Sweet's Syndrome Associated with a Benign IgA Gammopathy

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A 71-year-old woman was presented with 5-year history of recurrent, multiple, painful or tender, erythematous plaques on her lower limbs accompanied by fever and arthralgia. Histopathological findings showed a dense infiltration of mature neutrophils in the upper and mid dermis without leukocytoclastic vasculitis. These clinical and histopathological findings were consistent with Sweet's syndrome. The laboratory investigations demonstrated elevated ESR and IgA gammopathy, but no leukocytosis or neutrophilia. Her eruption revealed good responses to systemic steroid therapy.

We herein describe a patient with Sweet's syndrome without leukocytosis, probably associated with a benign IgA gammopathy. (Ann Dermatol 11(4) 276~279, 1999).

Key Words : Sweet's syndrome, IgA gammopathy, Leukocytosis

Sweet's syndrome(SS) was first described by Sweet as an uncommon but distinct clinical entity in 1964[1]. According to Sweet's original description the definition of this entity had four cardinal features: 1) fever, 2) peripheral leukocytosis, 3) tender red plaques on the limbs, face, and neck, and 4) a dense dermal infiltrate of mature neutrophils[1,2]. SS has been described in association with a variety of clinical conditions such as inflammatory diseases(autoimmune disorders or antecedent infections), hemoproliferative diseases or solid tumors, and pregnancy[3]. However, its association with a monoclonal gammopathy has rarely been reported in literature[4-8].

We herein report a case of SS without leukocytosis, probably associated with a benign IgA gammopathy.

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CASE REPORT

A 71-year-old woman was presented with an acute onset of multiple, tender and painful, erythematous, annular plaques on her lower limbs (Fig. 1). Her body temperature was 38℃ and she complained of general malaise and arthralgia. These symptoms had been present for 1 week. She had experienced similar skin eruptions several times since 1993 and they had improved with steroid therapy at each attack.

Laboratory investigations showed normal leukocyte count (5100/mm^3 with 55% segmented neutrophils) and elevated erythrocyte sedimentation rate (ESR, 60mm/hr). Chest radiograph, urinalysis, serum chemistry and liver function test were all within normal limits. Serum immunoglobulin analysis revealed an increased IgA level (3770mg/dl; normal 85-450mg/dl), but other immunoglobulin and complement levels were normal. In 1993, when she first visited our department due to similar lesions, the leukocyte count, ESR, and IgA level were 7100/mm^3, 60mm/hr, and 634mg/dl, respectively.

A skin biopsy specimen taken from the right leg showed a dense infiltration of numerous neu-

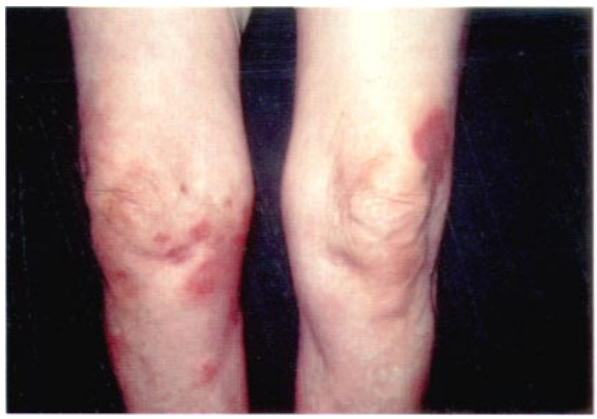

Fig. 1. Multiple painful erythematous annular plaques on the lower limbs.

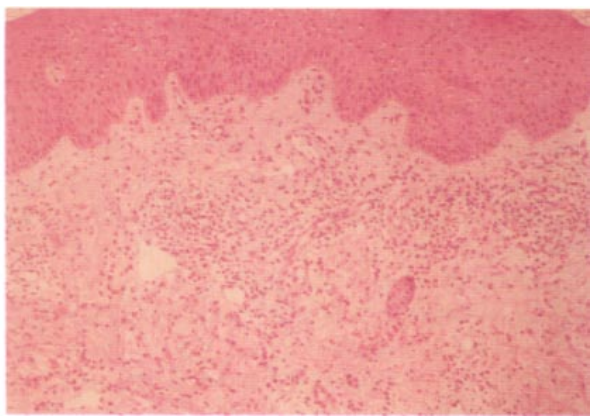

Fig. 2. Histopathological findings showing a dense perivascular neutrophilic infiltration in the upper and mid dermis (H&E, ×100).

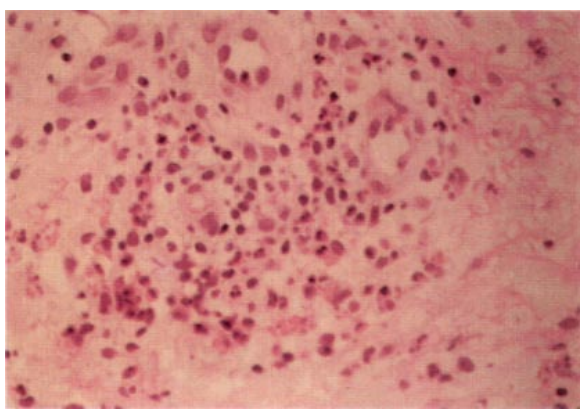

Fig. 3. Numerous neutrophilic infiltration around the vessels without vasculitis (H&E, ×400).

trophils with mononuclear cells without any evidence of vasculitis predominantly in the upper and mid dermis, along with papillary dermal edema, red blood cell extravasation, and vascular dilatation (Fig. 2, 3). Vascular dilatation and inflammatory cell infiltration were also focally observed in the subcutaneous fat layer. Direct immunofluorescence of the lesional skin was negative for immunglobulins and complements.

A diagnosis of Sweet's syndrome was made on the clinical and histopathological findings. Her skin lesions improved with intramuscular triamcinolone acetonide 40mg for 1 day and oral triamcinolone (16 mg/day) for 1 week.

DISCUSSION

Sweet's syndrome(SS), acute febrile neutrophilic dermatosis, is clinically characterized by painful, erythematous plaques on the face, neck and extremities. The eruptions may be accompanied by fever, arthralgia, malaise and headaches. Histologically, the lesions reveal a perivascular infiltrate predominantly of neutrophils in the upper and mid dermis, but there is no true evidence of vasculitis[1,2]. Su and Liu[9], in 1986, proposed two major criteria and four minor criteria for the diagnosis of SS and the revised version was proposed by von den Driesch[10] in 1994. To make the diagnosis, both of the major and at least two of the minor critera must be fulfilled. Our case was consistent with these diagnostic criteria. The differential diagnosis in this case must include urticarial vasculitis, erythema multiforme, erythema elevatum diutinum, erythema nodosum and Behcet's disease. However, these conditions could be differentiated by the characteristic histopathologic findings and clinical features.

Although the laboratory findings in SS are nonspecific, an elevated ESR(>20mm/hr), segmented nuclear neutrophils and stabs greater than 70% in the peripheral blood smear, and leukocytosis (>8000/mm^3) during onset, are included in the minor criteria[10]. Most physicians are aware of the association between leukocytosis and SS. In fact, however, neutrophilic leukocytosis are often, but not invariably, present in patients with SS. From the laboratory studies in 38 patients with SS, leukocytosis of more than 10,000/mm^3, were present in only 60% of patients[10]. Neutrophilia may be more common in the idiopathic subtypes than in the

paraneoplastic subtypes. Cohen and Kurzrock[11] noted that neutrophilia is found in less than 50% of patients with malignant associated syndrome and patients with hematologic malignancy typically do not have neutrophilia at the time of SS onset. Moreland et al.[12] suggested that this condition may be due to bone marrow suppression from hematologic disease process or from chemotherapy. The laboratory investigations in this case revealed elevated ESR levels, but no leukocytosis or neutrophilia during the 5-year follow up period, and there was no evidence of internal malignancy or chemotherapy.

SS has been described in association with many diseases. They include inflammatory diseases, hemoproliferative diseases, solid carcinomas, and miscellaneous conditions such as pregnancy, vaccination and sarcoidosis[3]. In a recent review, parainflammatory and paraneoplastic occurrence is found in approximately 25% of the cases[10]. In Korea, among 32 patients with SS, Kim and Bang[13] reported 18 patients associated with Behcet's disease, meningitis, lupus erythematosus, stomach cancer, myelodysplastic syndrome, leiomyoma and osteoporosis. However, SS associated with a monoclonal gammopathy has rarely been reported in literature[4-8]. Ilchyshyn et al.[4] reported a case of SS associated with IgG paraproteinemia and leading to chronic lymphatic leukemia. Bunker[5] described a similar case but with no evidence of an underlying hematologic malignancy. The present case showed a benign monoclonal IgA gammopathy on the laboratory examination during each attack. However, considering that other neutrophilic dermatoses such as subcorneal pustular dermatosis, erythema elevatum diutinum and pyoderma gangrenosum are sometimes associated with monoclonal gammopathy which is most of a benign IgA type[14], this finding is not surprising and likely to be not rare.

In the present case, it is interesting that IgA gammopathy was coexistent with normal peripheral blood leukocyte count, although the causal relationship was not defined. Recent studies have shown that IgA may affect some neutrophilic functions such as migration, phagocytosis or bactericidal action[15]. Furthermore, it was experimentally shown that the inhibition of neutrophilic chemotaxis in patients with chronic neutrophilic dermatoses correlated with increased serum IgA levels[15]. However, in spite of normal peripheral blood leukocyte count in our patient, the mechanism of accumulation of neutrophils in the skin remains unexplained. One possibility is that the neutrophils are sequestered in the skin by an increase in the local production of chemotactic factors such as complement fraction, interleukin-1 and interleukin-8[16,17]. Thus, although the peripheral blood leukocyte counts are normal as shown in this case, the skin may be a site of sequestration of viable neutrophils. Our case suggests that the monoclonal IgA gammopathy may alter the functions of neutrophils and play a role in the pathogenesis of the SS without leukocytosis. It would be interesting to systematically search for IgA levels in the serum of patients with SS without leukocytosis.

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