A Sweet Case of *Mycoplasma*

Jackie Hsieh, MD, Ali Yalcindag, MD, Daniel T. Coghlin, MD

abstract

Sweet syndrome, also known as acute febrile neutrophilic dermatosis, is an uncommon inflammatory disorder marked by fever and swelling of the skin that can be very painful. It is especially rare in the pediatric population. Infection is a well-known trigger for Sweet syndrome, but this entity has, to our knowledge, never been described after *Mycoplasma* infection. Herein, we describe the first pediatric case of febrile neutrophilic dermatosis associated with *Mycoplasma* infection.

A 6-year-old boy presented with left leg pain and swelling, as well as decreased ability to bear weight. He was in his usual state of health until a few hours before presentation. He was sitting on the ground playing video games when he started complaining of leg pain and inability to walk. The parents noted some swelling on the medial aspect of his left leg as well as a rash characterized by red, raised lesions on both legs. The rash was not pruritic and he denied any trauma. Of note, the patient did have a cough and sore throat ~1 week before these symptoms, but he never had a fever and his upper respiratory symptoms had resolved by the time of this presentation.

When the patient was examined in the emergency department, he was normotensive, tachycardic, and febrile to 100.9°F. His medial left thigh had a 4- to 5-cm area that was noted to be swollen, erythematous, and warm. There were also small erythematous papules bilaterally on the dorsum of ankles and hands. The patient was in obvious discomfort, including inability to ambulate or tolerate any palpation of the area. The patient was initially thought to have a left leg cellulitis and was started on clindamycin and admitted for pain control. For the next day, his fevers persisted despite antipyretics and antibiotics. Because of this lack of response, he was switched from clindamycin to vancomycin; yet, he continued to have fevers and then developed migratory swelling in 1 area of the body that would then resolve 24 to 48 hours later. These swellings were edematous, erythematous, and severely painful for the patient (Fig 1). Regions included his right posterior head, left face and eye, right abdomen, left arm, and both legs. The patient's papular rash also appeared on the extensor surfaces of both elbows and knees (Figs 2 and 3). An MRI of his left leg showed subcutaneous and fascial edema and enhancement involving the anterior, medial, and posterior calf, including the soleus muscle, suggestive of infectious myositis; however, his creatine kinase level was normal. Multiple ultrasounds failed to demonstrate any synovitis. As the clinical picture became less consistent with infection, antibiotics were discontinued a few days into his hospital course.

Rheumatology, Immunology, Infectious Disease, and Dermatology were consulted. Multiple laboratory studies were collected, and a skin biopsy of an elbow papule led to the final diagnosis. The biopsy showed neutrophilic dermatosis and no signs of vasculitis, consistent with Sweet syndrome. Given the association between Sweet syndrome and malignancy, the patient had

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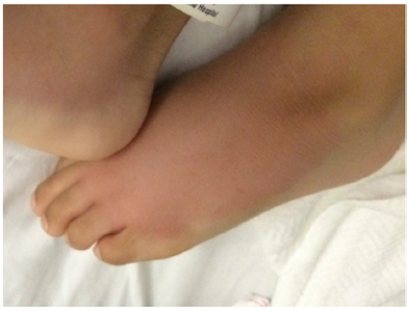

FIGURE 1
Erythematous swelling of our patient's left foot.

a bone marrow biopsy that was unremarkable. He was started on steroid therapy and discharged from the hospital after improvement of his pain and swelling.

On the patient's initial labwork, he was found to have positive anti-streptolysin O titers with negative anti-DNase B antibodies and negative Group A *Streptococcus* throat DNA probe. He also had positive *Mycoplasma pneumoniae* immunoglobulin (Ig)M and IgG levels. Convalescent *Mycoplasma* titers 5 weeks later showed an increase in IgM, suggesting recent infection with *Mycoplasma* as the trigger for this case of Sweet syndrome. To our knowledge, this is the first reported association between Sweet syndrome and a pediatric case of *Mycoplasma* infection.

DISCUSSION

Sweet syndrome, also known as acute febrile neutrophilic dermatosis, was first described by Dr Robert Sweet in 1964.[1] It presents with painful plaques or nodules accompanied by fever. Although there are a variety of presentations of Sweet syndrome, the most common clinical appearance is usually pseudovesicular in appearance, which our patient did have in some areas of his body, most notably his elbows and knees. A skin biopsy of these lesions revealed the characteristic dense interstitial neutrophilic infiltrate without vasculitis. Additionally, our patient

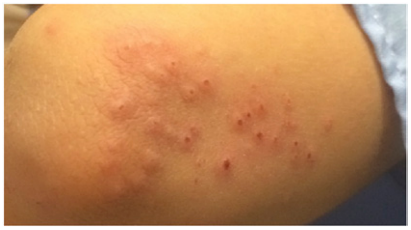

FIGURE 2
Rash on the elbow.

had edematous swellings that were likely a result of the pronounced edema in the upper dermis, another possible presentation of Sweet syndrome.[2] Sweet syndrome is uncommon, but has been more prevalently described in adults and is rarely seen in children, with only ~70 pediatric cases reported in the literature.[3] The mechanism behind Sweet syndrome is not completely known. Existing literature posits that it is a hypersensitivity reaction to a number of possible triggers, including hematologic and solid malignancies, inflammatory bowel disease, immunodeficiencies, certain medications, and infections.[2,4,5] There also have been case studies of Sweet syndrome after vaccination in both children and adults.[6,7] Symptoms in classic Sweet syndrome appear ~1 to 3 weeks after infection, inflammatory bowel disease flare, or exposure to any of the aforementioned factors. The treatment of Sweet syndrome is steroids.[8] If Sweet syndrome is suspected, a biopsy of the lesions is important to obtain for diagnosis. Meanwhile, a bone marrow biopsy is also recommended to rule out malignancy if a source of the Sweet syndrome is not found.

In terms of association with infection, Sweet syndrome has been described to follow upper respiratory infection and gastrointestinal infections.[2] In our patient, he experienced cough and throat discomfort ~1 week before diagnosis with Sweet syndrome. *M pneumoniae* infection presents often with a nonproductive cough and posterior pharyngitis, and can be without pneumonia, as our

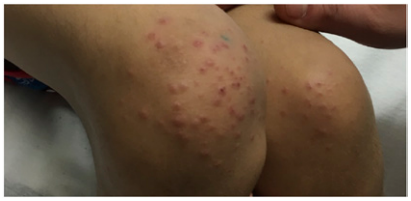

FIGURE 3
Rash on both knees.

patient experienced. Additionally, *Mycoplasma* IgM titers were positive and increased on a repeat level many weeks later, demonstrating evidence of infection.[9] Although Sweet syndrome has been described to be associated with *Streptococcus* infections, in this particular case, the patient's throat culture was negative and anti-DNase B antibodies were negative. Despite the positive anti-streptolysin O, the sensitivity and specificity of a throat culture are both high, including some studies that report them to be 97% and 99%, respectively.[10] Moreover, anti-DNase B antibodies should have been detectable for up to 6 to 9 months after infection. Thus, this patient's Sweet syndrome was more likely to have been associated with *Mycoplasma* infection rather than streptococcal infection.

This case highlights the importance of recognizing Sweet syndrome as a mimicker of common causes for soft tissue swelling. Initially, this patient had a soft tissue swelling that persisted for a few days, and appeared consistent with cellulitis. Areas of swelling also appeared over joint spaces and were concerning for joint effusions or hematogenous spread of infection, such as in osteomyelitis. Additionally, these symptoms were accompanied by fever and elevated inflammatory markers, including leukocytosis, thrombocytosis, elevated C-reactive protein, and erythrocyte sedimentation rate. These signs and symptoms are certainly suspicious for infectious etiology, in particular soft tissue

infection. Another diagnosis that may be considered other than cellulitis is a vasculitis such as Henoch-Schönlein purpura, given the erythematous lesions. Some other autoimmune considerations that are more likely in adults include sarcoidosis and Löfgren syndrome, although these are more likely to cause erythema nodosum and are not associated with the classic pseudovesicular plaques of Sweet syndrome. It is important to consider Sweet syndrome in the differential diagnosis of soft tissue infections to minimize exposing a child to unnecessary antibiotics and pain. Although Sweet syndrome is characterized by major and minor criteria, many of the criteria, including fever and inflammatory markers, are nonspecific.[2] One distinguishing factor that pointed our team away from cellulitis was that the lesions were of abrupt onset and were markedly painful. Some of them were also clear and edematous in appearance, which was less consistent with cellulitis. Second, there were migrating areas of edema located throughout the body, pointing to a systemic and nonfocal source of inflammation. Moreover, these areas of swelling were associated with abruptly-appearing tender erythematous papules, which are characteristic of Sweet syndrome. Another unique marker was that our patient had 70% neutrophils in the setting of leukocytosis, which is one of the criteria for Sweet syndrome (neutrophilia >70%).[2] Finally, the patient had persistent fever despite antipyretics and multiple broad-spectrum antibiotics, also concerning for autoimmune or systemic inflammation. Once Sweet syndrome is suspected, a biopsy would confirm presence of neutrophilic dermatosis without vasculitis, after which steroid therapy can be initiated. Our patient improved after 1 week with prednisone therapy.

This case also demonstrates another post-*Mycoplasma* condition that already includes acute disseminated encephalomyelitis, transverse myelitis, Guillain-Barré, and now Sweet syndrome. Identifying it in this context is important for future recognition, and may warrant testing for *Mycoplasma* in suspected cases.

CONCLUSIONS

Mycoplasma may trigger Sweet syndrome. We recommend testing for *Mycoplasma* when evaluating potential triggers of Sweet syndrome. This case also highlights that not all febrile soft tissue swelling is infectious. Although rare, Sweet syndrome is important for primary care providers and hospitalists to distinguish from cellulitis, given Sweet syndrome's severe pain, its response to steroids, and its association with serious illnesses.

ABBREVIATION

Ig: immunoglobulin

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