Pulmonary Involvement In Sweet's Syndrome (Acute Febrile Neutrophilic Dermatosis)*

Preleukemic and Leukemic Phases of Acute Myelogenous Leukemia

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A 60-year-old man developed histologic lesions characteristic of acute febrile neutrophilic dermatosis in skin and lung during preleukemic and leukemic phases of acute myeloid leukemia. These lesions showed improvement and resolution during oral prednisone therapy, requiring higher doses during each relapse. The response to prednisone therapy was enhanced by concomitant administration of effective antileukemic chemotherapy.

Acute febrile neutrophilic dermatosis is an uncommon, recurrent, often dramatic skin disease characterized by painful plaque-forming inflammatory papules. These are associated with fever, arthralgia and peripheral leukocytosis. The typical skin lesions are red to bluish-red papules or nodules. They have a tendency to coalesce and form irregular, sharply bordered plaques. There is pronounced inflammatory edema giving an "illusion of vesiculation." They may occasionally become studded with tiny pustules and central clearing may lead to arcuate or annular patterns. These lesions are painful, tender and enlarge over a period of days to weeks and eventually resolve without scarring. The most common areas of involvement are face, neck, and extensor aspects of upper extremities. Over half of these recur, often in previously involved sites.

CASE REPORT

This 60-year-old man was well until November 1982, when he developed low-grade fever and malaise. He had normochromic normocytic anemia and thrombocytopenia, and the diagnosis of refractory anemia with excess blasts (RAEB) was made on bone marrow biopsy. He was treated with folate and pyridoxine. One week later, he developed fever and an expanding, ecchymotic, bullous lesion on the dorsum of his right hand. Results of aerobic and anaerobic cultures were negative. The skin lesion progressed during an empiric trial of broad spectrum antibiotics and he was hospitalized. Chest roentgenogram on admission showed right lower lobe pulmonary infiltrates (Fig 1). Biopsy and culture of the skin lesion and cultures of blood and sputum were obtained, and antibiotic therapy continued without benefit. The skin biopsy resulted in the diagnosis of "acute febrile neutrophilic dermatosis," also known as "Sweet's syndrome" (Fig 2). Antibiotic therapy was discontinued and treatment with oral prednisone, 60 mg daily, was begun. He became afebrile, and significant improvement of the skin lesion and chest roentgenogram were noted prior to discharge on 5 Jan 1983.

Over the next two weeks the patient noted recurrent fever and cough while prednisone was being tapered to 20 mg per day. Chest roentgenogram showed recurrence of right lower lobe pulmonary infiltrate, and hemogram demonstrated hemoglobin 6.9 g/dl, leukocyte count 21,500/cu mm, and platelet count 21,000/cu mm. He was admitted to the hospital and results of cultures of blood, sputum, and bronchoscopic washings were negative. The neutrophilic dermatosis of the right hand was healing well at this time. He received transfusions of red blood cells, broad spectrum antibiotics, and oral prednisone, 100 mg daily. After ten days of therapy, the patient became afebrile, leukocytosis resolved, and improvement in the right lower lobe infiltrate was noted prior to discharge. Prednisone was tapered to 40 mg daily for two weeks, after which he developed recurrent fever to 38.5°C. He was admitted to the hospital and the chest roentgenogram showed progressive bilateral pulmonary infiltrates. On 13 February 1983, a right axillary thoracotomy and open...
lung biopsy were performed. The histology of the lung specimen was similar to that of the previous skin biopsy. Prednisone was again increased to 100 mg orally daily, and tapered to 50 mg daily upon discharge one week later. Serial chest roentgenograms over the next month showed resolution of the infiltrate.

The patient underwent repeat bone marrow biopsy on 22 March 1983 for persistent transfusion-dependent anemia and thrombocytopenia, and the diagnosis of acute myeloid leukemia (FAB classification M-2) was made. He developed increasing fever and bilateral pulmonary infiltrates on oral prednisone 50 mg daily, and on 2 April 1983 underwent contralateral open lung biopsy. Results of routine bacterial cultures, as well as special stains for acid-fast bacilli, fungi, viral organisms, and *Pneumocystis carinii* were negative. Review of several sections of the lung biopsy specimen showed neutrophilic infiltrates and small areas of fibrosis (Fig 3). Oral prednisone was increased to 100 mg daily for two weeks, again associated with clinical and roentgenographic improvement, and gradually tapered to 20 mg daily.

Antileukemic chemotherapy with cytosine arabinoside, 2 mg/m² twice daily was begun 26 April 1983. In May 1983, purpuric lesions affecting the hands, arms, and groin developed, and biopsy of one of these lesions demonstrated histologic features of neutrophilic dermatosis noted on the initial skin biopsy. Oral prednisone was increased from 50 mg to 120 mg daily with gradual clearing of skin lesions and pulmonary infiltrates. Initial remission was punctuated by recurrent episodes of leukemic relapse controlled by chemotherapy. Serial chest roentgenograms over the next ten months showed only residual right lower lobe abnormalities. In April, 1984, during a course of chemotherapy, he developed pancytopenia, fever, and new right lower lobe infiltrates. An empiric trial of broad-spectrum antibiotics and high dose prednisone was of no benefit and he expired five days later. Permission for post-mortem examination was refused.

**Comments**

In 1964, Sweet described the features of "acute febrile neutrophilic dermatosis" which has since come to be known as Sweet's syndrome. In his original description, the cardinal features included: (a) fever; (b) polymorphonuclear leukocytosis; (c) raised painful plaques on the extremities, face, and neck; and (d) a dense dermal cellular infiltrate with mature neutrophils on histology. The etiology is unknown. There is a history of upper respiratory infection in the majority of patients with this syndrome, suggesting hypersensitivity as a possible pathophysiologic mechanism. A significant association with hematologic malignancies, particularly acute leukemia, has been reported, with manifestations of Sweet's syndrome usually preceding the diagnosis of leukemia. Storer et al. have shown an association of this syndrome with Sjogren's syndrome, ulcerative colitis, metastatic adenocarcinoma, and testicular carcinoma.

Sweet's syndrome has been noted to occur predominantly in females. No racial predilection has been noted. It is frequently associated with systemic symptoms of fever, arthralgia, conjunctivitis, and episcleritis. Albuminuria and anemia have also been reported. Matta et al. reported a case of renal involvement and a case of hepatic involvement, both proven by biopsy. Pulmonary involvement in Sweet's syndrome has not been reported previously.

Our patient had open lung biopsies from both lungs at different times, and the histologic changes were similar in both specimens and also similar to those changes noted in skin. Numerous negative culture results, lack of response to

**Figure 2.** Punch biopsy of the skin lesion from the dorsum of the right hand demonstrating marked edema of the dermal and papillary dermis, with extensive neutrophilic infiltration. A few eosinophils are also seen. There is no evidence of vasculitis or atypical cellular infiltrate (original magnification ×100).

**Figure 3.** Section from open lung biopsy of left lung demonstrates chronic interstitial pneumonitis, minimal fibrosis and a marked intraalveolar neutrophilic infiltrate. There was no evidence of necrosis or vasculitis (original magnification ×100).
antibiotics, histology of lung biopsies similar to skin biopsies, and the prompt response to increasing doses of prednisone therapy strongly support the conclusion that this patient had Sweet’s syndrome involving skin and lung. Skin and pulmonary changes were both present during the preleukemic (RAEB) phase and flared during neoplastic transformation to acute myeloid leukemia. Pulmonary manifestations were active while skin lesions were relatively quiescent and were more difficult to treat. The effective control of skin and pulmonary manifestations was less difficult while the patient was receiving effective antileukemic chemotherapy.

In summary, this patient developed histologic lesions characteristic of acute febrile neutrophilic dermatosis in skin and lung during preleukemic and leukemic phases of acute myeloid leukemia. These lesions showed improvement and resolution during oral prednisone therapy, requiring higher doses during each relapse. The response to prednisone therapy was enhanced by concomitant administration of effective antileukemic chemotherapy.

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REFERENCES