Respiratory Failure in an Infant with Rapidly Evolving Cutaneous Lesions: Sweet Syndrome

Raymond A. Stemrich[1†], Gabriel Brutico[1†], Abhay Metgud[1†], and Lindsay M. Dittman[1,2]
[1]Geisinger Commonwealth School of Medicine, Scranton, PA 18509
[2]Geisinger Medical Center, Danville, PA 17822
[†]Doctor of Medicine Program
Correspondence: rstemrich1@gmail.com

Abstract

Acute febrile neutrophilic dermatosis, or Sweet syndrome, is an uncommon condition in adults and is especially rare in the pediatric population. Its low prevalence and variable clinical presentation in adult and pediatric patients often lead to delayed diagnosis and potential complications. This report presents a 10-week-old male with no significant history delivered via C-section after an uncomplicated pregnancy who developed persistent oral lesions. The lesions began to evolve rapidly, starting as small vesicles and becoming large, indurated, fluid-filled pustules spreading to the face, trunk, and extremities. Initial evaluation did not reveal a clear diagnosis and the patient decompensated quickly. Once intubated and in the PICU, a skin biopsy revealed neutrophilic infiltrates consistent with Sweet syndrome. After a prolonged admission and steroid therapy, the skin lesions improved, and the patient recovered to baseline. Although Sweet syndrome is rare with a wide variation in clinical presentations and disease course, it should be considered as a differential diagnosis for any patient presenting with rapidly evolving cutaneous lesions, especially in the absence of a clear etiology. A prominent feature of the condition is resolution with corticosteroid treatment and many patients improve following initiation of the therapy.

Introduction

Acute febrile neutrophilic dermatosis, or Sweet syndrome (SS), is an uncommon condition that impacts both adult and pediatric patients. It is exceedingly rare in infants and children, with only a small number of cases reported in the literature (1, 2). The criteria for diagnosing Sweet syndrome are based on findings seen in the adult population, which are then extrapolated to the pediatric cases. Although useful for generation of differential diagnoses, there is significant variation between the adult and pediatric forms of the condition (1–3). New research suggests that the pediatric category should be further stratified into neonatal, infantile, and juvenile forms to account for the variable presentations seen in that patient cohort (3). The case below describes one clinical presentation of SS in a pediatric patient, highlighting an unexpected and severe respiratory complication.

Case Presentation

The patient is a 10-week-old male born at 40 weeks gestation via C-section for arrest of dilation. The pregnancy was uncomplicated with no maternal history of infections or significant medical conditions. He had neonatal hyperbilirubinemia, but he did not require phototherapy. Gastroesophageal reflux was the only issue noted after discharge and he received his 2-month vaccinations at approximately 6 weeks of age.

Two weeks prior to his admission, the patient saw his pediatrician for vesicular lesions in his mouth and he was diagnosed with an unspecified viral illness. He was prescribed amoxicillin for a concurrent otitis media, which improved, but the oral lesions persisted and prompted an emergency department visit. He was diagnosed with hand, foot, and mouth disease.

The rash worsened after discharge, spreading to his face, neck, and extremities, prompting the family to return to the emergency department. He also developed a low-grade fever (100.6°F) during this time. Per the family, the rash started as pinpoint "pimples" that rapidly grew and evolved into larger, firm lesions with yellow coloration. The initial lesions in his mouth were improving; however, the rash on his body continued to worsen. His mother reported that he appeared to be in discomfort during bottle and breast feedings and would only take about one ounce at a feeding as a result.

On examination, his vitals were within normal limits. He had vesicular lesions on the soft palate. He had small vesicular and pustular lesions along the right upper eyelid, and lesions on his neck, face, hands, and lower extremities ranging from small vesicles or pustules to indurated, nodular, and umbilicated lesions, with the largest roughly 1.5 cm in size (Figure 1). Some of the lesions had surrounding erythema. The soles, palms, and diaper area were spared, and there was no noted desquamation. Initial laboratory findings included an elevated leukocyte count (18.8 K/uL) with an increased absolute neutrophil count (9.29 K/uL), and an elevated CRP (46 mg/L). The respiratory viral panel and early cultures were negative. Differential diagnoses were broad, including herpes simplex virus and bullous impetigo. Peripheral blood cultures and herpes simplex virus PCR were obtained from surfaces and serum. He was subsequently started on cefazolin, vancomycin, and acyclovir.

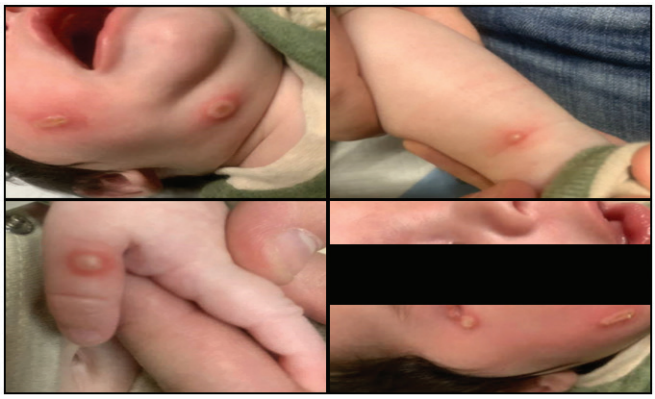

Figure 1. Vesicular/pustular lesions found on face, ankle, and hand. Mature lesions were firm and indurated with surrounding erythema.

Less than 12 hours after admission, the patient developed respiratory failure with rapid decompensation. He had tachycardia with heart rates >200 beats per minute and increased work of breathing as evidenced by intercostal and subcostal retractions and oxygen saturations as low as 70%. The patient had persistent hypoxia despite escalations in respiratory support from high-flow nasal cannula to CPAP and eventually BIPAP. His chest X-ray showed evidence of tracheal narrowing with bilateral apical atelectasis, but no parenchymal infiltrates. He was intubated without issue and transferred to the pediatric intensive care unit. A respiratory viral panel was completed and was negative. There the patient was noted to have severe anemia (hemoglobin 5 g/dL) and received a transfusion of packed red blood cells. His endotracheal tube was noted to have been plugged with a significant amount of blood. Laryngoscopy was performed, and there was no evidence of laryngeal lesions causing obstruction. A bronchoscopy was not performed. Laboratory testing did not reveal any etiology for the anemia, although a thorough evaluation was not conducted. The working theory was blood loss secondary to endotracheal tube placement; however, the procedure was completed without issue.

The patient was in the PICU for 5 days, was extubated after 4 days, and then admitted to the pediatric unit for an additional 18 days. During this time, a skin biopsy was performed, which revealed dermal papillary edema and dense neutrophilic infiltrates, consistent with neutrophilic dermatosis. The histopathology results and clinical picture were consistent with Sweet syndrome. The patient was started on prednisolone 1mg/kg BID with rapid subsequent improvement in skin lesions. Once the pending cultures resulted as negative, all antibiotics and antiviral medications were discontinued. A peripheral blood smear, full body MRI, dihydrorhodamine assay, primary immunodeficiency panel, and autoimmune evaluation (including ANA, SS-A, SS-B, and U1-RNP) were ordered. The additional testing was negative, with the primary immunodeficiency panel indicating two variants of unknown significance.

After 23 days of admission, the patient returned to his baseline and was discharged home with close follow-up with dermatology and endocrinology. His final diagnoses included classic (idiopathic) Sweet syndrome and iatrogenic adrenal insufficiency secondary to lengthy steroid treatment. To date, systemic corticosteroids have continued to control disease activity and the patient has not developed any additional skin lesions.

Discussion

Sweet syndrome is a rare condition in the pediatric population, accounting for just around 5% of all occurrences, with male patients less than 3 years of age more commonly impacted, in contrast to the female predominance in the adult form (2).

Within the pediatric population, the syndrome is associated with paraneoplastic disease (15–25% of cases), post-infectious entity (22–45%), or is labeled idiopathic without any recognized association (21–42%). In patients less than 3 months of age, immunodeficiencies, autoimmune diseases, and chronic conditions (i.e., neonatal lupus and metabolic disorders) can be associated with Sweet syndrome. In patients older than 3 months, association with infectious etiologies, such as viral illnesses, may be more likely (1–4).

Pediatric Sweet syndrome is diagnosed using the same criteria as the adult population (Table1); however, the criteria do not always apply in the pediatric age group and clinical presentations vary widely (3). This case reports on an infant who initially presented with oral lesions, which are typically a rare clinical finding in the pediatric form of the syndrome. Mucosal involvement is reported in only about 5% of patients. Mucosal involvement has been associated with underlying hematologic malignancy in the adult population; however, no such association has been shown in the pediatric population (2, 3).

Major Criteria
1. Abrupt onset of typical cutaneous lesions
2. Predominantly neutrophilic infiltration of the dermis on biopsy
Minor Criteria
1. Preceded by associated infections, vaccinations, malignancies, inflammatory disorders, drug exposures, or pregnancy
2. Presence of fever and consitutional signs and symptoms
3. Leukocytosis, elevated ESR, positive CRP
4. Significant response to systematic corticosteroids
ESR= Erythryocyte sedimentation rate CRP= C-Reactive Protein *Must include both Major Criteria and at least 2 Minor Criteria

Table 1. Criteria to diagnosis Sweet syndrome* (Adapted from McClanahan et al., and Uihlein et al.)

This patient rapidly decompensated and developed respiratory failure requiring intubation and mechanical ventilation. Although the condition is often associated with a preceding respiratory infection, true pulmonary Sweet syndrome has been reported in approximately 5% of pediatric cases with chest radiographs showing pulmonary infiltrates and perhaps visualization of lesions in the respiratory tract (3). Respiratory symptoms typically present later in the disease, but can present both prior to and concurrent with the cutaneous lesions (3, 5). In this patient, no signs of infiltrates were seen on chest X-ray and laryngoscopy did not reveal lesions in the upper respiratory tract, but bronchoscopy was not done to evaluate the lower respiratory tract. The temporal relationship between the worsening of the patient's skin lesions and the development of respiratory decompensation without any identifiable etiologies indicate that they were likely part of the same process.

Regardless of age, the treatment, management, and surveillance of Sweet syndrome is similar. One hallmark of the condition is its

response to systemic corticosteroids, which typically resolves the cutaneous lesions rapidly after a tapered treatment. Management includes evaluation for associated malignancies, immunodeficiencies, autoimmune conditions, and inflammatory processes, especially in the pediatric population (1–3). Pediatric patients should also undergo cardiac evaluation, as complications may be silent but progress to fatal complications (1, 3). Finally, close monitoring by dermatology for exacerbation of cutaneous lesions are essential. This is particularly important in pediatric patients who have the greatest risk of recurrence and may develop refractory disease. A course of corticosteroids is the treatment of choice for flares of cutaneous lesions; however, to minimize the long-term effects of chronic steroid use, steroid-sparing therapies such as potassium iodide have proven effective (1–4).

Conclusion

This case report highlights the variability in clinical presentation and course of Sweet syndrome, especially in the pediatric population. It is often not considered as a possible diagnosis due to the low prevalence of this condition in children. Delayed recognition may lead to significant complications. Although cases of pulmonary Sweet syndrome are noted in the literature, it is exceedingly rare, and often defaults as a diagnosis of exclusion without clear evidence of lesions in the airways. Nonetheless, it should be acknowledged as a potential complication and the care team should be prepared to manage an acute decompensation.

Disclosures

The authors declare that there is no conflict of interest regarding the publication of this article.

References

1. Nelson CA, Stephen S, Ashchyan HJ, James WD, Micheletti RG, Rosenbach M. Neutrophilic dermatoses: Pathogenesis, Sweet syndrome, neutrophilic eccrine hidradenitis, and Behcet disease. *J Am Acad Dermatol*. 2018;79(6):987–1006.
2. Uihlein LC, Brandling-Bennett HA, Lio PA, Liang MG. Sweet Syndrome in Children. *Pediatr Dermatol*. 2012;29(1):38–44.
3. McClanahan D, Funk T, Small A. Sweet Syndrome in the Pediatric Population. *Dermatol Clin*. 2022;40:179–90.
4. Cohen PR. Sweet's syndrome – a comprehensive review of an acute febrile neutrophilic dermatosis. *Orphanet J Rare Dis*. 2007 Jul 26;2:34.
5. Arakaki R, Shofner JD, Kroshinsky D. An infant with pulmonary-cutaneous Sweet syndrome. *J Pediatr*. 2012;161(5):959–61.