Bullous Sweet’s Syndrome in a Patient with Metastatic Colorectal Cancer

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A fifty-two-year-old Bahraini male with metastatic colon cancer developed pustules in the upper limbs which increased in size and number and were associated with pain, ulceration and itchiness. A biopsy revealed diffuse dermal and perivascular neutrophil infiltrate, confirming the diagnosis. This case revealed that the bullous variant of Sweet’s syndrome is closely linked to malignancies, including solid tumors; however, it is uncommon.


Sweet’s syndrome was described in 1964 as an “acute febrile neutrophilic dermatosis”. It presents with fever, neutrophilia and tender erythematosus lesions on the skin including papules, nodules and plaques. The classic histopathological finding of this disease is a diffuse infiltration of mature neutrophils in the upper dermis. The presentation of Sweet’s syndrome can be malignancy-associated, drug-induced, and idiopathic or classical. The skin lesions associated with malignancy are frequently atypical, vesicular, bullous or even ulcerative, in addition to the typical plaques and nodules.

Sweet’s syndrome is an uncommon disease, with a worldwide distribution and no obvious racial predilection. The average age of onset is 30–60 years, however, infants, children and the elderly may also be affected; there is a female predominance of 4:1. Up to 20% of patients have internal malignancies, and in this subgroup, there is no female predominance.

Malignancy-associated Sweet’s syndrome commonly presents with an underlying hematopoietic neoplasia, acute myeloblastic leukemia being the most common. Sweet’s syndrome may also be associated with solid tumors, adenocarcinomas making up 57% of tumors. The most common associated malignancies were of the genitourinary organs, breast and gastrointestinal tract. The incidence of solid malignancy associated Sweet’s syndrome is increasing with time; it is likely due to increased awareness of the disease as well as the increased use of growth factors.

The colorectal cancer was invasive and had infiltrated into adjacent structures including fat, fascia, bladder base, seminal vessels and prostate. The patient had a colorectal resection and colostomy. He received three cycles of palliative chemotherapy (Cetuximab and Irinotecan). The patient had a perianal abscess (MDR Acinetobacter and extended-spectrum beta-lactamases Escherichia coli) and a urinary tract infection (UTI).

The patient was given courses of metronidazole, meropenem, tigecycline and colistin. During the skin lesion onset, the patient was on the following systemic medications: Zyrtec (Cetirizine), Lyrica (Pregabalin), Lactulose, Omeprazole, Albumin 20% IV, Morphine Sulphate, Dopamine, Clexane (Enoxaparin). He was prescribed Betadine and beta-sitosterol 0.25% cream for the perianal area after incision and drainage.

On examination, the patient was afebrile. There were multiple punched out tender ulcers with yellowish, greenish pus on the dorsal aspect of the upper extremities. The lesions measured from 2.5 cm² to 5 cm² in diameter, surrounded with indurated rim along with the lymphatic distribution, see figures 1, 2 and 3.

Figure 1: Sweet’s Syndrome Lesions on the Dorsal Aspect of Patient’s Hands Bilaterally

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The initial differential diagnosis was pyoderma gangrenosum, disseminated fungal infection (Mucormycosis and Aspergillus), neutrophilic dermatosis associated with malignancy and ulcers associated with chemotherapy.

Complete Blood Count was performed, see table 1.

Table 1: Complete Blood Count

<table>
<thead>
<tr>
<th>Result</th>
<th>Unit</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>White Blood Count</td>
<td>9.29 x 10^9L</td>
<td>3.6 - 9.6</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>7.4 ↓ g/dl</td>
<td>12.0 - 14.5</td>
</tr>
<tr>
<td>Platelets</td>
<td>591 ↑ x 10^9L</td>
<td>150 - 400</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>74.6 %</td>
<td>42.2 - 75.2</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>15.10 ↓ %</td>
<td>20.5 - 55.1</td>
</tr>
</tbody>
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A punch biopsy revealed epidermis with a subcorneal pustule and mild spongiosis; heavy diffuse dermal and perivascular neutrophilic infiltrate occupying the reticular dermis, and extending to the superficial subcutaneous tissue. There was leukocytoclasia surrounding the vascular spaces with endothelial swelling but no vascular damage. Papillary dermal edema was also noted. No atypical pathology was seen. The report concluded that the features were consistent with the clinical diagnosis of Sweet’s syndrome. The patient’s condition deteriorated and expired in August 2016.

DISCUSSION

Von den Driesch proposed the following criteria to diagnose Sweet’s syndrome: sudden onset of tender/painful erythematous plaques or nodules, non-specific respiratory or gastrointestinal tract infection associated with malaise and fever, raised ESR, neutrophils and leukocytosis, good response to corticosteroids or potassium iodide. One major and two minor criteria are required to diagnose such case. Sweet’s syndrome is also known as acute neutrophilic dermatosis. Walker et al added histopathologic evidence of a dense neutrophilic infiltrate without evidence of leukocytoclastic vasculitis as a criterion for diagnosis.

Sweet’s syndrome was associated with hematologic malignancies and, to a lesser extent, with solid tumors; 1,683 cases of Sweet’s syndrome were reported between 1964 and 2012, approximately 21% were associated with malignancy. A review of Sweet’s syndrome revealed that 15% were associated with hematologic cancers and the remaining 6% was associated with solid cancer. Another review of 39 patients revealed that 37% was associated with carcinoma of the genitourinary organs, 23% with breast carcinoma and 17% with carcinoma of gastrointestinal tract.

Our patient had two major criteria (an abrupt onset of painful bullous, ulcerating lesions and neutrophilic infiltration) and two minor criteria (the presence of an underlying malignancy and a neutrophil count >70%).

The most likely cause of this patient’s Sweet’s syndrome is the presence of malignancy. Other causes of Sweet’s syndrome were excluded, such as drug-induced Sweet’s syndrome. The patient was afebrile and a temporal relationship between drug ingestion and clinical presentation could not be determined.

Our patient had a bullous variant of Sweet’s syndrome. This variant is more commonly seen in malignancy-associated diseases, the majority of which are hematological in origin, as multiple case studies have reported.
Solid tumors are less likely to present with Sweet’s syndrome. However, few cases have been reported in the literature, including cases with concurrent colorectal cancer. The following cases presented with the bullous variant of Sweet’s syndrome: A fifty-three-year-old female who had resected adenocarcinoma of the rectum was diagnosed with bullous Sweet’s syndrome after radiotherapy. Another case of a 44-year-old Caucasian female who had cervical cancer (FIGO IIIB) and was treated with chemotherapy and radiation therapy developed bullous Sweet’s syndrome. The third case was a 68-year-old white female who was diagnosed with squamous cell laryngeal carcinoma and treated with modified dissection of the neck, chemotherapy and radiotherapy developed bullous Sweet’s syndrome.

CONCLUSION

Our case demonstrated that the bullous variant of Sweet’s syndrome is closely linked to malignancies including solid tumors, although it is uncommon. In addition, although Sweet’s syndrome typically presents with pyrexia, it may also occur in afebrile patients as seen in our case.

The management of the case was severely limited by the patient’s condition and comorbidities.

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Competing Interest: None.

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REFERENCES