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Bullous Sweet Syndrome. A Case Report and a Review of the Literature

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Abstract

Observation: Acute febrile neutrophilic dermatosis, or Sweet syndrome (SS) is rare or rare dignosable disease characterized in typical cases by four cardinal clinical symptoms: fever, neutrophilic leukocytosis, characteristic edematous painful plaques predominantly localized on face, neck and upper extremities, neutrophilic infiltration of the dermis. Rare bullous variant of SS in 23-year old woman was described in this article. No underlying condition and evidence of any infection disease were noticed was found despite intensive work-up.

Introduction

English dermatologist Robert Douglas Sweet described results of his 15 year observations on 8 patients with an interesting clinical condition in Brtitish Journal of Dermatology, 1964 [**1**]. All this patients complained of fever and edematous painful plaques predominantly localized on face, neck and upper extremities and had had neutrophilic leuko cytosis. Despite this clinical picture resemble an infection disease intensive work up revealed no evidence of any infection and treatment with systemic antibiotics was ineffe ctive. Therefore systemic corticosteroids had been administered with dramatic improvement of skin lesions and patients, general condition. So this new syndrome was named acute febrile neutrophilic dermatosis (AFND). According to the clinical course of SS it can be divided to acute and chronic remitting. In addition in the cases of atypical forms such characteristic signs as fever and periferal neutrophilia may absent. So the term Sweet syndrome (SS) is more appropriate in our opinion than AFN

Case Report

A 23-year old woman presented with fever (38,7 C) with chills, rash on her face, neck and upper extremity, arthralgia, malaise, headache.

She told that her complaints began from acute onset of rash on her face and fever. She saw the doctor who prescribed an antibiotics for presumed skin infection without any improvement.

Physical examination reveals multiple 1- to 10-cm tender well-demarcated erythematous, and violaceous edematous papules and nodules predominantly localized on her face (**Figure 1**), neck and both upper extremities (**Figures 2 and 3**), unilateral conjunctivitis for 5 days. Because of marked infiltration the lesions had vesicular or bullous appearance but true blister located on erythematous basis were also seen.

Her medical history and the remainder of the physical examination was unremarcable. She were not pregnant and didn't take any drugs. Abdominal USG and chest X-ray examination revealed no pathology. Laboratory tests showed leukocytosis with neutrophilia (WBC 18,280/uL with segments:75.1%), increased CRP (19 mg/dL), and elevated ESR (60 mm/h).

Histological examination of skin biopsy samples obtained from early lesions on her right dorsal hand revealed an edema of the all dermal layers and disperse mixed infiltration with neutrophils and lymphocytes predominance in the dermis. There was no sign of vasculitis. Blood and lesional tissue culture obtained to check for bacterial and fungal infections were both negative.

Diagnosis of bullous Sweet syndrome was established. After an appropriate therapy with prednisolone (1mg/kg) systemic and skin condition demonstrated full recovery without scar formation. Recurrence was not detected in a follow up period for more than 2 years.

Discussion

Acute febrile neutrophilic dermatosis, or Sweet syndrome (SS) is rare disease characterized in typical cases by four cardinal clinical symp toms: fever, neutrophilic leukocytosis, characteristic edematous painful plaques predominantly localized on face, neck and upper extr emities, neutrophilic infiltration of the dermis.

Diagnostic criteria:

Diagnostic criteria (proposed by Su and Liu and revised by von den Driesch) [**2,3**] include the presence of 2 major and 2 minor clinical findings, as follows:

Major criteria:

Abrupt onset of tender or painful erythematous plaques or nodules, occasionally with vesicles, pustules, or bullae

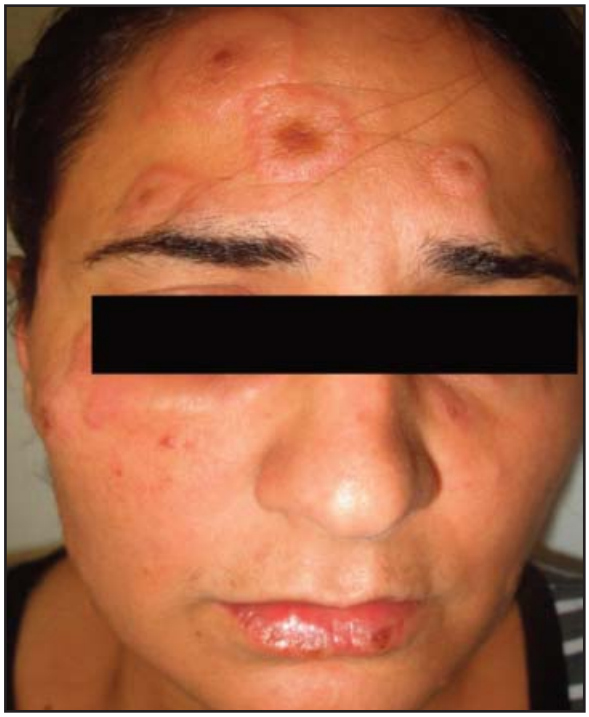

Figure 1. Due to marked edema some plaques can resemble vesicles. So they are called pseudovesicles - a pathognomonic sign of Sweet syndrome . Conjunctivitis. Cheilitis

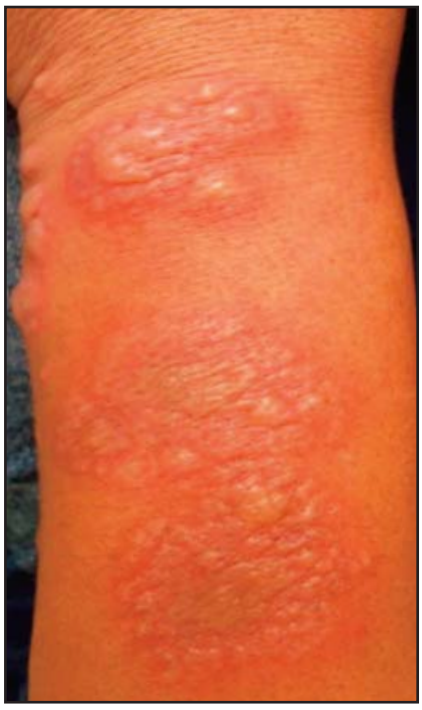

Figure 2. Vesicles located on erythematous and edematous base can mimic herpetic (or zoster-like) eruptions

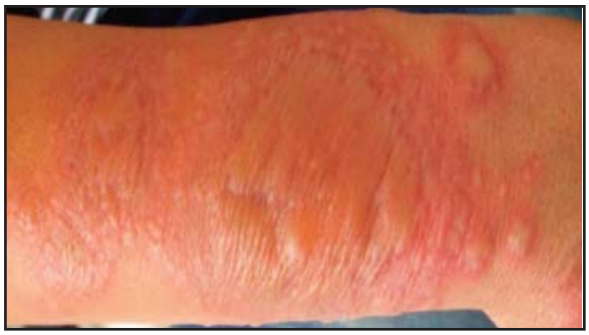

Figure 3. Multiforme rash presented with erythematous, urticarial and vesico-bullous eruptions

Predominantly neutrophilic infiltration in the dermis without leukocytoclastic vasculitis

Minor criteria:

Preceding nonspecific respiratory or gastrointestinal tract infection or vaccination or associated with inflammatory disease, hemoproli ferative disorders, solid malignant tumors, or pregnancy

Periods of general malaise and fever (body temperature >38°C)

Laboratory values during onset showing a erythrocyte sedimentation rate >20 mm, positive C-reactive protein (CRP) result, elevated segmented nuclear neutrophils, bands >70% in peripheral blood smears, and leukocytosis (count >8000/μL) (meeting 3 of 4 of these values is necessary)

Excellent response to treatment with systemic corticosteroids or potassium iodide

Diagnostic criteria for DISS (proposed by Walker and Cohen) include all 5 criteria below; all of the following are required for the drug eruptions to be considered a diagnosis of drug-induced Sweet syndrome [**4**].

Abrupt onset of painful erythematous plaques or nodules

Histopathologic evidence of a dense neutrophilic infiltrate without evidence of leukocytoclastic vasculitis

Pyrexia (38°C)

Temporal relationship between drug ingestion and clinical presentation, or temporally related recurrence after oral challenge

Temporally related resolution of lesions after drug withdrawal or treatment with systemic corticosteroids.

There is 6 etiologic forms of SS:

idiopathic or classical (ISS)

autoimmune diseases associated SS (ADASS)

drug induced (DISS)

malignancy-associaed (MASS)

pregnancy associated (PASS)

infection diseases associated (IDSS)

Diagnosing of defined etiologic forms of SS is most important factor influencing treatment choice in context of eliminating triggering agents. Classical Sweet's syndrome has a worldwide distribution, usually presenting in middle age women with a 4:1 female to male ratio, no racial disparity, and recurrence in one-third of patients [**5**]. The diagnosis of autoimmune diseases associated SS is performed in cases of association SS with different autoimmune diseases. Different examples of these associations were described in the literature such as: systemic lupus erythematosus [**6**] dermatomyositis [**7**] pemphigus vulgaris[**8**] Crohn's disease and Sjogren syndrome [**9**] etc. Malignancy-associated Sweet's syndrome was first described by *Cohen* et al. [**10**] In this subtype, the clinical manifestations can precede, follow, or appear concurrent with the diagnosis of neoplasm in patients. Approxi mately 21% of patients newly diagnosed with SS were previously or subsequently diagnosed with either a hematologic (15%) or solid cancer (6%) [**11,12**] Finally, in drug-induced Sweet's syndrome, there is nearly always a temporal relationship between medication administration and symptom development. In 1996, Walker and Cohen described the diagnostic criteria for druginduced Sweet's syndrome [**4**]. G-CSF is the most commonly reported drug that causes Sweet's syndrome. In addition several other drugs such as all-trans-retinoic acid [**13**] trimetoprim/sulfamethoxazole [**14**] azathioprine [**15**] piperacillin/tazobactam [**16**] etc. can provoke development of DISS.

In addition to etiologic there are also several clinical forms of SS divided into 2 groups: typical and atypical [**17**] Among the last ones bullous SS (BSS) is one of the most important on account of association with underlying hematological malignancies. Although BSS induced by drugs also had been reported. *So Lund J.* et al. reported case of BSS in female patient taking carbamazepineand hydralazine [**18**] Besides work-up of our patient and observation for more than 2 years revealed no underlying ma-

lignancies or other underlying conditions. Recurrence was also not detected.

Bullous variant is a rare and atypical subtype of SS that presents predominantly with neutrophilic bullous lesions, but not with typical erythematous plaques [**19,20**] But in some cases such as own classical edematous plaques (pseudovesicles) can coexist with bullous one. Vesicles and pustules can sometimes be seen to a certain degree in half of SS cases [**21**]. bullous variant is different from usual SS in that bullae are the dominant eruptions in bullous variant. In this case, important differential diagnosis was bullous pyoderma gangrenosum [**22**] However, rapid dramatic res ponse to steroid systemic therapy and healing without scar formation even ulcerative lesions in addition to diagnostic criteria are diagnostic clues for SS.

SS can resemble a large variety of different skin diseases. By-turn latest can also mimic SS (Sweet-like dermatoses). Differential diagnosis may be difficult in such cases but it is very important in the context of possibility of underlying malignancy. In addition SS and SS-like dermatoses can occur simultaneously in the same patient. *So C.Y. Neoh* et al. describe a 47-year-old male patient with concurrent lesions of SS on the limbs and pyoderma gangrenosum on the chest. MDS with refractory anaemia and bone marrow infection with Penicillium species was also revealed [**22**].

Conclusion

According to the opinion of some authors SS may be rare diagnosable disease. But in fact Sweet R.D. himself describes only 8 cases at the observation period of 15 years. So SS is rare disease. We found that only a few cases of bullous Sweet syndrome have been reported in the literature. So physicians must keep in mind SS when consult any patient with fever, rash and elevated segmented nuclear neutrophils. In addition when bullous lesions developed in patient with SS it is important to perform necessary investigations to rule out underlying malignancy, especially hematological disorders.

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