

Sweet Mystery Case Report of a Rare Presentation of Myelodysplastic Syndrome as the Sweet's Syndrome

This article was published in the following Scient Open Access Journal:

SOA: Clinical Medical Cases, Reports & Reviews

Received August 07, 2017; Accepted August 28, 2017; Published September 04, 2017

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Abstract

Acute febrile neutrophilic dermatosis (Sweet's syndrome) is characterized by pyrexia, neutrophilia, and the abrupt appearance of erythematous, painful, cutaneous plaques.

We describe the case of an 83-year-old man, who was presented to our hospital with increased frequency of urination, progressive fatigue, weight loss, and fever. Along with this, patient was concerned about the rapidly developing open skin ulcers for about 3-4 weeks. Initial lab-reports showed anemia, leukocytosis and elevated PSA. Imaging was negative for any abnormality. Surgical biopsy of the skin lesion was performed and it revealed the diagnosis of sweet's syndrome. Patient was treated with intravenous steroids with rapid improvement in his condition and eventual complete resolution of the skin ulcers. His prostate biopsy and gastro-intestinal evaluation came negative for malignancy. Bone marrow biopsy was done for persistent anemia and thrombocytopenia and the patient was found to have high-grade Myelodysplastic syndrome.

Keywords: Sweet syndrome, Myelodysplastic Syndrome, Anemia, Rare entity

Background

The case highlights an unusual presentation of sweet's syndrome in a previously healthy male. Acute febrile neutrophilic dermatosis (Sweet's syndrome) is characterized by pyrexia, neutrophilia, and the abrupt appearance of erythematous, painful, cutaneous plaques, primarily on the upper extremities, head, and neck [1]. Histologically, the salient feature is a dense neutrophilic dermal infiltrate. Approximately 10 to 15 percent of published cases of Sweet's syndrome occurred in patients with cancer [2]. Response to systemic steroids is dramatic in virtually all patients, regardless of the presence of malignancy [2].

The patient in this case report presented with classic features of sweet's syndrome and responded well to the steroid treatment. However, his disease remained a clinical mystery for quite some time, until the bone marrow biopsy was done and he was found to have poorly differentiated, high-grade Myelodysplastic syndrome.

Case Description

An 83-year-old white male came in the emergency department with the complaint of increased frequency of urination. On initial evaluation patient described a 3-week history of progressive fatigue, weight loss, fever and increased frequency of urination. Along with this, patient was concerned about the rapidly developing open skin ulcers from the last 3-4 weeks. He went to a convenient care and was given Oral Ciprofloxacin for one week. He found no relief and decided to come to the ER. Regarding the skin lesions, patient mentioned not having any idea when did the skin lesions develop, he started noticing them since the last one month.

The patient had no significant past medical, surgical, allergy or medication history. He was a retired farmer and was living by himself.

On physical exam, the patient had toxic-appearing cachectic look, with fever, hypotension and tachycardia. He was found to have skin lesions in the form of ulcers, about 4-5 cm in diameter with heaped up edges and central ulceration around his lips, and on torso. The lesions were firm and painful to touch, along with bilateral axillary lymphadenopathy.

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Investigations

Initial basic lab evaluation revealed anemia, leucocytosis and acute kidney injury. Outside hospital's lab showed elevated PSA of 47 ng/dl. Fecal occult test done in the hospital and it was reported positive.

CT Chest Abdomen and Pelvis - Bilateral trace pleural effusions, mild mediastinal lymphadenopathy, non-specific and minimal pericholecystic stranding, non-specific.

Histopathology - Hematoxylin and Eosin stained at 10 X magnification showing ulcerated skin with superficial and deep neutrophilic infiltrates in the dermis (Figure 1a).

Bone Marrow Biopsy - Bone marrow aspirate and core biopsy show trilineage dysplasia. The bone marrow core biopsy is hypercellular for patient's age (50-60%). Core biopsy shows enlarged atypical and hyperchromatic megakaryocytes. CD61 stain showed numerous megakaryocytes in loose clusters. CD34 stain showed less than 5% blasts. The findings are consistent with Myelodysplastic/Myeloproliferative neoplasm.

Flow Cytometry- No abnormal immunophenotypic cell populations seen in flow cytometry.

Chromosome Analysis, FISH, Bone Marrow (MML) - The result is abnormal. Each metaphase had a complex karyotype including 85 of the nuclei with 5q deletion. Also 9q deletion, trisomy 8 and monosomy 3 is found. The result is associated with either de novo or therapy-related MDS or AML.

Differential Diagnosis

- Idiopathic Sweet's syndrome
- Sweet's syndrome likely secondary to underlying possible Prostate cancer (elevated PSA)
- Sneddon Wilkinson disease
- Pyoderma Gangrenosum
- Granuloma Faciale

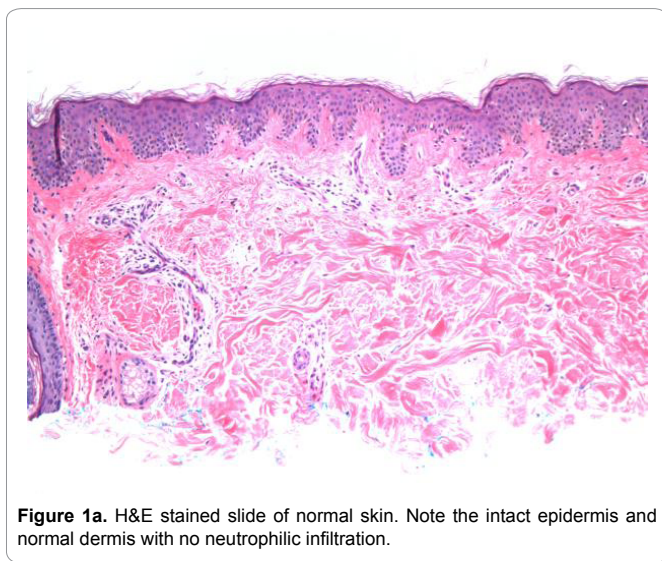


Figure 1a. H&E stained slide of normal skin. Note the intact epidermis and normal dermis with no neutrophilic infiltration.

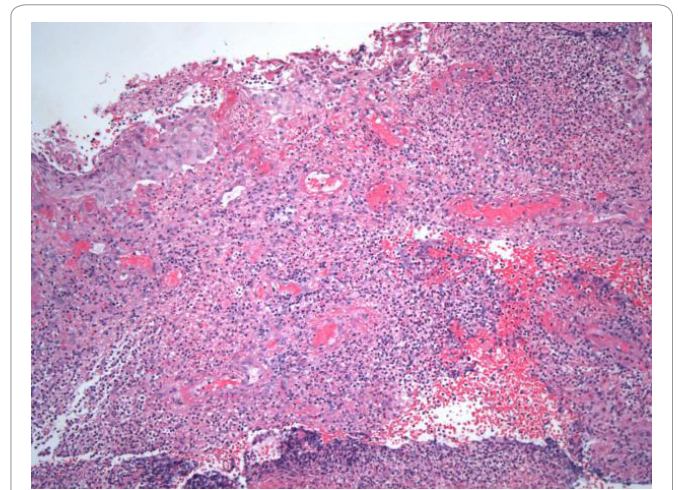


Figure 1b. H&E stained slide (from the skin lesion on the chest) at 100 x magnification showed epidermal sloughing ulceration, and superficial and deep neutrophilic infiltrates in the dermis. H&E X 100.

Treatment

Based on the initial broad differentials, a broad range of antibiotics were started including Doxycycline, Levofloxacin, Vancomycin and ceftriaxone based on the broad differentials. Consultations were placed for Infectious disease and Urology teams. Antibiotics were discontinued accordingly as the blood and fungal cultures came back negative, and imaging studies also did not show any remarkable findings. Patient initially showed some improvement, followed by a rapid decline requiring intensive care for some time during his hospital course. The biopsy results from the skin lesions on his chest reported neutrophilic dermatosis (Figure 1b), consistent with the diagnosis of sweet's syndrome. Patient received high dose steroid therapy in the form of intravenous methylprednisone 1mg /kg/day. He showed remarkable improvement on steroid treatment and his skin lesions also showed the signs of healing. He was discharged to a skilled nursing care facility with several out-patient follow-ups including Urology, Hematology, Gastroenterology and primary care.

Outcome and Follow-Up

Patient did fairly well during his stay at the nursing home in terms of his energy levels and appetite. He continued prednisone taper and underwent several outpatient procedures including prostate biopsy, Colonoscopy and Upper GI Endoscopy, all of which came back negative for any underlying pathology. Patient was evaluated by Hematology team for his consistent anaemia, leucocytosis and thrombocytopenia. Peripheral blood smear, flow cytometry and mutation studies for JAK-2, Bcr-Abl came back negative. Bone marrow biopsy revealed enlarged atypical and hyperchromatic megakaryocytes, findings consistent with high risk Myelodysplastic syndrome with complex karyotype (Figure 2). The karyotype was complex due to the 5q deletion found in the genetic analysis. Also, chromosome 9q deletion, trisomy 8 and trisomy 9 were also found in chromosomal analysis. Because of his advanced age and high risk of complications, patient was recommended supportive therapy. Patient also opted for palliative care and later hospice care and passed away peacefully 20 days after the diagnosis was revealed.

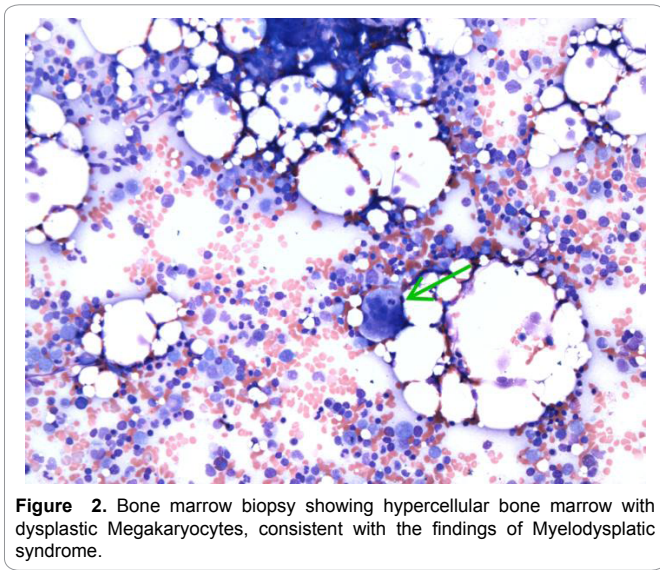


Figure 2. Bone marrow biopsy showing hypercellular bone marrow with dysplastic Megakaryocytes, consistent with the findings of Myelodysplastic syndrome.

Discussion

Sweet's syndrome or acute febrile neutrophilic dermatosis is an uncommon entity first described by Dr Robert Sweet in 1964 [1]. The exact incidence rate of Sweet's syndrome is not known, however several studies have been published since 1964 [1]. It is characterized by fever, leucocytosis, and abrupt onset of tender erythematous skin lesions on the face, neck and extremities. It is mainly divided into three categories: 1) Idiopathic or classical Sweet's syndrome, 2) Drug induced and 3) malignancy associated sweet's syndrome [2-4]. The basic pathogenesis of sweet's syndrome is unclear, some of the possible association described in the literature includes possible bacterial infection leading to the formation of skin lesions about 1-3 weeks after the upper respiratory tract infection or tonsillitis, hypersensitivity to bacterial, viral or tumor antigens, autoantibodies, immune complexes or leukocytoclastic antigens may contribute to the pathogenesis of sweet's syndrome [2,5].

The diagnostic criteria for sweet's syndrome established by Su and Liu in 1986, later modified by Von Den Driesch in 1994, [2,6] includes the following:

a. Major criteria

1. Sudden onset of extremely painful erythematous papules and nodules
2. Neutrophilic dermal infiltrates with the absence of leukocytoclastic vasculitis

b. Minor criteria

1. Fever (>38C), recent infections, recent vaccinations
2. Arthralgia, conjunctivitis or associated malignancy
3. Leucocytosis with neutrophilia >70% on peripheral smear, elevated ESR and CRP.

There are studies in the literature relating sweet syndrome with certain malignancies including solid tumors such as Prostate cancer, Breast cancer, as well as hematological malignancies such as Myelodysplastic syndrome. Studies by Kurzrock et al. [6], and

Cohen et al. [7], have reported febrile neutrophilic dermatosis or Sweet's syndrome and they found that 85% of the cases are associated with underlying hematological malignancy, and 15% with solid tumors. Among the most common hematological malignancies causing sweet syndrome includes Acute myelogenous leukemia (42%) followed by Lymphoma (11%) and Myelodysplastic syndrome (9%). There are several case reports in which the patients presented with different forms of sweet's syndrome associated with hematological malignancy. In a case reported by Li et al., the patients exhibited arthralgia before the development of skin lesions, and had multi-organ involvement shown by pleural effusions, cardiomegaly, liver dysfunction, conjunctivitis and acute kidney injury. Patient was later found to have MDS [8]. Another case of sweet's syndrome, discussed by Garcia et al demonstrated an atypical picture of neutrophilic dermatosis [5]. The patient presented with the picture of granuloma faciale followed by sweet's syndrome like skin lesions that later changed to Pyoderma gangrenosum type of skin eruptions. The patient was later found to have high grade MDS. The authors have outlined that atypical clinic-pathological features of the patient's skin lesions might be due to underlying MDS [5,8]. There are reports of cases of sweet's syndrome secondary to underlying leukaemia presenting as pustules, ulcerations and semi-translucent plaques. Cooper et al, highlighted the term of 'leukemic neutrophilic dermatosis' to the skin lesions in MDS [9]. Also, the presence of lesions with neutrophilic dermatosis has been linked with poor prognosis in myelodysplastic syndrome cases, as reported by Avivi et al. [10]. A new entity in the category of sweet's syndrome has been recently published by Shin, defining subcutaneous sweet's syndrome in their case report [11]. The patient presented with erythematous tender plaques on the dorsum of his foot and the biopsy results showed neutrophilic infiltrates in the subcutaneous tissue extending up to the level of dermis. The inflammatory infiltrate of sweet's syndrome is located in the reticular dermis, however it can also involve the subcutaneous tissue. As per Shin et al, recurrent neutrophilic panniculitis and fever require evaluation of an underlying hematological disorder [12].

In conclusion, patient presenting with tender cutaneous eruptions and biopsy showing neutrophilic dermatosis requires a careful and thorough work-up for infection, medication use and an underlying hematological malignancy. This report re-emphasizes the association of sweet's syndrome with underlying hematological malignancy, such as Myelodysplastic syndrome and the need for malignancy work-up in sweet syndrome.

Learning Points/ Take Home Messages

- Rare entity
- Generalized cutaneous lesions require careful haematological work-up
- The need of malignancy work-up in sweet's syndrome
- Sweet's syndrome must be considered as a differential diagnosis in patients with febrile illness and skin rash.

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