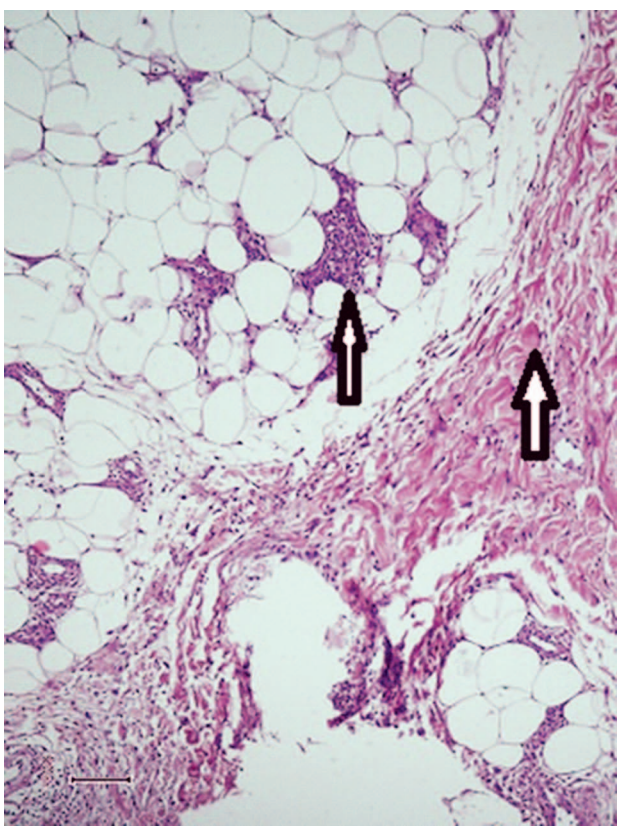

Figure 3. Septal fibrosis of subcutaneous fat (H&E*×40).

vasculitis and septal fibrosis of subcutaneous fat (Figure 3).

Consequently, the upper and lower extremity specimens were compatible with neutrophilic dermatosis including Sweet's syndrome and erythema nodosum (EN), respectively. According to clinicopathological findings, our patients had concurrent Sweet's Syndrome and EN with a high probability.

Because of the reported underlying solid tumors such as breast and colon cancers, especially with Sweet's syndrome, in addition to ruling out acute myelogenous leukemia (AML), we advised our patient to receive colonoscopy, mammography and Pap smear test to screen for the 3 most common malignancies of middle aged women [1,2,5].

Our patient was treated with prednisolone 30 mg daily and evidence of improvement was seen after 7 days. The dose of oral corticosteroid was tapered and finally discontinued within 4 weeks. Her follow-up visit was 6 months later with no evidence of recurrence.

DISCUSSION

Sweet's syndrome, the prototype of neutrophilic dermatoses, was initially reported in 1964 and EN, which is the best known septal panniculitis, was first described in the early 18th century [1,2]. However, the similarities between Sweet's syndrome and EN do not confine to clinical, histopathological, associated conditions, sex predominance and treatment, but in the supposed etiological hypothesis as well. Despite the poorly understood pathogenesis of both Sweet's syndrome and EN, the most debatable ones are dysregulation of T helper 1 (Th1) and thus uncontrolled production of interleukin-1, interleukin-3, interleukin-6, interleukin-8, granulocyte colony-stimulating factor (G-CSF), tumor necrosis factor-α (TNF-α), interferon-γ (*IFN-γ)* in Sweet's syndrome and local and systemic secretion of Th1 cytokine profile (IFN-γ and IL 2, G-CSF and TNF-α) in EN. The mentioned cytokines stimulate the inflammation cascade both in the circulatory system and the skin and cause systemic and cutaneous manifestations. On the other hand, such a cytokine profile (Th1) is associated with cellular immunity, or to be more precise, delayed type hypersensitivity. The latter is contrary to the supposed pathogenic role of the immune complex in Sweet's syndrome. The previously mentioned cytokines cause activation of neutrophils to produce reactive oxygen products, tissue damage and inflammation consequently. It means that neutrophils may play an important role in the pathogenesis of Sweet's syndrome and EN [1,2].

The supposed hypothesis has been accepted to some extent in Sweet's syndrome, as a neutrophilic dermatosis, but remains controversy in EN [1,2]. The supporting data for the pathogenic role of these cells in EN are neutrophilic infiltration in early lesions, incremental amounts of activated neutrophils, induction following G-CSF use, and its responsiveness to colchicine and anti TNF-α agents, as seen in Sweet's syndrome [1,2]. Although concurrence of Sweet's syndrome and EN is considered rare [1,2], there are at least 3 case series which show this coexistence in about 30% of the cases of Sweet's syndrome [6]. Our case report, besides the recently reported cases, may indicate that such coexistence is not fortuitous. The discussed similarities and reported concurrent Sweet's syndrome and EN may reveal two manifestations of the same spectrum or different manifestations of the same disease.

Tabanlıoğlu et al, supported the latter supposition after finding septal neutrophilic infiltration and leukocytoclasia in favor of sweet panniculitis within an EN-like lesion specimen in a case of concurrent Sweet's syndrome and EN [3]. Sweet's panniculitis is an uncommon variant of Sweet's syndrome in which the subcutaneous fat is infiltrated by neutrophils with or without dermis involvement [3]. On the contrary, our report is more compatible with the first supposition with no evidence of Sweet's panniculitis in the specimen of the EN lesion. Because of the reported underlying malignancies, as Wasson et al, has emphasized [5], we referred our patient to receive the screening tests of the most common malignancies of the 6th decade of life in females. Other evaluations for inflammatory bowel disease (IBD) and autoimmune diseases were normal. The excellent response to oral prednisolone in our patient is similar to the previous reports and supports the immunity basis of Sweet's syndrome and EN.

In conclusion, we report post streptococcal concurrent Sweet's syndrome and EN in a woman who responded well to oral prednisolone. Our report puts further emphasis on the increasingly

recognized association and closer relationship between Sweet's syndrome and EN than an accidental coexistence, and if so, EN should be preferably classified as a neutrophilic dermatosis.

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