

Sweet Syndrome in Pediatrics. A case report

Síndrome de Sweet en Pediatría. A propósito de un caso

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Abstract

Introduction: Sweet's syndrome is a very rare dermatosis in pediatrics, of unknown pathogenesis, clinically characterized by fever, neutrophilia, raised and painful plaques on the skin of the face, neck, and limbs, and histologically by dermal infiltration of neutrophils. **Objective:** To present a clinical case of Sweet Syndrome in a pediatric patient. **Clinical case:** 3-years-old female child, with history of complex chromosomopathy 46XX add(8), with a 7-day history of plaques and blisters on the back and later also on the limbs, associated with high fever, without response to antibiotic treatment prescribed due to suspicion of bullous impetigo. Physical examination showed multiple erythematous-violaceous plaques, with bullous center on the back, upper and lower limbs, along with plaques and erythematous nodules on the left arm and thigh. Laboratory tests showed leukocytosis with neutrophilia (absolute neutrophil count 45954/mm³) and elevated CRP (347 mg/L). Biopsy of skin lesions reported histopathological findings compatible with Sweet's Syndrome. Treatment with prednisone 1 mg/kg/day was indicated with good clinical response. After two weeks of treatment, she presented crusty plaques of smaller size, without bullous lesions. **Conclusions:** Sweet's syndrome is an uncommon dermatosis in pediatrics, therefore, a high index of suspicion should be held in the presence of fever associated with persistent skin lesions. While most cases are idiopathic, screening for associated conditions, mainly proliferative disorders, infections, and immunodeficiencies must be performed.

Keywords:

Sweet's syndrome;
neutrophilic
dermatosis;
Steroids;
Fever

Introduction

The Sweet's Syndrome (SS) or acute febrile neutrophilic dermatitis, first described in 1964, is clinically characterized by fever, neutrophilia, painful raised plaques in the limbs, face, and neck, and histologically by dermal neutrophilic infiltration¹. It is a very rare condition in children, representing only 5% of the total cases reported as Sweet's Syndrome². A recent review, 2015, reports less than 70 cases in pediatrics³. No cases of SS have been reported in children or adolescents in the national literature. The pathogenesis is not entirely clear, although it has been associated with infections, immunodeficiency, drugs, neoplasms, and other systemic diseases⁴. Some authors speculate that a genetic predisposition may determine geographical variations in the incidence, since almost half of all reported cases have occurred in Japan, finding an association with human leukocyte antigen BW 54 (HLA-Bw54) in these patients, which could play a role². There are diagnostic criteria initially proposed by Su and Liu in 1986 and later modified by Driesch, which consider necessary the presence of two major and at least two minor criteria⁵ (Table 1).

The objective of this report is to describe the clinical, laboratory and histopathological characteristics of a clinical case of SS in pediatrics, highlighting the characteristic skin lesions and the good response to steroidal treatment.

Clinical case

3-year-old female patient, with history of complex chromosomal abnormality 46, XX, add⁸, suction-deglutition disorder corrected with Nissen surgery and secondary gastrostomy, recurrent urinary tract infection, non-obstructive left-sided renal nephrolithiasis, recurrent obstructive bronchial syndrome, iron deficiency anemia, convulsive syndrome, and moderate psychomotor developmental delay. The patient received

pharmacological treatment with valproic acid, ferrous sulfate, nitrofurantoin, levocetirizine, and nebulized ipratropium bromide and budesonide.

The patient consulted due to a seven-day history of plaques and blisters on the back and the subsequent appearance in the upper and lower limbs, associated with fever up to 39°C (102°F). She was evaluated at the primary health care emergency service, where antibiotic treatment with cefadroxil 40 mg/kg/day for seven days was indicated due to suspicion of bullous impetigo. After 72 hours of antibiotic therapy, the febrile symptoms persisted and skin lesions increased in the described areas, therefore, she was taken to the emergency service of the pediatric hospital where she was hospitalized.

There was no history of respiratory or gastrointestinal infections in previous weeks.

The patient was evaluated by the Dermatology team; physical examination revealed multiple erythematous-violaceous plaques, most of them with a blistered center and some with a crusted center located in the lumbar region, upper and lower limbs (Figure 1 A and B Figure 2 A and B), with erythematous and indurated plaques and nodules on the left arm and thigh. (Figure 3) No sole foot involvement or mucosal lesions were observed. She did not have adenopathies.

Among the laboratory tests performed in the emergency service were leukocytosis with left shift and neutrophilia (leukocyte count 62100/uL with 11% bacilliforms (6831/mm³), absolute neutrophil count (45954/mm³), and an increase of C-reactive protein (CRP 347 mg/L).

Sweet's Syndrome was suspected and skin biopsy was indicated for histopathological study. Two skin samples were taken, one with a bullous lesion on the right arm and another one with an erythematous nodule on the left forearm, after the administration of local anesthesia without vasoconstrictor and intravenous sedation with benzodiazepine, performed by the anesthesiologists team. The histology described skin with psoriasiform epidermal hyperplasia, spongiosis,

Table 1. Diagnostic criteria reviewed for the diagnosis of Sweet Syndrome (5)

| Criteria | Description |
|----------------|--|
| Major Criteria | - Abrupt onset of tender erythematous plaques or nodules, occasionally with vesicles, pustules or bullae. - Dense neutrophilic infiltrate on biopsy, without leukocytoclastic vasculitis. |
| Minor Criteria | - Fever, temperature > 38°C - Association with an underlying hematologic malignancy, inflammatory disease, or pregnancy or preceded by an upper respiratory or gastrointestinal tract infection. - Abnormal laboratory values at presentation (3 of 4): erythrocyte sedimentation rate > 20 mm/h, positive C-reactive protein; leukocyte count > 8000/uL, >70% neutrophils, - Excellent response to treatment with systemic corticosteroids |



Figure 1. Clinical Image. **A:** Blisters and crusted ulcers in the thoracolumbar region. **B:** Blisters and crusted ulcers in the left arm.



Figure 3. Clinical Image. Papules and erythematous nodules on left arm and forearm.



Figure 2. Clinical Image. Blisters in right upper extremity. **A:** Blister of hemorrhagic content, erythematous base of 2 cm diameter in the inner side of the right arm. **B:** Tense blister of hemorrhagic content, violaceous of 2.5 cm diameter in right forearm.

and papillary edema, with superficial erythrocytes extravasation. Perivascular inflammatory infiltrate with polymorphonuclear neutrophils that extended to the deep dermis and subcutaneous tissue, with the presence of foci of necrosis (Figure 4 A, B and C), compatible with SS.

Treatment with prednisone 1 mg/kg/day was started with good clinical response, without the appearance of new lesions, fever remission, and decreasing inflammatory parameters, therefore the patient was discharged and outpatient monitoring was indicated. She went to a medical check-up a week later, completing two weeks of steroidal treatment, she remained afebrile, with smaller crusting plaques and incipient erythematous-violaceous scars in previously affected areas. Due to the good therapeutic response, the progressive reduction of corticosteroid treatment was started for six weeks, with clinical check-ups every two weeks. Due to the multiple underlying pathologies, the multidisciplinary

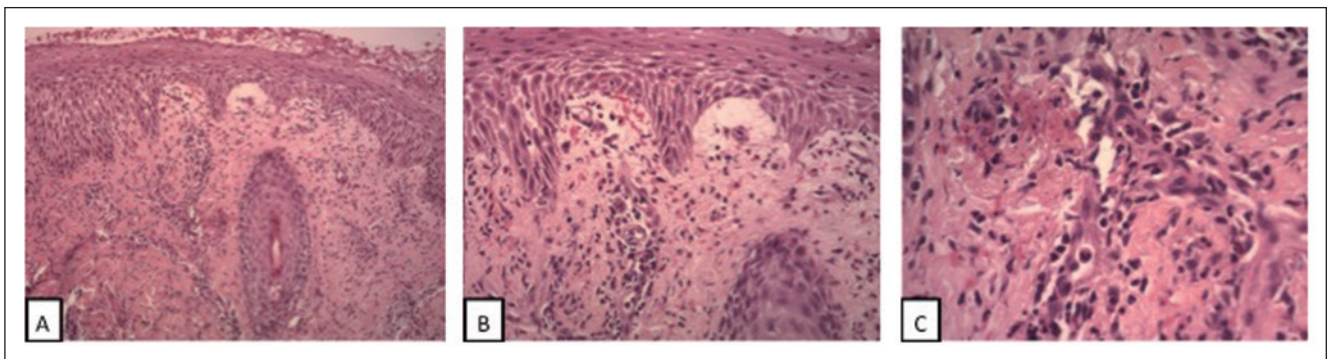


Figure 4. Histopathological study. **A:** Epidermis with psoriasiform hyperplasia and spongiosis. There is edema and extravasation of erythrocytes in the papillary dermis (H/E 40X). **B:** Perivascular inflammatory infiltrate with polymorphonuclear neutrophils, which extends to the reticular dermis and subcutaneous tissue. Some foci of necrosis are appreciated (H/E 100X). **C:** Perivascular inflammatory infiltrate with multiple neutrophils and extravasation of erythrocytes in the dermis. (H/E 400X).

management was maintained and the laboratory study performed (hemogram, ESR, biochemical profile, liver profile, renal function, LDH), requesting HIV, ANA, and immunoglobulin titers, which dismissed the presence of immunodeficiency and hematological neoplasms.

Discussion

In pediatrics, Sweet's Syndrome is a very rare condition. An equitable distribution by gender has been described but with a slight predominance in the male gender among children under three years of age⁶. The average age of diagnosis in pediatric cases is five years⁶. Cutaneous lesions are typically sensitive and appear as red or violaceous nodules or papules, and may develop plaque-like lesions, and sometimes bullous lesions. They are normally distributed asymmetrically and heal without leaving scars. They can be preceded by several days to weeks of fever⁷. The most common symptoms and/or signs are arthritis, myalgia, and compromise of the general condition³. The most frequent laboratory findings are neutrophilia and high ESR, thus diagnosis is often delayed, as it is mistaken for an infectious disease^{7,8}. Among the proposed diagnostic criteria, the histopathology highlights the presence of dermal neutrophilic infiltration, without leukocytoclastic vasculitis⁵. This infiltrate often extends throughout the entire dermis, compromising even the subcutaneous tissue or epidermis. Perivascular neutrophils, lymphocytes, and reactive leukocytosis can be observed, but there should be no fibrinoid changes or vasculitis⁹. SS can occur in three clinical scenarios: classic or idiopathic, paraneoplastic, and drug-induced⁷. In pediatrics, up to 45% of idiopathic cases have been described after a transient gastrointestinal or respiratory infection, 30% associated with chronic inflammatory conditions, and 25% of cases were paraneoplastic, where the greatest association is with acute myeloid leukemia, osteosarcoma, and myelodysplastic syndrome^{4,6,10,11}. Due to these associations with various pathologies, screening schemes for pathologies associated with SS have been proposed, which include clinical aspects such as blood pressure measurement, basic laboratory tests: hemogram, ESR, LDH, and uric acid, in addition to detection of HIV, ANA, and serum immunoglobulin levels. It is also suggested to perform an echocardiogram and in case of bone pain, an imaging study, simple x-ray and/or MRI scan in case of high clinical suspicion¹⁰. Among children, there are few drug-induced cases, which have been associated with a granulocyte colony-stimulating factor, transretinoic acid, cotrimoxazole, and azathioprine⁸. In our case, neoplastic disorders and drugs involved were dismissed and it was diagnosed as classic or idiopathic Sweet's Syndrome.

The prognosis of this pathology depends mainly on the severity of the associated conditions¹¹. Despite the fact that the first line treatment corresponds to corticosteroids in an equivalent dose of prednisone 1-2 mg/kg/day, spontaneous resolution of the skin lesions has been detected without treatment⁴. In our case, there was a good initial therapeutic response with the use of systemic corticosteroids, therefore, progressive reduction of the dose was indicated, with strict clinical monitoring. In cases associated with drugs, improvement and subsequent resolution are observed after the interruption of the associated drug⁸. Recurrence of lesions has been described in 45% of pediatric cases, especially in those associated with neoplasms⁶, thus follow-up is important for the investigation of new skin lesions.

Conclusions

The Sweet's Syndrome is an uncommon dermatosis in pediatrics, therefore a high rate of suspicion must be maintained in the presence of fever associated with persistent skin lesions. Although most cases are idiopathic, screening for neoplastic disorders, infections, and immunodeficiencies should be made. Treatment with systemic corticosteroids is effective in the complete resolution of skin lesions, however, patients should have a follow-up due to the risk of lesions recurrence.

Ethical responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

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Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

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