Classic Sweet Syndrome with Mucosal Involvement

Madiha Ahmed, Azeem Khan, Rameez Rao, Anh Bui, and Stephen Carlan

ABSTRACT

Sweet syndrome is an uncommon disorder of unknown etiology and characterized by skin and systemic inflammation. Classic Sweet syndrome is not associated with malignancy or drug exposure and typically involves elderly females. A 67-year-old female with a past medical history of multiple sclerosis and chronic kidney disease presented with worsening erythema of bilateral lower extremities, and diffuse, tender pustular lesions in her extremities, eye lids, nares, oral commissures, and tongue. A biopsy revealed marked neutrophilic inflammation suggestive of Sweet syndrome and she was started on high dose methylprednisolone which immediately improved her condition. As with most progressive inflammatory diseases, early recognition and early treatment improves the prognosis. This case is unusual because of mucosal involvement at presentation. Classic Sweet syndrome can often be diagnosed by exclusion after failed treatment for either infectious or autoimmune disorders.

Keywords: Methylprednisolone, mucosal ulcers, Sweet syndrome.

I. INTRODUCTION

Sweet Syndrome was first described by Dr. Robert Douglas Sweet in 1964 [1]. It belongs to a group of uncommon inflammatory abnormalities known as neutrophilic dermatoses. This group includes a heterogeneous group of inflammatory skin disorders that include Sweet syndrome, pyoderma gangrenosum, and subcorneal pustular dermatosis [2]. Even though this condition has been reported in hundreds of case reports since its first description, the underlying etiology is not clearly understood. The following case describes a single patient presenting with erythema that was initially mistaken for cellulitis, only to be diagnosed with Sweet syndrome later in the clinical course. The patient’s convoluted course highlights the challenges in identifying this skin condition that can have atypical presentation, hence posing a diagnostic challenge. In addition, a description of the definition, pathogenesis and management is included.

II. CASE REPORT

A 67-year-old female with a past medical history of multiple sclerosis and chronic kidney disease presented to the hospital with worsening erythema of bilateral lower extremities. Two days prior, she was diagnosed with cellulitis at the skilled nursing facility. Due to extensive medication allergies, she was started on aztreonam and vancomycin at the facility which was continued on arrival to the hospital. Upon presentation to the hospital, her vital signs were remarkable for temperature of 100.6 F and labs were remarkable for white blood cell count of 18.0 x 103/ul [normal range of 4.4-10.5 x 103/ul] with 84% neutrophils, c-reactive protein (CRP) 224 mg/L [normal 0-9.9 mg/L], and erythrocyte sedimentation rate (ESR) of 100 mm/hr [0-30 mm/hr]. Over the next few days, she showed no signs of improvement despite being on the antibiotic regimen. She also developed diffuse, tender pustular lesions in her extremities, eye lids, nares, oral commissures, and tongue (Fig. 1) as well as...
purulent discharge in bilateral eyes for which she was given antibiotic eyedrops for suspected bacterial conjunctivitis, with no improvement.

The lesions became hemorrhagic bullae which burst and turned into ulcers. We performed extensive infectious disease and autoimmune workup which all came back negative. A punch biopsy of one of the lesions was then performed which showed marked neutrophilic inflammation suggestive of Sweet syndrome (Fig. 2).

She was started on high dose methylprednisolone which immediately improved the skin lesions with complete resolution of all cutaneous manifestations within 7 days.

**Fig. 1.** (A) Erythematous right lower extremity. (B) Tender pustular lesions on face with oral mucosal involvement (C) Hemorrhagic bulla on left hand.

**Fig. 2.** (A and B) Histologic sections of a punch biopsy show squamous epithelium surrounded by widespread neutrophilic inflammatory (black arrows) infiltrate and fibrin deposition.

### III. DISCUSSION

There are three subtypes of Sweet syndrome: classical or idiopathic, drug-induced and malignancy-associated. The most common presentation of classical Sweet syndrome includes fever, leukocytosis and tender, erythematous skin lesions that usually affect the face, neck and upper extremities [3]. Classical Sweet syndrome may be associated with infection, usually of the upper respiratory or gastrointestinal tract and inflammatory bowel disease, however, in many instances, like this case, there is no known precipitating event that can be identified. In addition, up to 80% of cases of classic Sweet syndrome are women. The diagnostic criteria for classical Sweet syndrome was originally proposed in 1986 and was subsequently modified by [4]. Table I summarizes the diagnostic criteria for the diagnosis of classical Sweet syndrome [5]. The case we describe in this report was characterized by bullous formation, which is usually associated with underlying malignancy, mainly hematological, however this patient did not have any underlying hematological malignancy [6] and was also up to date on age appropriate cancer screening which had been negative. This case was also characterized by mucosal involvement which is an atypical presentation of classical Sweet Syndrome and is seen in only 2% cases worldwide [3].

Malignancy-associated Sweet syndrome can be the first cutaneous manifestation of an undiagnosed malignancy or an unsuspected cancer recurrence in an oncology patient. Approximately 21% of Sweet syndrome patients have an associated malignancy. Most commonly these malignancies are hematological disorders like acute myelogenous leukemia (AML) and Hodgkin disease solid tumors, however it can also be seen in adenocarcinomas of the breast, genitourinary tract, and gastrointestinal tract [7]. In drug-induced Sweet syndrome, there is usually a temporal relationship between medication administration and symptom development. The most commonly reported drug causing Sweet syndrome is granulocyte-colony stimulating factor, trans-retinoic acid proteosome inhibitors, hypomethylating agents, tyrosine kinase inhibitors and lenalidomide [8].

The pathogenesis of Sweet syndrome is not clearly understood. There has been a strong association observed with infections, autoimmune diseases, neoplasms, and drugs that suggests that an unusual hypersensitivity reaction mediated by cytokines, followed by infiltration of neutrophils might have a role to play in the disease pathogenesis. Circulating autoantibodies, cytokines, dermal dendrocytes, HLA serotypes, immune complexes and leukotactic mechanisms have all been suggested as possible mediators in the pathway. The most accepted theory regarding the pathogenesis of malignancy-associated Sweet syndrome, is the overproduction and inappropriate regulation of inflammatory cytokines, and granulocyte colony stimulating factor (G-CSF) and granulocyte macrophage colony stimulating factor (GM-CSF) [9].

Currently there are no guidelines for the treatment of Sweet syndrome, however systemic corticosteroids are considered to be the first line of treatment. In patients who have a contraindication to corticosteroids, oral therapy with either potassium iodide or colchicine can be considered for resolution of symptoms and lesions. Since Sweet syndrome can be a manifestation of underlying malignancy, it has been recommended that newly diagnosed Sweet syndrome patients undergo a malignancy workup [10], since there have been cases of neoplasms that were concurrently or subsequently diagnosed in previously cancer-free Sweet’s syndrome patients.

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### TABLE I: IN CLASSICAL SWEET SYNDROME, THE PRESENCE OF BOTH MAJOR CRITERIA (1 AND 2) AND TWO MINOR CRITERIA (3-6) IS NEEDED TO ESTABLISH THE DIAGNOSIS

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<thead>
<tr>
<th>Diagnostic Criteria for Classical Sweet Syndrome</th>
<th>Major</th>
<th>Minor</th>
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<tr>
<td>Abrupt onset of painful erythematous nodules or plaques.</td>
<td>Histopathological findings of dense neutrophilic infiltrate without evidence of leukocytoclastic vasculitis</td>
<td>Fever &gt;38 °C</td>
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<td>Association with hematologic or visceral malignancy, inflammatory disease, or pregnancy, or preceded by upper respiratory tract infection, gastro-intestinal infection or vaccination</td>
<td>Excellent response to treatment with systemic corticosteroids or potassium iodide</td>
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<td>Abnormalities in laboratory tests (three of four): erythrocyte sedimentation rate &gt; 20 mm/h; high C-reactive protein, leukocytes &gt; 8000, with &gt; 70% neutrophils</td>
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### IV. CONCLUSION

Classic Sweet syndrome is uncommon and early treatment is critical. Mucosal involvement is rare and its presence can delay a diagnosis. An awareness of the disease is important so proper biopsies can be performed and early treatment begun. Through this case report we aim to improve awareness of this condition so as to reduce diagnostic delay and improve patient outcomes. We also hope to facilitate an understanding of the disease process which is still not completely understood.

### CONFLICT OF INTEREST

Authors declare that they do not have any conflict of interest.

### REFERENCES