Sweet Syndrome After Autologous Stem Cell Transplant

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Abstract

Sweet syndrome (acute febrile neutrophilic dermatosis) is a rare clinical entity characterized by skin lesions, neutrophilia, fever, and neutrophilic infiltration of the dermis. It may be a consequence of malignant disease, comorbidities, or drugs. We present a case of acute febrile neutrophilic dermatosis in a patient after autologous stem cell transplant.

Key words: Adverse events, Dermatosis, Fever, Neutrophilia

Introduction

In oncology practice, skin lesions are common, not only associated with malignancy but also as an adverse event from drugs. Sweet syndrome, which is acute febrile neutrophilic dermatosis (AFND), is a rare clinical entity characterized by skin lesions, neutrophilia, fever, and neutrophilic infiltration of the dermis. It may be a consequence of malignant disease, comorbidities, or drugs.1 We present a case of AFND in a patient after autologous stem cell transplant.

Case Report

A 64-year-old woman presented with cervical lymphadenopathy. Excisional biopsy resulted in the diagnosis of mantle cell lymphoma. She had bone marrow infiltrating, CD20-positive disease and was treated with rituximab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone; course B, methotrexate, and cytarabine regimen (hyper-CVAD). After 4 courses of hyper-CVAD, refractory disease was treated with rituximab, ifosfamide, carboplatin, and etoposide (R-ICE) combination.

After a complete response, an autologous stem cell transplant was planned. With high-dose regimen, stem cells were infused and prophylactic antibiotic therapy was started with trimethoprim-sulfamethoxazole, levofloxacin, and fluconazole. After infusion of stem cells, filgrastim (10 μg/kg/d) was initiated. Engraftment was achieved on day 14 after autologous stem cell transplant.

On day 20 after transplant, the patient complained of erythematous lesions on the radial aspects of bilateral index fingers. Physical examination showed targetoid lesions with erythematous plaques. On the next day, the lesions progressed over the dorsal aspects of both hands (Figure 1). On the second day after the lesions were noted, she developed fever. The evaluation for infection was inconclusive including viral serology, galactomannan test, radiography, and

Figure 1. Erythematous Maculopapular Lesion at the Dorsum of the Hand
blood and urine cultures. Laboratory evaluation was normal except for neutrophilia. On days 4 and 5 after onset, the lesions on the hands progressed to other parts of the body. The lesions transformed into erythematous papules, plaques, and vesicular lesions over the arms, anterior aspects of the legs, and posterior aspect of the thorax (Figure 2 and 3).

The clinical diagnosis of drug eruption was made, and skin biopsy of the dorsal hand lesions was performed. Pathologic evaluation was consistent with the diagnosis of neutrophilic dermatosis (Figure 4). Methylprednisolone (40 mg/d) was started. On the second day of treatment, the lesions and neutrophilia disappeared progressively. The patient was free of fever and lesions on the seventh day of treatment.

**Discussion**

Sweet syndrome (AFND) was first described by Robert Douglas Sweet in 1964, as painful erythematous plaques accompanied by fever and neutrophilic leukocytosis. The cause is not well defined, but hypersensitivity reactions and cytokine release are the main suspects in the cause and pathogenesis. There are 3 main subtypes defined according to the cause. The classical form (idiopathic) is the most common subtype observed after infections of the upper airway and gastrointestinal system. Inflammatory bowel disease, pregnancy, and autoimmune diseases are rare causes of this form. The second form (malignancy-associated subtype) usually is encountered with hematologic malignancies rather than solid tumors. Leukemia is the most common malignant cause, and genitourinary and breast cancers are the most common etiologic solid tumors. The third form (drug-associated subtype) is caused by numerous drugs, especially antibiotic, antineoplastic, and antiepileptic drugs. Granulocyte colony stimulating factors are the most commonly reported agents that cause AFND.

Clinical presentation of AFND predominantly includes skin lesions. The lesions usually are edematous, sensitive, and inflamed plaques and nodules that appear initially on the head, neck, and upper extremities. Initial painful lesions may have pseudo-vesicular appearance caused by superficial dermal edema and may cause confusion in the diagnosis. Occasionally, the mucosa may be involved with
ulcers in the oral cavity. Fever usually is a finding of the drug-associated form. Nonspecific complaints such as arthralgia, headache, and myalgia may be noted. Extracutaneous manifestations may be seen at the initial presentation. Pulmonary, cardiac, renal, and central nervous system involvement may be life threatening. Laboratory evaluation reveals neutrophilia and increased acute phase reactants. Biopsy of the lesion reveals neutrophilic infiltration of the dermis. Well-defined major and minor criteria are used for definitive diagnosis of the syndrome.

Classic manifestations of the disease were encountered in our patient. The marked improvement after treatment also was consistent with AFND. The causative factor in our patient was challenging because numerous drugs were used in treating the autologous stem cell transplant and underlying malignancy. Malignancy-related AFND was not in the differential diagnosis because the disease was in remission. Although progressing lesions with vesicles raised concerns about possible herpetic infection, further tests eliminated the diagnosis of atypical zoster. Infectious pathology also could not be documented on further evaluation.

There are numerous drugs that have been associated with Sweet syndrome. Colony stimulating factors have been well-defined as a cause. The use of published diagnostic criteria suggested the diagnosis of drug-induced AFND. Drugs may be difficult to confirm as causative because it may be difficult to address the specific drug in patients receiving multidrug therapy. The most commonly associated drugs (granulocyte colony stimulating factors) and, rarely, trimethoprim-sulfamethoxazole have been documented previously. After discontinuation of both these drugs, the symptoms progressed abruptly.

To the best of our knowledge, our patient is the first reported patient who had Sweet syndrome that occurred after autologous stem cell transplant. Skin eruption in transplant patients must always alert the clinician about possible infectious pathogens. After stem cell transplant, because of multiple drug exposure and comorbidities, clinicians must consider this rare entity in the differential diagnosis of skin lesions.

References