Case Report

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Internal Medicine Section

Sweet Syndrome Masquerading as Severe Infection: A Case Report

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ABSTRACT

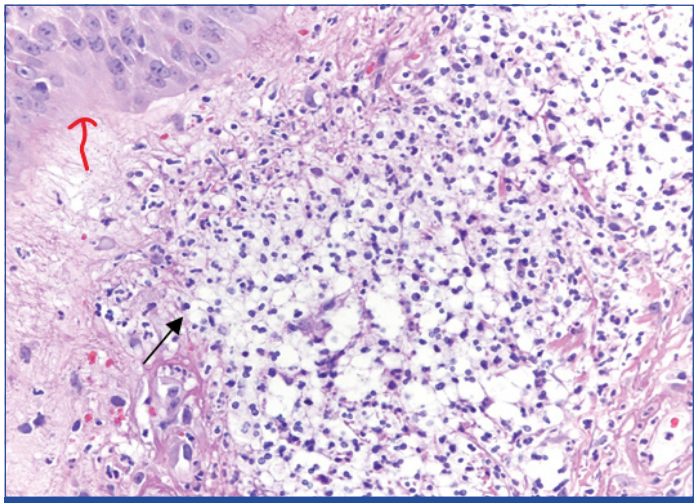
Sweet Syndrome is an uncommon condition noted to occur worldwide, and it usually occurs in females aged between 30 to 50 years. Its exact prevalence is unknown. Hereby, authors report a case of 34-year-old female with a past medical history of Anti-Neutrophil Cytoplasm Antibody (ANCA) vasculitis, End Stage Renal Disease (ESRD) on haemodialysis and history of recent hospitalisation for sepsis secondary to multifocal pneumonia presented with fever and disseminated bullous rash. Patient was started on board spectrum antibiotics in view of Systemic Inflammatory Response Syndrome (SIRS) positivity. Subsequently, she underwent skin biopsy due to lack of improvement of symptoms on antibiotics. It showed dermal neutrophilic infiltrates suggestive of sweet syndrome. Patient was then started on high dose intravenous steroids with subsequent improvement of her symptoms. She was gradually transitioned to oral steroids and was discharged in a stable condition. Thus, Sweet syndrome is an uncommon condition which can easily be confused with other medical conditions like infection or vasculitis. Careful assessment and thorough work up including skin biopsy are vital in confirming the diagnosis.

Keywords: Bullous rash, Sepsis, Vasculitis

CASE REPORT

A 34-year-old female was referred from an outside facility with painful, bullous rash with haemorrhagic crusting on face (around both eyes, nares, and lips) and left upper extremity measuring about 1.5 cm diameter for three days. Patient had been recently hospitalised at an outside facility for multifocal pneumonia and empyema for which she was treated with antibiotics (vancomycin and piperacillin/tazobactam) and chest tube insertion. Her hospital course was complicated with splenic laceration secondary to chest tube insertion which required interventional radiology guided embolisation. On the fifth day of hospital stay, patient developed painful, non pruritic bullous nodular rashes about 1.5 cm in diameter associated with haemorrhagic crusting and moderate tenderness to palpation on face and left upper extremity. Patient was transferred to hospital three days after development of the rash. Her past medical history included Anti-Neutrophil Cytoplasm Antibody (ANCA) vasculitis, end stage renal disease with renal transplant complicated by graft rejection and now on haemodialysis, and history of parathyroidectomy for secondary hyperparathyroidism.

The patient was admitted to Medicine Unit and her complete blood count was done which revealed: haemoglobin was 8.2 g/dL, haematocrit was 26%, white cell count was 20,000/µL, and platelets were 424000/µL. Patient was Systemic Inflammatory Response Syndrome (SIRS) positive in the setting of tachycardia, fever, tachypnea, and leukocytosis. She was initiated on broad spectrum antibiotics (vancomycin and piperacillin/tazobactam). Dermatology team was consulted who initially recommended to hold steroids and other immunosuppressive agents due to concern for infection. She subsequently developed bilateral corneal ulcerations associated with conjunctival palpebral defects concerning for vasculitis flare versus Steven-Johnson syndrome requiring treatment with amniotic membrane transplants. Rheumatology team was consulted due to concern for vasculitis flare who recommended further evaluation with vasculitis labs, which came back negative. No improvement was noticed in the first few days after initiation of antibiotics. Subsequently, skin biopsy was done which showed exuberant perivascular and dermal neutrophilic infiltrate favouring Sweet syndrome with no evidence of vasculitis noted [Table/Fig-1]. Fungal and bacterial aetiologies were ruled out with appropriate stains.



[Table/Fig-1]: Histology (40X magnification) of a left forearm punch biopsy showed moderate to marked oedema of the dermis with a robust, dermal perivascular to nodular neutrophilic infiltrate (see black arrow); the epidermis was uninvolved by this process (red arrow).

The patient was then started on high dose steroids thus intravenous solumedrol 40 mg twice daily for seven days with subsequent improvement in her symptoms including fever and rash. She was then transitioned to oral prednisone 60 mg twice a day with slow taper regimen. This hospital course was complicated by haemorrhagic shock due to worsening splenic haematoma associated with splenic laceration sustained during the previous hospitalisation. Splenectomy was performed followed by a few days of Intensive Care Unit (ICU) stay requiring vasopressors, blood transfusion, and intubation. Patient was discharged on a steroid taper regimen and was advised to follow-up after one week in dermatology clinic. During the follow-up visit, she was continued on steroid taper for three and a half more months with another follow-up visit afterwards to assess for the resolution of the lesions and the extension of steroid therapy.

DISCUSSION

Sweet syndrome or acute febrile neutrophilic dermatosis was first described by Dr. Robert Douglas Sweet in 1964 when he reported the development of inflammatory skin lesions with systemic findings

in eight women [1]. It commonly affects individuals between the ages of 30 to 50 years, but it can be seen in other age groups as well. Women are more likely to get affected compared to men [2]. Exact aetiology of this condition remains unclear, but it has been seen in the setting of vast array of medical illnesses due to which it has been divided into three subtypes: 1) Classical sweet syndrome (also known as idiopathic Sweet syndrome), which is usually seen with infections and different inflammatory illnesses; 2) Malignancy-associated Sweet syndrome, which is observed in association with different haematologic malignancies (AML etc.,) and solid tumours; 3) Drug induced Sweet syndrome, which is caused by multiple drugs including granulocyte colony stimulating factor [3-6].

Histologically, the hallmark feature of this condition is an intense dermal infiltrate of mononuclear cells (especially neutrophils), and the epidermis is often spared. Additionally, there may be marked oedema of papillary dermis. It is important to perform gram, Periodic Acid-Schiff-diastase (PAS-D)/Grocott Methenamine-Silver (GMS), and Acid- Fast Bacilli (AFB) stains to rule out infectious aetiologies. Classical or malignancy associated Sweet syndrome's diagnosis requires meeting of both major criteria and two of the four minor criteria. Major criteria include new painful erythematous nodules or plaques and histopathologic evidence of dense neutrophilic infiltrate without evidence of leukocytoclastic vasculitis. Minor criteria include good response to systemic steroid or potassium iodide; fever above 38°C; association with pregnancy or inflammatory disease, underlying visceral or haematologic malignancy, or illness preceded by gastrointestinal infection, vaccination, or upper respiratory infection; lab abnormalities at presentation (three of four of the following included erythrocyte sedimentation rate >20 mm/hour, positive C-reactive protein, >8000 leukocytes, >70% neutrophils) [7].

The differential diagnosis of Sweet syndrome is broad, as cutaneous lesions associated with Sweet syndrome may look similar to the lesions seen in other disorders which include bechet's disease, erythema nodosum, erythema multiforme, pyoderma gangrenosum, cellulitis, drug eruptions, cutaneous metastatic crohn's disease, halogenoderma, malignancy, vasculitis, and autoimmune bullous diseases [8]. Systemic steroids are the mainstay of treatment for Sweet syndrome. Colchicine, potassium iodide, or dapsone can be an option in adults in whom steroids cannot be used. Immunomodulatory therapy or pulsed intravenous glucocorticoids can be used for refractory disease [9]. The present case was an example of classical Sweet syndrome.

Most cases of classical Sweet syndrome reported in the literature either occurred abruptly without preceding illness or were associated with upper respiratory tract infection or inflammatory bowel disease [10]. Rarely, it may present with oral manifestations in the setting of a haematological disorder [11]. It may also have atypical presentation such as panuveitis. There are few cases reported in the literature about pulmonary involvement of Sweet syndrome [12-14]. Nishimoto K et al., described a case of Sweet syndrome manifesting as lungs infiltrates on Computed Tomography (CT) scan. However, further work up including bronchoalveolar lavage was negative for infectious aetiology and patient subsequently improved with steroid therapy [13]. In a similar case, patient was noted to present with acute onset dyspnea in the setting of interstitial lung infiltrates. Patient was started on antibiotics due to suspicion for pneumonia with no improvement in symptoms. However, patient had resolution of symptoms with steroid therapy confirming Sweet syndrome as the underlying cause [12]. In the present case, Sweet syndrome was preceded by sepsis due to multifocal pneumonia and empyema. However, lungs imaging did not show any new infiltrates at the time of presentation. One of the unique aspects of present case was that it presented an uncommon association between ANCA vasculitis reported ESRD and Sweet syndrome. Very few of those cases are related in the literature. One such case was presented by Miraliakbari HM et al., of a 60-year-old female with ESRD due to granulomatosis with polyangiitis. She presented with two days of somnolence, fever, nausea, and purple coloured exudative plaques on the forehead and index finger. She was initially diagnosed with herpes zoster and was started on acyclovir. Her lesions progressed to involve both sides of the face. Skin biopsy revealed neutrophilic dermal infiltrate. She was diagnosed with Sweet syndrome and was started on prednisone. Acyclovir was discontinued. She responded to the treatment and was discharged after five days. The patient in this case did not present with sepsis or pneumonia unlike the patient in our case [15].

The present case posed a significant diagnostic challenge particularly given her history of vasculitis. Her initial presentation favoured infectious pathology prompting treatment with antibiotics. However, later development of ophthalmic symptoms pointed towards vasculitis flare further adding to the diagnostic dilemma. Lack of improvement on antibiotics, negative vasculitis labs, and diagnostic skin biopsy helped confirm the diagnosis. Thus, it is often a challenge to initiate appropriate treatment in a timely manner in such cases due to significant overlap in the clinical presentation between different medical conditions as described above.

A multidisciplinary approach is often helpful in such cases but can also pose a challenge when there are differing opinions between specialties. In the present case, the primary team and ophthalmology felt strongly about the need for steroid treatment earlier in the course than other consultants. It required several negative cultures and two biopsies before consultants recommended initiation of steroids. While subspecialists are critical to evaluation and care in most of these cases, it can be challenging for primary teams to feel empowered to make medical decisions that may contradict their recommendations. Clear lines of communication are vital to ensure that care is not compromised by these differing opinions.

CONCLUSION(S)

Sweet syndrome is an uncommon entity which can easily be confused with other medical conditions such as sepsis or vasculitis. Careful consideration of presentation, risk factors, results (particularly negative cultures), and skin biopsy are vital to avoiding delays in the appropriate care.

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