

Sweet's syndrome associated with neoplasms*

*Síndrome de Sweet asociado a neoplasias**

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Abstract: Sweet's syndrome was described in 1964 by Robert Douglas Sweet, as an entity he named acute febrile neutrophilic dermatosis. It is characterized by five main features: 1) sudden appearance of erythematous and tender plaques on the face, neck and extremities; 2) fever; 3) polymorphonuclear leukocytes; 4) predominantly neutrophilic dense infiltrate in the dermis, and 5) rapid response to steroid therapy. Sweet's syndrome can be classified into five groups: idiopathic, parainflammatory, paraneoplastic, drug-induced, and pregnancy-related. Twenty percent of cases are associated with malignancies; 85% out of them involve hematologic malignancies and the remaining 15%, solid tumors.

A series of seven cases of Sweet's syndrome associated with neoplasms which were diagnosed from 2002 to 2006 is presented. Six cases were related to oncohematologic diseases and one to solid tumors. These results highlight the importance of the diagnosis of the syndrome, since it may predict tumor relapse or underlying disease progression. The timely use of diagnostic and treatment methods may improve the quality of life of these patients. The fact that oncology patients take multiple medications (a colony-stimulating factor) which may be associated with the onset of this entity must also be considered in excluding possible causes.

Keywords: Prognosis; Skin Neoplasms; Sweet's syndrome

Resúmen: El síndrome de Sweet fue descrito en el año 1964 por Robert Douglas Sweet, como una entidad a la cual denominó dermatosis neutrofílica febril y aguda. Se caracteriza por cinco rasgos principales: 1) aparición brusca de placas eritemato-dolorosas en cara, cuello y extremidades; 2) fiebre; 3) leucocitosis polimorfonuclear; 4) denso infiltrado dérmico a predominio neutrofílico; 5) rápida respuesta al tratamiento esteroideo. Se puede clasificar en cinco grupos: idiopático, parainflamatorio, paraneoplásico, secundario a drogas y asociado a embarazo. En el 20% de los casos se asocia a enfermedades malignas, representando las hematológicas el 85% y los tumores sólidos el 15% restante. Se presenta una serie de siete casos de síndrome de Sweet asociado a neoplasias, diagnosticados durante el período 2002-2006, de los cuales seis correspondieron a enfermedades oncohematológicas y el restante a tumores sólidos. Como comentario de dicha casuística, se hace hincapié en la importancia del diagnóstico de este síndrome, debido a que puede anunciar la recaída del tumor o la progresión de la enfermedad de base. De esta manera, mediante el uso de métodos de diagnóstico y tratamiento oportunos, se lograría mejorar la calidad de vida de estos pacientes. También debe tenerse en cuenta, que los pacientes oncológicos reciben múltiples medicaciones (factor estimulante de colonias), que pueden estar implicadas en la aparición de esta entidad, debiendo ser las mismas descartadas como posibles causas.

Palabras-chave: Neoplasias cutáneas; Pronóstico; Síndrome de Sweet

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INTRODUCTION

In 1964, Dr. Robert Douglas Sweet described a dermatosis that he called "Groom-Button disease" in honor of the first two patients in whom he observed this disease. Later it was named acute febrile neutrophilic dermatosis because of its clinical and humoral characteristics. Currently, the term Sweet syndrome is preferred.¹ The condition is characterized by five main traits: 1) sudden onset of painful erythematous plaques on the head, neck, and upper limbs; 2) fever; 3) neutrophilic leukocytosis; 4) dense predominantly polymorphonuclear dermal infiltrate; 5) rapid response to steroid therapy.^{2,3}

This disease was classified according to five categories: idiopathic or classic, parainflammatory, paraneoplastic, secondary to drugs, and pregnancy-related.^{4,1} Most patients belong to the first group. In 20% of cases, there was an association with malignant diseases in which 85% were hematologic and 15% were solid tumors. In hematologic neoplasms, acute myeloid leukemia is the most frequently observed type, and in solid tumors, approximately 2/3 of the cases correspond to genitourinary tract carcinomas.^{2,5-7}

There have also been cases published of Sweet syndrome associated with hematologic neoplasms and solid tumors⁵ and, more recently, an association with two solid tumors of the genitourinary tract.⁶

It is important to point out that many times the diagnosis of this syndrome is a presentation sign of a new or recurrent neoplasm. On the other hand, the presence of anemia and abnormal platelet count, absence of neutrophilia, location, and atypical presentation forms of the lesions should be an alert signal for the need to investigate neoplasms, since these findings are not common in the idiopathic form of this syndrome.^{2,5}

Although the spontaneous resolution of the clinical picture may occur in weeks or months, the treatment of choice is with steroids which produce remission in spite of a subjacent neoplasm.^{2,3,5}

We present seven clinical cases of Sweet syndrome associated with neoplasms diagnosed over the period of 2002 to 2006; six cases correspond to oncohematologic diseases and one to solid tumors. These seven cases match the diagnostic criteria established for this syndrome by Su and Liu, in 1986 (Chart 1).

We compare cases presenting with the idiopathic form and highlight differences observed relative to world medical literature. In charts 2, 3, and 4 these findings are summarized.

Case 1

Male patient, 25 years of age, with diagnosis of common type B acute lymphoblastic leukemia (ALL)

admitted for febrile neutropenia secondary to chemotherapy treatment and in need of granulocytic colony-stimulating factor (G-CSF). The origin of the fever was determined to be a gluteal abscess that had been treated with surgery and broad-spectrum antibiotics (vancomycin, imipenem, and ciprofloxacin), in spite of which the fever persisted.

During hospitalization, a lesion was noted on the patient's left knee comprised by a slightly painful rounded erythematous-violaceous plaque, 1.5 cm diameter, with well-defined margins and a center with a pseudovesicular aspect. The patient reported prior trauma and a pimple at the site many years before and the repeated appearance of the current lesion during each hospitalization for chemotherapy. A biopsy was performed for histopathological study and culture.

Since the fever continued, intravenous amphotericin was added to the dosing regimen.

In laboratory tests, pancytopenia was identified; blood, urine, and skin cultures were negative. The histopathological examination showed epidermal acanthosis and spongiosis, as well as significant dermal edema and polymorphonuclear infiltrate.

Based on the clinical characteristics and histopathological study, the diagnosis of Sweet syndrome was made.

The patient progressed with remission of neutropenia with 70% of blasts, and was diagnosed with chemotherapy-resistant leukemia. Considering the guarded prognosis, the patient was discharged with palliative measures.

Case 2

Male patient, 78 years of age, with a five-year history of anemic syndrome admitted due to fever,

CHART 1: Diagnostic criteria for Sweet syndrome (Su and Liu, 1986)

Major criteria

- I. Abrupt appearance of papules and/or painful erythematous plaques.
- II. Predominantly neutrophilic infiltrate with no signs of leukocytoclastic vasculitis.

Minor criteria

- I. Prior fever or infection.
- II. Fever, arthralgia, conjunctivitis or concomitant underlying malignancy.
- III. Leukocytosis.
- IV. Rapid response to steroid therapy but not to antibiotic therapy.

CHART 2: Epidemiology and clinical manifestations

| Case | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|-------------|-----|------|---------|-----|-----|-----|-------|
| Sex | M | M | M | F | F | F | F |
| Age | 25 | 78 | 66 | 68 | 54 | 57 | 65 |
| Association | ALL | CMML | MDS/AML | NHL | MM | NHL | BC/TC |
| Site | A | A | A | T | T | A | A |
| Lesion | T | A | A | A | T | A | A |
| Systemic | No | Yes | No | No | Yes | No | No |

M: male; F: female; ALL: acute lymphoblastic leukemia; CMML: chronic myelomonocytic leukemia; MDS: myelodysplastic syndrome; AML: acute myeloid leukemia; MM: multiple myeloma; NHL: non-Hodgkin lymphoma; BC: breast carcinoma; TC: thyroid carcinoma; A: atypical; T: typical

CHART 3: Laboratory

| Case | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|--------------------------|-----|-----|-----|-----|-----|-----|-----|
| Leukopenia | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Neutropenia | Yes | No | Yes | No | No | No | No |
| Anemia | Yes | Yes | Yes | Yes | Yes | Yes | No |
| Decreased platelet count | Yes | Yes | Yes | Yes | Yes | Yes | No |
| ESR | ↑ | ↑ | ↑ | ↑ | ↑ | ↑ | ↑ |

ESR: erythrocyte sedimentation rate

CHART 4: Treatment and prognosis

| Case | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|------------|-----|-----|-----|-----|----|-----|-----|
| Steroids | No | Yes | No | Yes | No | Yes | Yes |
| Resolution | S | NS | S | NS | S | NS | NS |
| Recurrency | Yes | No | Yes | Yes | No | No | Yes |
| Prognosis | P | P | P | G | G | G | G |

S: spontaneous; NS: non-spontaneous; P: poor; G: good

general malaise, left carpal monoarthritis, and pancytopenia.

Physical examination showed rounded erythematous-violaceous papular lesions, some coalescent in 0.5-1.0 cm diameter plaques, with well-delimited margins located in frontal region, upper lip, back, and upper limbs (Figure 1A).

Laboratory analyses showed pancytopenia with neutrophilia, increased erythrocyte sedimentation rate (ESR), and abnormal liver function tests.

During the hospital stay, chronic myelomonocytic leukemia (CMML) was diagnosed.

The patient developed lung infiltrates observed by radiography (Figure 1B) and computed axial tomography (CAT) of the chest. Antibiotics were empirically dosed without clinical or radiographic response. Blood, urine, skin, and bronchoalveolar lavage (BAL)

cultures were negative, and antibiotics were discontinued. The BAL showed the presence of neutrophilic alveolitis.

Due to progressive worsening of the liver function tests, a hepatic puncture biopsy of the liver was performed that showed the presence of lobular hepatitis. Additionally, a skin biopsy was done for histopathological study and cultures. The histopathology showed mild hyperkeratosis in the epidermis, and abundant inflammatory infiltrates with polymorphonuclear predominance and hemorrhagic areas in the dermis. Skin cultures were negative.

In light of the clinical picture and histopathological results, the diagnosis was made of Sweet syndrome with systemic involvement; 500 mg/day intrave-

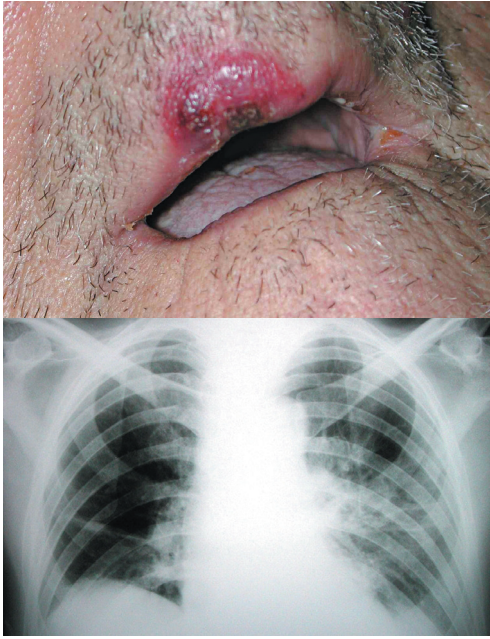


FIGURE 1: A: Oval, erythematoviolaceous plaque, with well-delimited margins and serum blood crust in the bottom, located in upper lip mucosa. B: Lung infiltrates predominating in the left middle and lower lobes

nous methylprednisolone was given for 5 days, followed by 80 mg/day oral prednisone with progressive tapering of the dose. The patient experienced a favorable clinical progress and was discharged from the hospital.

Case 3

Male patient, 66 years of age, diagnosed with myelodysplastic syndrome (MDS) under transformation to acute myeloid leukemia (AML) admitted for chemotherapy treatment and in need of G-CSF.

He progressed with febrile neutropenia, skin lesions, and pericatheter phlogosis.

Upon physical examination, asymptomatic mobile nodules of various sizes were observed (5 mm to 1 cm diameter) with well-defined limits, firm consistency, erythematous and infiltrated subjacent skin, located on the scalp, face, and neck (Figure 2A). Both ear lobes showed phlogistic signs and a strange pain to the touch. On the back, asymptomatic erythematous 1-cm diameter plaques were observed, some with pseudovesicular centers. On the back of both hands and on the legs, rounded 4-5 mm diameter purpural papules with well-defined limits were noted (Figure 2B). There were no mucosal lesions.

Culture sample collection and a skin biopsy were performed for histopathological study, cultures, and direct immunofluorescence (DIF) testing for Type 1 and Type 2 herpes simplex virus and varicella



FIGURE 2: A: Papules and nodules of various, with erythematous and infiltrated subjacent skin and pseudovesicles located on the posterior neck. B: Rounded purpural papules and plaques, 3 mm-1cm diameter, with well-defined limits on the back of both hands

zoster.

Antibiotics were introduced with intravenous vancomycin and imipenem, with no response. New lesions were noted on the back resembling a rosette. Remaining lesions became spotted and purpural, consistent with thrombocytopenia. Intravenous amphotericin was added to the dosing regimen.

The patient progressed with afebrile neutropenia; since cultures and DIF were negative, the antibiotic was discontinued. Histopathology revealed preserved epidermis and edematous dermis, with diffuse layered polymorphonuclear infiltrate (Figure 3) leading to the diagnosis of Sweet syndrome.

The patient experienced an involution of cutaneous lesions with improvement of general health condition and remission of neutropenia, and was discharged from hospital. One month later, during another hospitalization for chemotherapy, a Sweet syndrome relapse led to the patient's death.

Case 4

Female patient, 68 years of age, diagnosed with non-Hodgkin lymphoma (NHL) in remission was admitted presenting with malaise, fever, and skin lesions on left cheek and left wrist. She had personal antecedents of prior similar episodes that had not responded to antibiotic treatment.

Physical examination revealed a 1.5-cm diame-

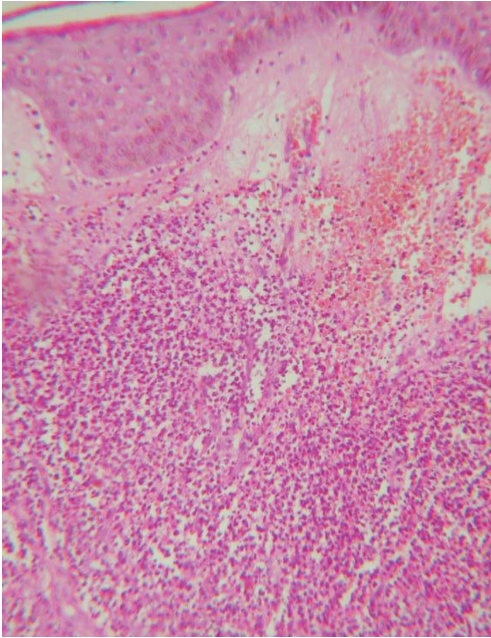


FIGURE 3: Preserved epidermis and edematous dermis, with diffuse layered polymorphonuclear infiltrate

ter rounded erythematous plaque with a central crust on the left cheek (Figure 4). On the ipsilateral wrist, an edematous erythematous plaque with well-defined polycyclic margins and a pseudo-ampullar surface in sectors was noted. The patient reported that the lesions were painful.

Laboratory tests showed anemia, leukopenia with neutrophilia, thrombocytopenia, and an increased erythrocyte sedimentation rate. Blood, urine, and skin cultures were negative. As the histopathology was compatible with Sweet syndrome, treatment with 60 mg/day oral prednisone was introduced and resulted in a good clinical progress.

Case 5

Female, 54-year-old patient diagnosed with multiple myeloma (MM) and plasmacytoma located in right arm; treatment had been initiated with chemotherapy and autologous bone marrow transplant.

Patient was admitted presenting with prolonged febrile syndrome, persistent deterioration of liver function tests, and skin lesions within two months after the transplant. The lesions were painful annular 1-3 cm diameter erythematous plaques with well-defined limits and pseudovesicles on margin, in a linear disposition along the upper right limb (Figure 5A). The patient also had erythematous papules on the left arm.

Empirical treatment was initiated with intrave-



FIGURE 4: Rounded erythematous plaque, 1.5 cm diameter, with a central crust on the left cheek

nous acyclovir 5 mg/kg every 8 hours.

A skin biopsy was performed for histopathological examination, cultures, and DIF for Herpes 1 and 2 virus and varicella zoster antigens.

Laboratory studies showed anemia, leukopenia without neutrophilia, increased erythrocyte sedimentation rate, serum immunoelectrophoresis with monoclonal IgG kappa component, and deterioration of liver function tests. Results of a puncture liver biopsy proved to be compatible with portal inflammation.

On the second day of hospitalization, the patient experienced central facial paralysis; nuclear magnetic resonance imaging showed no brain abnormalities. Respiratory involvement also occurred, with diffuse bilateral interstitial infiltrates seen on chest CAT, which led to broncopulmonary lavage with biopsy that proved negative for germs.

Skin, blood, and urine cultures were negative. The histology study of the skin showed preserved epidermis and a dense dermal polymorphonuclear infiltrate. The diagnosis was Sweet syndrome with systemic involvement.

The patient showed an improvement of the clinical picture with no need for steroid treatment, and was discharged from the hospital.

Case 6

Female patient, 57 years of age, diagnosed with non-Hodgkin mantle-cell lymphoma admitted for her second round of chemotherapy. After four days of treatment, her clinical condition had deteriorated. Patient was afebrile, with a skin eruption involving the neck, back, sternal area, and both proximal thighs. This lesion was surrounded by erythematous

papules with 3-4 mm diameter, some with a vesiculous center (Figure 5B). Additionally, painful aphthoid lesions were noted on left jugal mucosa and ipsilateral labia minor vulvar area.

Laboratory tests showed anemia, thrombocytopenia with neutrophilia, and increased erythrocyte sedimentation rate, with no other abnormalities.

Skin biopsy was performed for histopathological study, as well as sampling for cultures and swab of the skin and mucous lesion for DIF for Herpes 1 and 2 and varicella zoster antigen tests. Empirical treatment was started with intravenous antibiotics using piperacillin-tazobactam.

Cultures and DIF were negative; hence, the antibiotic treatment was discontinued. The histologic study was compatible with Sweet syndrome.

Treatment was introduced with oral 40 mg/day prednisone leading to good clinical progress and hospital discharge.

Case 7

Female patient, 65 years of age, with personal antecedents of breast carcinoma (1989), thyroid carcinoma (2000), and Sweet syndrome (2003). Eight months after the syndrome she was seen as an outpatient presenting with fever and skin lesions. The lesions comprised painful edematous and rounded erythematous plaques of various sizes, with well-defined limits, some with a pseudovesicular surface, located on the face (forehead, left eye, nasal dorsum, and upper lip), neck, back of chest, and backs of hands (Figures 6A and 6B). Additionally, the conjunctiva of the left eye showed hyperemia.

Comprehensive laboratory tests showed leuko-

penia with neutrophilia and increased erythrocyte sedimentation rate. The histopathological examination of one of the lesions was consistent with Sweet syndrome; treatment with oral 20 mg/day prednisone was introduced with good clinical improvement. The patient was studied in search of new neoplasms or reactivation of prior lesions, and was found disease-free.

COMMENTS

Sweet syndrome or acute febrile neutrophilic dermatosis is a disease of unknown etiology characterized by the presence of fever, neutrophilic leucocytosis, abrupt appearance of painful erythematous plaques and nodules predominantly on the head, neck, and upper limbs, with dense dermal polymorphonuclear infiltrate without vasculitis and a rapid response to steroid treatment.^{2,3,8}

Most patients present with the classic or idiopathic form represented by paraneoplasia in 20% of cases. Most are hematologic neoplasms, as in the cases presented. The most common malignant disease is acute myeloid leukemia.⁷ However, associations with myeloproliferative and lymphoproliferative disorders, as well as with myelodysplastic syndrome and carcinomas have also been reported.^{2,9} The correlation with multiple myeloma is not very common,¹⁰ and in most cases corresponds to tumors that secrete immunoglobulin G, as in case # 6.¹¹ As to solid tumors, 2/3 of the cases are represented by genitourinary tract tumors, although there have been cases described in association with carcinomas of the breast, endometrium, ovaries, vagina, cervix, testicles, kidneys, stomach, rectum, and melanoma.^{5-7,12,13} Associations between hematologic diseases and solid tumors have been reported,⁵ and recently a case was published of this syndrome associated with two solid tumors.⁶ In case # 7, the patient had a prior history of two solid tumors that had been promptly treated. The appearance of Sweet syndrome and its later recurrence alerted to the importance of careful follow-up in search of new neoplasms, relapses, or progression of former lesions. Usually Sweet syndrome coincides with or precedes the neoplasm, but its apparition up to one year after the syndrome has also been reported.^{14,15,16}

In idiopathic Sweet syndrome there is predominance in women between 30 and 50 years of age, although cases have been described as early as the seventh week of life up to 85 years of age.^{3,17} In the cases presented, as well as in those published in international medical literature, no predominance in the female gender has been noted, and age at onset was between the sixth and seventh decades of life.^{2,5}

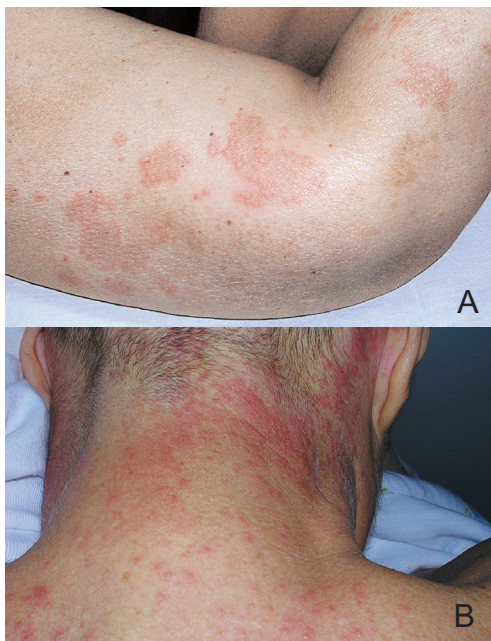


FIGURE 5: A: Erythematous annular plaques with well-defined limits, with pseudovesicles on margin, in the upper right limb. **5B:** Rounded erythematous papules with 3-4 mm diameter, some with a vesiculous center, located on the posterior neck

Clinically, typical location and presentation forms were observed in all cases, with erythematous papules, plaques, and nodules, with pseudovesiculation and spontaneous pain on the head, neck, and upper limbs.¹⁸ Further, concurrent with medical literature, more severe and atypical forms were noted in necrotic and purpureal vesicular lesions with bullas on the trunk, backs of hands, and lower limbs.^{2,4,5} In cases # 2 and # 7, lesions were observed on labial semi-mucosa, and in case # 6, on jugal and vulvar mucosas. Involvement of oral mucosa with a polymorphic aspect was noted in 30% of patients with pseudo-aphtoid lesions as was seen in case #6.¹⁶ This is more common in patients with malignant diseases, especially hematologic in nature.^{3,19} In these cases,



FIGURE 6:A: Rounded edematous and erythematous plaques, with a pseudovesicular surface, distributed on the face as mountain chains



FIGURE 6:B: Rounded erythematous plaques of various sizes, with purpuric center, well-defined limits, located on the periungueal region and back of hands

however, the skin lesions have a more pseudovesicular aspect and frequently ulcerate.¹

The nonspecific involvement of the genital mucosa is not common, as was verified in case # 6.¹⁶

Extracutaneous involvement is seen in a high proportion of patients (about 50%) with Sweet syndrome associated with neoplasms, especially those affecting muscular-skeletal tissue and kidneys. Less frequently, there can also be ocular, pulmonary, hepatic, digestive, pancreatic, splenic, ganglionic, cardiac, and central nervous system involvement.^{2,3,5,16} Cases # 2 and # 7 showed ocular involvement in the form of conjunctival hyperemia with no posterior sequelae, which is in agreement with what is presented in literature.⁵ Conversely, cases # 2 and # 5 showed pulmonary and hepatic involvement, verified by laboratory tests and imaging. In both cases, BAL and puncture liver biopsies showed a neutrophilic infiltrate,²⁰ confirming systemic involvement in Sweet syndrome. Steroid therapy produced remission of skin lesions and extracutaneous manifestations, as reported in literature.

The appearance of new pulmonary infiltrates with negative sputum, BAL, and serial blood cultures in a patient with underlying neoplasms makes it vital to exclude Sweet syndrome as a possible cause, since timely initiation of steroid treatment produces rapid clinical improvement.^{2,5,18}

The patient with multiple myeloma experienced central facial paralysis with no changes seen on nuclear magnetic resonance of the brain. This patient showed improvement coinciding with the involution of the skin lesions.

Cases of Sweet syndrome have been published with neurologic manifestations indicating that the most common symptoms are seizures, headaches, and changes in consciousness. Imaging studies may be normal, but in some cases lesions have been found in basal ganglia, white matter, and brainstem. Cerebrospinal fluid analysis shows lymphocytic pleocytosis and incremented lumbar protein leak. Neurologic manifestations in this syndrome are habitually transitory, but in some cases may be recurrent. In relapses, it may be beneficial to use low doses of steroids, dapsone, colchicine, or indomethacin.²¹

Extracutaneous manifestations indicate that the syndrome is a systemic disease with a high possibility of multiorgan involvement.²

Laboratory results, both in idiopathic Sweet syndrome and paraneoplastic patients, show an increased erythrocyte sedimentation rate, as was noted in the cases presented.⁵ Although neutrophilic leukocytosis is one of the diagnostic criteria, it is absent in up to 50% of cases associated with neo-

plasms, and does not, therefore, exclude the diagnosis.^{2,5,7,22} Anemia and abnormal platelet count are frequent in oncohematologic disease patients, which coincides with the natural history of the underlying disease and chemotherapy treatment. Neutropenia can also be explained by what was previously mentioned, as was seen in cases # 1 and # 3.⁵

Based on what was previously stated, when dealing with a patient bearing lesions consistent with Sweet syndrome, anemia, abnormal platelet count, and absence of neutrophilia, a comprehensive search for subjacent or recurring hematologic diseases should be made.^{2,5,23}

Although proteinuria is the most common manifestation of renal involvement,⁵ it was not found in the cases we presented.

Blood, urine, sputum, and skin cultures proved to be negative for bacteria, mycobacteria, fungi, and viruses, ruling out an infectious process and explaining the lack of response to antibiotic treatment in these patients.⁵

The histopathological examination of the skin lesions shows no significant difference between the idiopathic and paraneoplastic forms, except for the possibility of identifying leukemia cutis in skin lesions of oncohematologic patients.³ This is represented by immature and atypical myeloid cells in the skin infiltrate.²⁴ We did not observe this concurrence in our cases.

The pathognomic histopathologic characteristic is the presence of dense infiltrate mainly comprised of mature neutrophils located primarily in the upper and mid dermis. Less common are lymphocytes, histiocytes, and eosinophils. Frequently there is leukocytoclasia, endothelial tumescence, and erythrocyte extravasation. The prominent edema of the upper dermis may lead to vesicle or bulla formation. The epidermis may be normal or show slight acanthosis and/or hyperkeratosis.⁵ The representation previously described was observed in the cases presented.

It is important to remember that the histological study enables the confirmation of absence of infectious agents, tumor cells, and vasculitis. It should also be differentiated from other neutrophilic dermatoses such as pustular psoriasis, leukocytoclastic vasculitis, and gangrenous pyoderma, among others.^{3,5} A variant of Sweet syndrome was recognized on the backs of hands in which leukocytoclastic vasculitis was found secondary to the inflammatory process, but the diagnosis was not excluded.^{14,25}

Spontaneous involution of the clinical picture may take weeks to months.³ In patients with neutropenia following chemotherapy (cases # 1 and #

3) that require the use of G-CSF, clinical involution of symptoms was observed with remission of neutropenia while the patient was receiving the G-CSF. It should be remembered that G-CSF administration is responsible for most cases of drug-related Sweet syndrome.³ Additionally, we need to bear in mind that the use of chemotherapy agents and radiotherapy may act as causes for the syndrome.^{14,26,27}

The treatment of choice, both for idiopathic Sweet syndrome and that associated with neoplasms, is systemic corticoids that produce a rapid response to the clinical picture, as observed in the cases described.⁵ Prednisone is used with oral doses between 30 and 60 mg/day for four to six weeks, with a progressive tapering of the dose. In some patients, in order to suppress recurrences, low doses of prednisone are needed with 10 to 30 mg a day or every other day, during two or three months. In refractory cases, pulse therapy is used with up to 1000 mg/day of intravenous methylprednisolone during three to five consecutive days,³ as was necessary in case # 2.

Since neoplasm patients show different degrees of immunosuppression either from the underlying disease or the treatment given, in many situations the use of steroids may be more detrimental than beneficial.^{5,23} That is why it is important to remember other available treatments, such as potassium iodate, colchicine, indomethacin, dapsone, clofazimine, and cyclosporin, among others. The first two drugs are considered first choice along with corticoids.^{3,5,23} Recently a case report was published of recalcitrant Sweet syndrome associated with myelodysplastic syndrome that responded successfully to treatment with thalidomide.²⁸

Recurrence was observed in 30% of patients with the idiopathic form, growing to 70% in the paraneoplastic form. Relapses were associated with a guarded prognosis, since in many cases it coincided with the progression of the underlying disease or recurrence of an earlier neoplasm. Thus, the diagnosis of Sweet syndrome in an oncology patient should alert to this possibility.^{1,2,5}

As to the cases presented the following things were observed:

1- In case # 1, Sweet syndrome coincided with the progression of the underlying disease to a chemotherapy-resistant leukemia.

2- In case # 2, the syndrome coincided with the progression of an anemic syndrome to a form of chronic myelomonocytic leukemia.

3- In case # 3, the progression of a myelodysplastic syndrome to an acute myeloid leukemia was noted,^{28,29} coinciding with the appearance of the

Sweet syndrome. On the other hand, recurrence of the disease announced a guarded prognosis that culminated with the patient's death.

4- In the patient with solid tumor antecedents (case # 7), although the tumors were under control, relapse of the syndrome required an extensive search for a new neoplasms or recurrence of the former tumors.

Consequently, with the onset of lesions consistent with Sweet syndrome in an oncology patient, pertinent studies should be conducted to rule out the progression or reactivation of the underlying disease in order to introduce the opportune treatment.^{2,3,5,29}

CONCLUSION

Neoplasm-associated Sweet syndrome represents 20% of cases of the syndrome. Most of these are made up of hematologic diseases.⁷

In this group of patients, absence of female predominance and onset between the sixth and seventh decades of life were noted.^{2,5}

In cases of suspected Sweet syndrome associated with neoplasms, locations and atypical presentations need to be kept in mind, as well as the possibility of systemic involvement.^{2,4,5} On the other hand, with the appearance of lesions consistent with Sweet syndrome in a patient with anemia and abnormal platelet count, the possibility of a

subsequent neoplasm must be ruled out. The absence of neutrophilia does not exclude this diagnosis since neutropenia can be evident due to the subsequent disease or the chemotherapy treatment these patients receive.^{2,5,22,23} Additionally, G-CSF is one of the frequent causes of drug-related Sweet syndrome and this possibility must therefore be ruled out.³

In immunosuppressed patients, the coexistence of fever, neutrophilia, and skin lesions requires the consideration, first of all, of the possibility of infectious conditions that should be excluded first, since this determines the subsequent treatment. Therefore, antibiotics are used empirically, although Sweet syndrome does not respond to them.^{5,7} Steroid use promotes a rapid clinical response, if the absence of an infectious process has been confirmed.²³ Therefore, with cultures and histopathological study, processes can be differentiated in order to choose the correct treatment option.⁷

Lastly, in patients with paraneoplastic Sweet syndrome, there is a high percentage of recurrences that many times coincide with the progression or relapse of the underlying disease. Thus, the syndrome should be considered as a marker of a guarded prognosis and long-term follow-up should be made in search of subsequent neoplasms in order to introduce adequate treatment that will improve prognosis and quality of life for these patients.^{1,2,5,23,30} □

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