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Sweet’s Syndrome in a patient with Crohn’s disease: a case report

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Abstract

Sweet’s syndrome also known as acute febrile neutrophilic dermatosis has been associated with malignancy, autoimmune disease and collagen vascular disease. The association of Crohn’s disease and Sweet’s syndrome is rare. We report a case of Sweet’s syndrome in a patient with Crohn’s disease.

A sixty three year old man with a history of Crohn’s disease presented with one week duration of abdominal pain, diarrhea and hematochezia. He also noticed eruption of painful skin rashes all over his body at the same time. Colonoscopy and esophagastroduodenoscopy (EGD) showed inflammation involving different parts of the gastrointestinal tract consistent with Crohn’s disease. Punch biopsy of the skin lesion was consistent with Sweet’s syndrome, which has a rare association with Crohn’s disease.

Crohn’s disease should be excluded in patients presenting with Sweet’s syndrome and diarrhea. Alternatively, Sweet’s syndrome should be considered as a diagnosis when a patient with Crohn’s disease develops skin lesions.

Introduction

Sweet's syndrome, also known as acute febrile neutrophilic dermatosis, has rarely been associated with Crohn's disease. We report a case of Sweet's syndrome in a patient with Crohn's disease.
**Case Presentation**

A 63 year-old man with history of Crohn’s disease for past thirty years and hyperlipidemia presented with one week duration of abdominal pain, diarrhea and hematochezia. Abdominal pain was generalized, 6 by 10 in intensity on the pain scale and dull in character. It was worsened by food intake and relieved by bowel movement. Abdominal pain was associated with fever, chills, nausea and vomiting. The patient also complained of painful rashes all over his body that erupted all of a sudden, about a week ago. The rashes were non pruritic and had started on the dorsum of his hands and spread to involve his face, neck, chest and legs. He denied using any new cream, soap, detergent, perfumes or any change in his bed sheets or clothing. He also denied contact with pets, recent travel, similar rash in any family member, or being bitten by an insect. He denied having similar rash in the past. His history was significant for Crohn’s disease for past thirty years which had been in remission for several years, but for the past few months, he was having on and off troubles with diarrhea and rectal bleeding. Colonoscopy two years ago showed inflammatory bowel disease with segmental nature, rectal sparing and primarily involving the ascending and sigmoid colon. His medications included asacol which he had been taking for past few months and azathioprine which was started two weeks prior to his admission in an effort to taper off the steroid. He was previously on prednisone which was started two months ago with his last dose being four days prior to admission. His vitals on presentation were: Temp-100.5°F, BP-95/58mmHg, HR-120/min and RR-21b/min. On physical examination his abdomen was mildly distended with tenderness to palpation in the left lower quadrant. He also had multiple papular rash and plaques, with surrounding erythema, scattered all over his face, neck, chest and legs.
These were tender to palpation. Lab work showed an elevated white blood count (WBC) of 20.7 x 10^9 with 78 percent neutrophils and 14 percent bands. Comprehensive metabolic panel was significant for low sodium of 133 mEq/L and mildly elevated renal function with a BUN of 20mg/dL and Cr of 1.3mg/dL and. His erythrocyte sedimentation rate (ESR) and C reactive protein were also high at 49mm/hr and 161.6 mg/L respectively. His Blood cultures were negative. Other lab works included fungal serology, potassium hydroxide mount, gram stain, Acid fast bacilli smear, bacterial culture, fungal culture and an Acid fast culture of the skin rash, which were all negative.

The patient was started empirically on intravenous vancomycin for possible MRSA folliculitis, pending result of the workup. Computed tomography (CT) scan of abdomen done on admission showed inflammation involving the colon, gastric and duodenal region. Magnetic resonance angiography (MRA) of the abdomen was negative for mesenteric artery occlusion. Colonoscopy and esophagastroduodenoscopy revealed pancolitis and gastroduodenitis consistent with Crohn’s disease. Biopsy specimen taken from stomach, duodenum, ileum, ileocecal valve, and colon revealed pancolitis, duodenitis and gastritis with no evidence of granuloma. The patient was diagnosed with exacerbation of Crohn’s disease and started on intravenous methylprednisolone 60 mg q 12 hrs, with continuation of azathioprine and asacol. He was also given a dose of intravenous Infliximab. The skin rash did not improve despite being on antibiotic for three days. A Punch biopsy of the skin lesion revealed dense dermal infiltrate composed predominantly of neutrophils, with no evidence of vasculitis consistent with the diagnosis of Sweet’s syndrome.
The antibiotic was stopped. The patient’s symptoms and rash rapidly improved with systemic corticosteroid treatment.

Discussion

Sweet’s syndrome also known as acute febrile neutrophilic dermatosis was first described by Robert Douglas Sweet in 1964 (1). Sweet’s syndrome is characterized by fever, neutrophilia, cutaneous eruptions consisting of erythematous papules and plaques, and a dermal nonvasculitic neutrophilic infiltration on skin biopsy (2, 3). These plaques are painful but non pruritic (4). Other skin manifestations such as pustule, vesicles, purpura, ulcers and hemorrhagic lesions have been described (1). Seventy five percent of patients have some prodromal illness, most commonly an upper respiratory tract infection (5). Common complications of Sweet’s syndrome include arthralgia, arthritis, conjunctivitis, iridocyclitis, and rarely involvement of the central nervous system (4). Sweet’s syndrome is more common in females. The overall female to male ratio is 3.7:1, with the mean age being 52 years (1).

Sweet’s syndrome should be regarded as a cutaneous marker of systemic disease. It has been associated with malignancies in about 20 to 25 percent of patients (6). Most are hematopoietic, especially myelodysplastic syndromes and acute myeloid leukemia. 15
percent are due to solid tumors like breast, genitourinary and gastrointestinal malignancies (7). Other causes of Sweet’s syndrome are listed in table 1.

[Table 1]

Only a few cases of Sweet’s syndrome associated with Crohn’s disease has been reported in the literature (1). There is a higher incidence of colonic involvement and extraintestinal features in these patients. The skin lesions have been observed in patients with active Crohn’s disease, but sometimes it can proceed the onset of intestinal symptoms. It appears that the syndrome is not initiated by the underlying disease per se but rather shares with it a concurrent pathogenic mechanism.

The pathogenesis of Sweet’s syndrome is poorly understood. Cytokines, such as granulocyte colony stimulating factor (G-CSF), interleukin (IL)-1, IL-6, or IL-8, if deposited in the dermis, may be responsible for the immunopathologic and clinical manifestations of sweet’s syndrome. The fact that Sweet’s syndrome can occur after G-CSF treatment shows that IL-1, which is produced by acute myelocytic leukemia (AML) cells and stimulates the G-CSF gene, plays a role in the pathogenesis of Sweet’s syndrome (1).

For a definitive diagnosis of Sweet’s syndrome, both major and two minor criteria should be met. The two major criterias are 1) Abrupt onset of painful erythematous plaques or nodules occasionally with vesicles, pustules, or bullae and, 2) Neutophilic infiltration in the dermis without leukocytoclastic vasculitis. The minor criterias are 1) Skin lesion preceded by a nonspecific respiratory or gastrointestinal tract infection, vaccination or
associated with inflammatory disease such as autoimmune disorders, infections, hemoproliferative disorders, solid malignant tumors or pregnancy, 2) Accompanied by periods of general malaise and fever (> 38°C), 3) Laboratory values during onset: ESR > 20mm, C reactive protein positive, segmented neutrophils >70% in peripheral blood smear, leukocytosis > 8000 (3 of 4 of these values are necessary), 4) Excellent response to treatment with systemic corticosteroids or potassium iodide (1,8).

Sweet’s syndrome is one of the groups of neutrophilic dermatoses that include pyoderma gangrenosum, whose association with ulcerative colitis and Crohn’s disease is well established. Sweet’s syndrome can be distinguished from pyoderma gangrenosum by the absence of vasculitis and lack of dermal necrosis, but histological features may occasionally overlap. The abrupt tendency for Sweet’s syndrome to form multiple eruptions on the upper half of the body and the lack of ulceration also distinguishes the rash from pyoderma gangrenosum. However, the two conditions can occur in the same patients, as may other neutrophilic dermatosis, vesiculopapular eruptions, or other cutaneous features of inflammatory bowel disease such as erythema nodosum or polyarthritis. The simultaneous occurrence of different rashes in the same person can be viewed as the dermatological expression of a neutrophilic reaction to a common stimulus (9).

Sweet’s syndrome, if left untreated, usually heals within six to eight weeks (5). Prednisone at an initial dose of 40-60 mg per day, with gradual taper over four to six weeks, is the standard treatment for Sweet’s syndrome (3, 5). Relapses are common if
steroids are tapered too quickly. In recurrent disease, therapy with colchicine, potassium iodide, dapsone, doxycycline, indomethacin, clofazimine, isotretinoin and cyclosporine have been described (1, 5).

Potassium iodide administered orally as 300 mg enteric-coated tablets, 3 times each day, for a daily dose of 900 mg, or as a saturated solution of potassium iodide (Lugol's solution), beginning at a dose of 3 drops 3 times each day (9 drops/day = 450 mg per day) and increasing by 1 drop 3 times per day, typically to a final dose of 21 drops/day (1050 mg) to 30 drops/day (1500 mg), typically results in resolution of fever and other symptoms within 1 to 2 days and skin lesions within 3 to 5 days of initiation of therapy. Vasculitis and hypothyroidism are potential adverse effects of potassium iodide (10).

**Conclusion**

Sweet’s syndrome should be considered an extraintestinal manifestation of Crohn’s disease, and should be differentiated from other more frequent inflammatory diseases that accompany Crohn’s disease, like erythema nodosum, pyoderma gangrenosum and leukocytoclastic vasculitis. Awareness of this association may guide appropriate diagnostic procedures and therapy.

**Competing interest** – the author declares they have no financial or non-financial competing interests
Authors’ contribution -
NM – corresponding author – Took care of the patient while in the hospital, wrote the manuscript, collected all the relevant data, and finalized the manuscript for submission to the journal. Author has read and approved the final manuscript.

ML – Co-author – Involved in giving intellectual advice, reviewing it and correcting any mistakes. The author has read and approved the final manuscript.

Consent - Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Acknowledgement: Dr Niveditha Reddy MD

References


Table 1

Causes of Sweet’s syndrome

<table>
<thead>
<tr>
<th>Malignancies</th>
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<tbody>
<tr>
<td>Hematopoietic: myelodysplastic syndromes and acute myeloid leukemia, hairy cell leukemia, B and T cell lymphoma, agnogenic myeloid metaplasia</td>
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<td>Solid tumors: breast, testicular, prostate, ovarian, vaginal squamous cell, genitourinary and gastrointestinal malignancies</td>
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<th>Viral infections</th>
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<tr>
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<tr>
<th>Bacterial infections</th>
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<td>Streptococcus, mycobacterium, yersinia, typhus, salmonella</td>
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<th>Autoimmune and collagen vascular diseases</th>
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<tr>
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<td>Complement deficiency</td>
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<td>Subacute necrotizing lymhadenitis</td>
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<td>POEMS syndrome</td>
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Legends

**Figure 1** – pustular lesions with central necrosis on the patient’s leg

**Figure 2** - Punch biopsy of the skin lesion showing neutrophilic infiltration in the dermis, with no evidence of vasculitis