**Background**

- Sweet’s Syndrome is a rare disease manifested by an acute febrile neutrophilic dermatosis of painful erythematous and purpuric papules and nodules. There are 2 major and 4 minor criteria used to formally define the disease (Table 1).³

- Sweet’s Syndrome is classified into three types: classic (associated with upper respiratory tract infection, inflammatory bowel disease or pregnancy), malignancy-related and drug-induced.² However, to date, there are only 4 cases in the literature of an association with systemic inflammatory response syndrome.

**Presentation of the Case**

- A 44-year-old woman with follicular lymphoma transformed to diffuse large B-cell lymphoma (in remission, on maintenance rituximab) developed fever with migratory joint swellings, cold sore outbreaks and painful, pruritic large erythematous nodules and plaques on both legs.

- These symptoms continued on a recurrent and relapsing course for 2 months, ultimately culminating in hospital admission when she further developed easy bruising secondary to anemia and thrombocytopenia.

- During this admission, she had renal failure secondary to acute tubular necrosis, unresponsive transient skin rashes and migratory arthritis with persistent anemia and thrombocytopenia.

- Skin biopsy was non-diagnostic; bone marrow biopsy demonstrated myelodysplastic syndrome. She was started on a course of oral corticosteroids, and due to a positive response, a diagnosis of Sweet’s Syndrome was considered.

- Her initial autoimmune serology was negative including normal complement levels. Acute phase reactants were extremely elevated with ESR of 140 and a CRP of 127. Rituximab was held due to minor failure and she was discharged on a four-week tapering course of oral corticosteroids.

- Three weeks hence she relapsed with recurrent fever, arthritis and skin lesions, necessitating re-admission. Deep skin biopsy demonstrated neutrophilic panarteritis, leading to a diagnosis of atypical systemic Sweet’s Syndrome.

- Acute phase reactants were markedly elevated: CRP 244.9 mg/mL, ESR 92 mm/hr, Ferritin 1928 μg/L and C3 was low at 0.72 g/L. Anemia and thrombocytopenia persisted with a marked neutrophilia. ANCA’s, EMA panel, ANA, anti-DNA, RF, anti-CCP and cryoglobulins were negative.

- Corticosteroids again produced resolution of symptoms and skin rash after 4 weeks. However, once tapering began she became acutely unwell and hypotensive, requiring readmission only 3 days after her discharge.

- Extensive culturing never demonstrated organisms. Her clinical course was complicated by deep venous thrombosis developed during the course of the infection, and required intubation and continuous epinephrine infusion support.

- She was readmitted with recurrent fevers, hypotension (DVT) and pulmonary infiltrates. Corticosteroids were again started, successfully controlling the infection.

- Extensive culturing never demonstrated organisms. Her clinical course was complicated by deep venous thrombosis and later, pulmonary infiltrates requiring intubation and continuous epinephrine infusion support.

- Laboratory investigations demonstrated persistent anemia, thrombocytopenia, neutrophilia and markedly elevated acute phase reactants.

- Again she received corticosteroids and broad spectrum antimicrobials despite negative cultures, but with no response. Hydroxyurea was added in an attempt to suppress her neutrophilia, and colchicine, a first to second line therapy for Sweet’s Syndrome was added also.

- Cutaneous lesions resolved, but systemic manifestations persisted. Deterioration continued, with each palmarich rash more common than the last, ultimately requiring intubation and continuous epinephrine infusion support.

- She was discharged from dermatology on an NSAI D and colchicine.

- After first taper she deteriorated once again. Immunomodulatory doses of IVIG treatment were unhelpful, and she died after 3 weeks of aggressive ICU therapy.

- Cause of death on autopsy findings indicated multi-organ failure with bilateral acute bronchopneumonia, and multiple palpable erythematous epidermal lesions on arms bilaterally; microscopic examination revealed neutrophilic dermatosis with no evidence of infection consistent with Sweet’s Syndrome, and finally splenomegaly with multiple subcutaneous infects and acute aplasias.

- Minor findings included ascities, hepatomegaly with congestion, and reactive lymphadenopathy with no evidence of residual or recurrent lymphoma.

**Discussion**

- Sweet’s Syndrome was first described by Dr. Robert Sweet in 1964 as an “acute febrile neutrophilic dermatosis.”² Since then, several hundred cases have been reported which expanded the clinical and pathological features of the disease.¹

- Our patient was found to have myelodysplastic syndrome associated Sweet’s Syndrome and, during the course of her illness, had satisfied all major and minor diagnostic criteria. Anecdotally, MDS-associated Sweet’s Syndrome appears to be generally harder to treat.

- Fever is the most common symptom associated with the skin manifestations of Sweet’s Syndrome. Arthralgias, malaise, and myalgias are also reported.¹²–¹³ Sweet’s Syndrome associated with systemic inflammatory response syndrome is very rare. Indeed, we could only identify four cases in the literature,¹³ two of which were not in English journals, but both reporting fatalities from the same.¹⁴

- Other extracutaneous manifestations of Sweet’s syndrome have been well documented, including lung involvement with pulmonary infiltrates and edema,¹⁵ cardiac failure,¹¹ hepatomegaly,¹² and splenomegaly;¹² the latter two were also features in our patient. The most commonly laboratory findings are an elevated ESR and peripheral leukocytosis with neutrophilia.¹⁺

- Circulating auto-antibodies, cytokines, immune complexes may all play a role in the pathogenesis of Sweet’s Syndrome.¹ An etiologic role for pro-inflammatory cytokines,¹⁺ especially granulocyte colony stimulating factor (G-CSF), has been shown in several cases of Sweet’s Syndrome.¹³–¹⁴ Indeed, Sweet’s Syndrome is more complicated than G-CSF administration.¹⁵–¹²

- Most cases of Sweet’s Syndrome respond rapidly to systemic corticosteroids,² or one of the other first line agents such as colchicine and potassium iodide. Corticosteroid-resistant² or intolerable cases are rare, but cases have been described of successful rescue therapy with the administration of anti-TNF therapy (Infliximab, etanercept). After such a prolonged ICU stay with concomitant high dose corticosteroids, however, we presumed infection was complicating her clinical picture and did not attempt this therapy.

**Conclusion**

- Although the extracutaneous involvement of Sweet’s Syndrome is well documented, there are to date only 4 cases of Sweet’s Syndrome associated with systemic inflammatory response syndrome, only one of which has been fatal; these latter two only being published in the non-English literature.

- Sweet’s Syndrome is an evolving dermatosis with each new reported case adding information to our understanding of the condition.