

Sweet's Syndrome Associated with Bacterial Meningitis

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We report an unusual case of Sweet's syndrome associated with bacterial meningitis in a 38-year-old woman. Sweet's syndrome is associated with various diseases. The etiology and pathogenesis are still undefined. The patient presented with fever, headache, and cerebrospinal fluid finding of bacterial meningitis. This is the first reported case of Sweet's syndrome associated with bacterial meningitis. (Ann Dermatol 8:(1)66-69, 1996).

Key Words : Sweet's syndrome, Bacterial meningitis

Acute febrile neutrophilic dermatosis, first described by Sweet¹ in 1964, is associated with many diseases such as infections, malignancy, Sjögren syndrome, lymphoma, ulcerative colitis, and inflammatory arthritis.^{1,3} The pathogenesis of this syndrome remains unknown, although it is believed to represent a hypersensitivity reaction to an infection or malignancy.⁴ We describe a patient of Sweet's syndrome associated with bacterial meningitis. This is the first such reported case.

REPORT OF A CASE

A 38-year-old woman was admitted to the department of neurology at Severance Hospital with a four-day history of headache, fever and confused mental state. Initial complete blood cell count showed a white blood cell count, 11,200/mm³ with 90% polys, 8% lymphocytes, and 2% monocytes. Hemoglobin was 11.0 g/dl and hematocrit 33.5%. Chest radiograph, urinalysis, serum chemistry, and liver function tests were all within normal limits. A computed tomographic (CT) scan of her brain showed a diffuse low density lesion on both temporal lobes, but after contrast enhancement

there was no enhancement.

The patient was treated with chloramphenicol and crystalline-penicillin, but her fever continued. On day 5 several pea to coin-sized, tender erythematous plaques were developed on the face and extremities (Fig. 1A & 1B).

Cerebrospinal fluid (CSF) analysis revealed protein 172 mg/dl, glucose 49 mg/dl, no red blood cells, 510 white blood cells (70 polys, 30 monocytes); this was consistent with bacterial meningitis. Results of CSF examination during admission are shown in Table 1. Culture examination of CSF showed few staphylococci. However, there was no growth on blood culture examinations. She was consulted to the department of dermatology for skin lesions.

A skin biopsy specimen from the left forearm was taken 7 days after admission and revealed a dermal infiltrate of polymorphonuclear leukocytes, mononuclear cells, and nuclear dusts without any evidence of vasculitis (Fig. 2A & 2B).

A diagnosis of Sweet syndrome was made on the clinical basis of fever, tender plaques, leukocytosis and histologic findings. On the 20th day of admission, the WBC count was 4,200/mm³ with 82% polys, 14% lymphocytes, and 4% monocytes and the fever subsided. Antibiotic therapy was stopped. Her skin lesions were improved with topical steroids thereafter.

The patient was discharged 28 days after admission and continued to show improvement.

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Table 1. Cerebrospinal fluid analysis

Date	Appearance	Pressure (mmHg)	WBC (No./mm ³)	diff.(poly/mono) (%)	RBC (No./mm ³)	Protein (mg/dl)	Sugar (mg/dl)
7.23	Colorless	210	510	70/30	0	172	49/118
7.25	Colorless	210	151	10/90	0	66	57/130
7.29	Colorless	150	330	86/14	5	94	39/122
8.2	Colorless	150	92	58/42	0	90	37/124
8.6	Colorless	220	40	28/72	0	72	44/108
8.13	Colorless	170	45	0/100	3	50	45/131

Fig. 1. A, Coin sized, slightly erythematous plaque on the face.

B, Erythematous plaques on the leg.

Fig. 2. A, A dermal infiltrate of polymorphonuclear leukocytes, mononuclear cells, and nuclear dusts. (Hematoxylin-eosin stain ; $\times 100$).

B, Higher magnification of figure 2A. (Hematoxylin-eosin stain ; $\times 400$).

DISCUSSION

We describe a case of Sweet's syndrome associated with bacterial meningitis. Our patient showed CSF findings compatible with partially treated bacterial meningitis. She developed skin lesions consistent with Sweet's syndrome during admission, and improved with antibiotic therapy and topical steroids. To date, no specific etiology has been found for Sweet's syndrome. It is postulated to be a form of hypersensitivity reaction to a bacterial, viral, or tumor antigen.³

There are three reports of neurologic involvement in Sweet's syndrome.⁵ Aseptic meningitis was diagnosed in a 7-week-old child, the youngest patient reported.⁵ Another patient showed neurologic and psychiatric symptoms.⁶ Accumulation of neutrophils in the CSF⁴ were present in a third patient. All of them responded well to therapy.

Dunn et al³ proposed that Sweet's syndrome may be a response to an inappropriate secretion of endogenous cytokines such as granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-1 β (IL-1 β), and interferon- γ . These cytokines are increased in the CSF of patients with aseptic meningitis.⁷ Sweet's syndrome has been reported in a patient with hairy cell leukemia treated with granulocyte colony-stimulating factor (G-CSF).^{7,8} G-CSF is a potent activator of human polymorphonuclear neutrophilic granulocytes and induces stem cells to differentiate to mature neutrophils.⁹ GM-CSF was not detected in the CSF from patients with bacterial meningitis in which high concentrations of tumor necrosis factor- α and IL-1 β had been reported.¹⁰

Going¹¹ suggests that Sweet's syndrome is initiated by a variety of stimuli; the common result is an excessive production of, or an abnormal response to, IL-1. IL-1 is an important inflammatory mediator, produced by various cells, especially those of monocyte/macrophage lineage, but including keratinocytes. IL-1 is a cytokine with multiple immunoregulatory effects. Its specific effect on neutrophils causes neutrophilic leukocytosis and increases metabolic activation. It also stimulates macrophages to secrete more GM-CSF and to increase IL-8 production which is a specific neutrophil chemoattractant. It is responsible for an acute phase reaction, possesses endogenous pyrogen activity, is chemotactic for neutrophils and

induces a neutrophil leukocytosis.^{11,12} In leukemia-associated Sweet's syndrome the initiating event could be the infiltration of the dermis by neoplastic monocytes secreting IL-1 which attracts neutrophils and stimulates the bone marrow to produce more neutrophils. Their phagocytosis by dermal macrophages would stimulate more IL-1 production.¹²

Cohen et al^{13,14} suggested the possibility that the pathogenesis of Sweet's syndrome may be secondary to an inappropriate secretion of one or more of the endogenous cytokines. These concepts focus on disturbances in the cytokine regulation pathways responsible for the characteristic clinical pictures of Sweet's syndrome: IL-1 causes illness, fever, arthritis; IL-8 causes local recruitment of neutrophils; G-CSF, GM-CSF causes systemic and local recruitment of neutrophils.^{9,11}

Assays for IL-1, GM-CSF, G-CSF, and IL-8 would certainly be of interest in understanding the possible mechanisms for the infiltration of neutrophils into the dermis.¹² Further studies will be needed to find the precise mechanism of Sweet's syndrome.

We believe that this patient represents a unique case of Sweet's syndrome associated with bacterial meningitis.

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