CASE REPORT

Zosteriform Sweet Syndrome

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ABSTRACT

Sweet's syndrome (acute febrile neutrophilic dermatosis) is a rare skin condition characterized by fever, leukocytosis, and erythematous plaques or nodules invaded by neutrophils. Sweet's syndrome has been reported in three clinical settings: classical or idiopathic Sweet's syndrome, malignancy-associated Sweet's syndrome, and drug-induced Sweet's syndrome. We reported a 57-year-old woman, a known case of breast carcinoma and receiving radiotherapy. She had developed itchy, painful, reddish lesions on her left wrist region extending to the hand of 10 days duration. She had no fever or other accompanying symptoms. Histological examination was consistent with sweet syndrome; revealed a dense dermal neutrophilic infiltrate, with marked edema, and no vasculitis.

CASE REPORT

A 57-year-old female presented to the dermatology OPD with the complaint of a large, painful reddish itchy lesion on her left hand of 10 days duration. The condition had a sudden onset and a rapidly progressive course. The patient had a history of breast adenocarcinoma and underwent left radical mastectomy 2 years back, and she was receiving regular sessions of radiation therapy.

Physical examination showed, a large, well-demarcated, zosteriform erythematous and indurated edematous plaque measuring approximately 10 x 7 cm on the extensor area of the left wrist encroaching on its ventral region and hand (Fig. 1, 2). The lesion was studded with multiple vesicles and papules with overlying scales and crust. Some tender nodules were felt, along with little small discrete papules and vesicles were

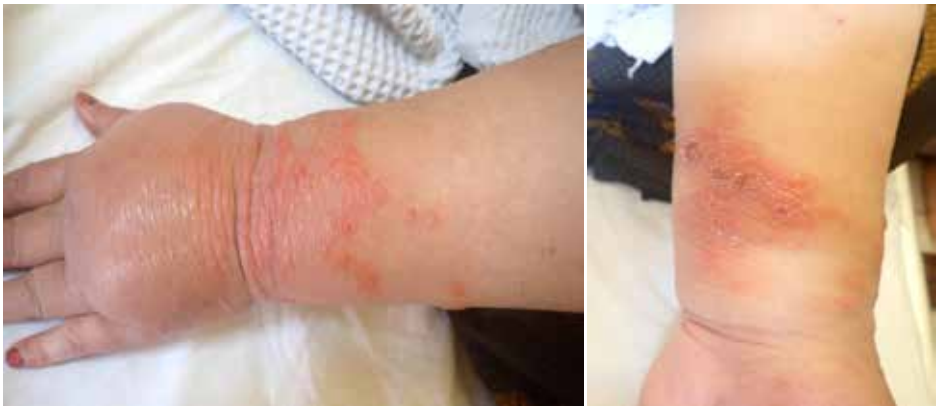

Fig. 1, 2 Well-demarcated erythematous and edematous plaque measuring approximately 10 x 7 cm on both aspects of the wrist with overlying vesicles and papules.

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noticed around the lesion. No lymphadenopathy was present. The review of other systems was unremarkable. Considering the clinical differential diagnosis of herpes zoster, contact dermatitis, tinea incognito, and zosteriform sweet syndrome, skin biopsy was taken.

Patients' routine biochemistry demonstrated neutrophilic leukocytosis (white blood count, 12.3×104 /µl with 89% neutrophils), increased ESR and CRP levels. The results of blood and wound cultures were negative. Other laboratory and radiological investigations including blood sugar, hepatic and renal profile, serology for hepatitis B and C and human immunodeficiency virus and routine chest x-ray were within normal limits.

A skin biopsy revealed dense neutrophilic dermal infiltrate involving superficial and mid-dermis, edema of papillary dermis with no evidence of vasculitis (Fig. 3). A Clinicopathological correlation was consistent with a diagnosis of sweet syndrome.

The patient was treated with oral prednisolone 0.5mg/kg/day for 2 weeks, then tapered over the next 2 weeks together with potent topical corticosteroid and experienced marked improvement. No recurrence after 1 year of follow-up.

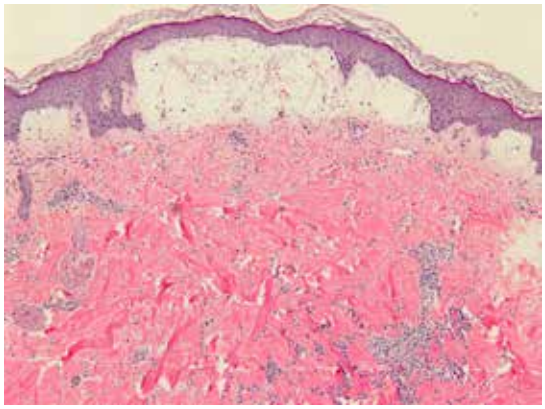

Fig. 3 Papillary dermal edema and inflammatory infiltrate containing numerous neutrophils with extravasated RBC's in superficial and mid dermis

FINAL DIAGNOSIS

Zosteriform Sweet Syndrome

DISCUSSION

Sweet's syndrome was first characterized as an "acute febrile neutrophilic dermatosis" by Robert Douglas Sweet in 1964. During the 15-year period from 1949 to 1964, Dr Sweet described the cardinal symptoms of a separate and severe sickness in eight female patients with a comparable constellation of findings: Fever, leukocytosis, painful erythematous skin plaques, and nodules are all symptoms.[1]

It is now understood that some cases of sweet's syndrome are not limited to the skin and various extracutaneous manifestations of sweet's syndrome have been described.[2] Dr Sweet himself preferred the disease be called as Gomm-Button disease in honor of the first two patients afflicted with the condition in Dr Sweet's practice.[1] Sweet's syndrome can signal the physician to the diagnosis of cancer or the recurrence of malignancy, hence it is critical that the oncologist does not miss the sentinel character of this skin lesion.[3]

The underlying molecular mechanisms causing sweet syndrome have remained a mystery. However, the association of this disease with infection, autoimmune diseases, neoplasms and drugs suggests an unusual hypersensitivity that may be mediated by cytokines, followed by infiltration of neutrophils that are probably activated by interleukin (IL)-1. Circulating autoantibodies, cytokines, dermal dendrocytes, HLA serotypes, immunological complexes, and leukotactic processes have all been implicated in the development of this condition. The presence of IL-1,

IL-2, and IFN- but not IL-4 implies that type 1T helper cells may be involved in the etiology of idiopathic forms of this syndrome.[4] Inflammatory cell markers, including CD3, CD163, myeloperoxidase, metalloproteinases and vascular endothelial growth factors, display significantly higher values in the lesioned skin of patients with Sweet's syndrome compared to non-Sweet's syndrome individuals or patients with other neutrophilic dermatoses.[5]

In malignancy-associated Sweet's syndrome, the most frequently proposed hypothesis for the pathogenesis is the overproduction and inappropriate regulation of inflammatory cytokines such as IL-1, IL-3, IL-6, IL-8, granulocyte colony stimulating factor (G-CSF) and granulocyte macrophage colony stimulating factor (GM-CSF).[6] In this subtype, the clinical manifestations can precede, follow, or appear concurrent with the diagnosis of neoplasm in patients. Approximately 21% of Sweet's syndrome patients have a malignancy; 85% of them are connected to hematological illnesses, most often acute myelogenous leukemia (AML). Sweet's syndrome has also been seen in individuals with Hodgkin disease, polycythemia vera, and 15% of patients with solid tumors, primarily adenocarcinomas of the breast, genitourinary tract, and gastrointestinal tract.[7-9]

Clinical prodromal features of sweet syndrome include fever which is the most common complaint in this disease and prior upper respiratory infection which present in 75–90% of patients with idiopathic sweet's syndrome and in only 20% of patients with malignancy-associated sweet's syndrome.[2] The cutaneous lesions in sweet's syndrome are painful, erythematous papules, plaques, nodules or even bullae or ulceration giving the morphology of pyoderma gangrenosum.[10] These skin lesions are seen in nearly 50% with malignancy-associated sweet's syndrome and 36% of patients with drug-induced sweet's syndrome.[11] Cutaneous pathergy, for instance, in post mastectomy lymphedema has also been observed to incite sweet's syndrome skin lesions.[12]

Our case showed an unusual presentation of sweet syndrome, a large, well-demarcated, zosteriform erythematous and indurated edematous plaque on the extensor area of the left wrist encroaching on the hand and studded with multiple vesicles and papules giving the appearance of zosteriform eruption. Different varieties and atypical cases of Sweet's syndrome can occur. Here we could not exclude malignancies and radiation as triggering factors in the development of skin lesions. There have been few reports of sweet's syndrome associated with radiation for the treatment of malignancies, in most patients, sweet's syndrome developed in the irradiated field during the course of radiotherapy and spread to non-irradiated fields.[13]

Neutrophilic dermatosis of the hands is thought to be a localized condition that can extend to adjacent areas and is not usually accompanied by fever and neutrophilia.[14] Another uncommon localized type is neutrophilic dermatosis at the site of lymphedema, which has a milder course with fewer systemic symptoms and fewer relapses, though its etiology is unknown.[15]

Extracutaneous manifestations of sweet syndrome have been reported to be present in 50% of patients affected with malignancy-associated sweet's syndrome which are more likely to be present in hematologic malignancy compared to solid malignancy.[16] It can affect individually other

organs, such as bones, brain, ears, eyes, kidneys, intestines, liver, heart, lung, mouth, muscles and spleen. Lungs are the most common extracutaneous site; symptoms range from upper respiratory tract infection with flu-like symptoms in its early stages to acute respiratory distress syndrome.[17]

Histopathological criteria of sweet syndrome include the presence of diffuse neutrophilic infiltrate in the dermis, edema, and fragmentation of the nuclei of neutrophils (karyorrhexis or leukocytoclasia). The epidermis appears normal and there is classically no evidence of primary leucocytoclastic vasculitis such as fibrin deposition or neutrophils within vessel walls. Perivascular and interstitial infiltrate composed predominately of neutrophils, scattered lymphocytes, histiocytes, and eosinophils.[17] The presence of subcutaneous neutrophilic inflammation in Sweet's syndrome lesions may be a more common finding in patients with either an associated hematologic dyscrasia or a solid tumor.[18]

The gold standard of the treatment in sweet's syndrome is treatment of the underlying malignancy, which can result in complete resolution of the individual's sweet's syndrome.[2] There are no specific guidelines for the treatment of malignancy-associated sweet's syndrome, therefore hematologists and oncologists treat sweet's syndrome same as classical sweet's syndrome. Sweet's syndrome caused by anticancer agents sometimes involves withdrawal or temporary discontinuation of anticancer agents, use of systemic corticosteroids, and/or rechallenge with either the same anticancer agents or different agents.[2]

Systemic corticosteroids are the mainstay of therapy for sweet's syndrome. Prednisone, at a dosage of 1 mg/kg/day, may be given as a single morning dose. After a clinical response is observed, prednisone can be lowered by 10 mg/day within a period of 4–6 weeks. Localized cutaneous lesions may be treated with high-potency topical corticosteroids including intralesional corticosteroids (such as triamcinolone acetonide) as a single injection or as multiple sequential treatments if necessary.[19]

Other treatments include potassium iodide which is more effective in vasculitis and hypothyroidism-associated sweet's syndrome[20] and in solid malignancy-associated sweet's syndrome with a good response.[21] Several larger studies have shown colchicine at a dose of 0.5 mg three times each day is an effective agent for the successful management of patients with sweet's syndrome.[22] Dapsone and cyclosporine can be given in combination with or without steroids in patients that do not respond to first line therapy.[21] Other second line stand-alone agents are indomethacin 150 mg orally for 7 days followed by 100 mg orally for 14 days have been shown with good response.[23] Other systemic drugs in isolated case reports have also been shown to be effective for the treatment of sweet's syndrome include chlorambucil and cyclophosphosphamide, antimetabolites, immunoglobulins, interferon-α, tumor necrosis factor and the anti-angiogenic agents, infliximab and thalidomide.[19]

In our case, systemic and local corticosteroid therapy rapidly cleared the skin lesions. Multidisciplinary collaboration is the base of providing quality medical care. Radio-induced sweet syndrome is generally well controlled by corticosteroid therapy and treatment could be achieved if there are minor symptoms. However, when patients are receiving antineoplastic agents, it is difficult to define underlying cause of sweet's

syndrome and its true significance.[24]

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