

## CASE REPORT

# Fatal Sweet Syndrome Associated to Chronic Idiopathic Systemic Inflammatory Response Syndrome

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**Abstract.** Sweet syndrome is one of the cutaneous processes more frequently associated to systemic diseases. Its association to the systemic inflammatory response syndrome has rarely been described. We report a case of chronic and relapsing Sweet syndrome associated to a chronic and idiopathic systemic inflammatory response syndrome that lasted seven years and proved fatal to the patient. Among the rare cases of Sweet syndrome associated to a systemic inflammatory response syndrome that have been described there have not been any fatal cases as occurred with our patient.

**Key words:** Sweet syndrome, systemic inflammatory response syndrome.

## SÍNDROME DE SWEET DE EVOLUCIÓN FATAL ASOCIADO A SÍNDROME DE RESPUESTA INFLAMATORIA SISTÉMICA CRÓNICO IDIOPÁTICO

**Resumen.** El síndrome de Sweet es uno de los procesos cutáneos ligados con mayor frecuencia a enfermedades de los órganos internos. Su asociación al síndrome de respuesta inflamatoria sistémica ha sido raramente descrita. Presentamos un caso de síndrome de Sweet de evolución crónica y recidivante asociado a un síndrome de respuesta inflamatoria sistémica crónico idiopático de 7 años de evolución que llevaron a la muerte del paciente. De los raros casos descritos de síndrome de Sweet asociado a síndrome de respuesta inflamatoria sistémica, no hay ninguno descrito que haya llevado a la muerte del paciente como en nuestro caso.

**Palabras clave:** síndrome de Sweet, síndrome de respuesta inflamatoria sistémica.

## Introduction

Sweet syndrome, also known as acute febrile neutrophilic dermatosis, was first described in 1964 as an eruption of painful plaques and/or nodules, with histologic findings revealing a dense dermal infiltrate composed mainly of neutrophils.<sup>1</sup>

The diagnostic criteria for Sweet syndrome were proposed by Su and Liu<sup>2</sup> in 1986 and subsequently revised by Von der Driesch in 1989<sup>3</sup> and 1994.<sup>4</sup>

In patients with neoplastic disease, Sweet syndrome is usually a marker of poor prognosis regardless of whether it presents before or after diagnosis of the malignant process.<sup>5</sup> However, the dermatosis itself is usually an acute, limited,

benign process that generally responds well to corticosteroid treatment. Reports of fatal outcomes of Sweet syndrome are uncommon.<sup>6-13</sup>

For normal host defense mechanisms to be maintained, the inflammatory response must be intact. However, in some cases, the inflammatory response can be very strong, leading to multiple organ failure. This is known as systemic inflammatory response syndrome, in which extensive release of proinflammatory cytokines such as interleukin 6 and tumor necrosis factor  $\alpha$  occurs. Under sustained antigen stimulation, the inflammatory response syndrome is chronic with progressive deterioration of the patient's general state of health and immune status.<sup>14,15</sup>

There have been few reports of Sweet syndrome associated with systemic inflammatory response syndrome.<sup>16-18</sup> We present the case of a patient who died after a 7-year history of chronic and recurrent Sweet syndrome associated with idiopathic systemic inflammatory response syndrome.

## Case Description

A 72-year-old man was seen in August 1998 for

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**Figure 1.** Pseudotumoral erythematous–edematous masses on the neck.

pseudotumoral erythematous masses on the anterior aspect of the trunk and face (Figure 1) accompanied by fever and malaise. The patient reported periodic outbreaks of similar lesions in the previous 3 years. The results of a biopsy performed in another hospital had already diagnosed neutrophilic dermatosis, and the laboratory and serological tests, analysis of tumor markers, and radiological examinations had all been normal or negative.

A skin biopsy of the trunk was undertaken once again. The results—an intense dermal edema with massive neutrophilic infiltration but no vasculitis (Figures 2 and 3)—were compatible with Sweet syndrome. Oral corticosteroid therapy was prescribed at a dose of 1 mg/kg/d and the skin lesions resolved rapidly. However, these lesions recurred on reducing the corticosteroid dose.

In March 1999, the patient was admitted to hospital for an episode of deep vein thrombosis and a new outbreak of skin lesions. He received treatment with acenocoumarol and cyclosporine was added to the corticosteroid therapy

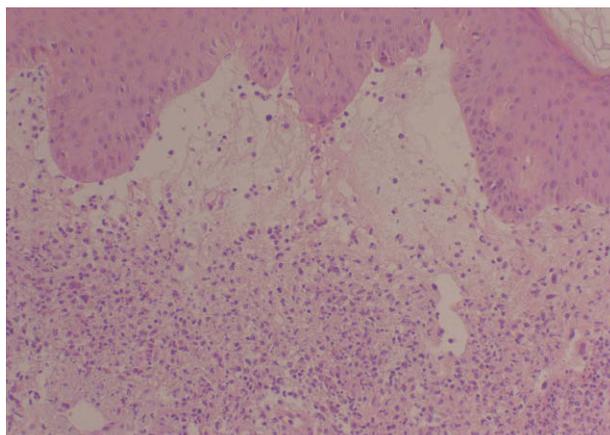
at a dose of 5 mg/kg/d. This regimen controlled his dermatosis.

In July 1999, despite continued therapy with cyclosporine, he suffered a further outbreak of skin lesions typical of Sweet syndrome along with oral sores. He was admitted once again for treatment, and while in hospital he developed nosocomial pneumonia and septic shock which necessitated admission to the intensive care unit and mechanical ventilation. In this period, the immunosuppressant therapy was completely suspended and the patient presented minimal skin lesions. He was discharged in March 2000 after negative or normal findings in extensive laboratory tests, radiological examinations, analysis of tumor markers, serological studies, and histopathological studies including a bone marrow biopsy. None of the findings could explain the cause of the neutrophilic dermatosis.

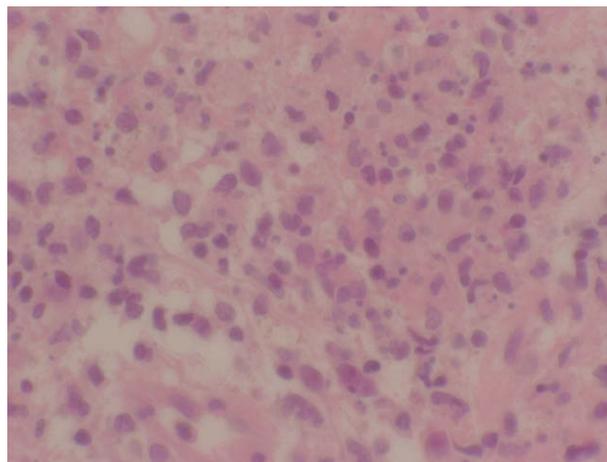
In May 2000, he presented with a further outbreak of severe skin lesions and once again received oral corticosteroid therapy accompanied by azathioprine at a dose of 100 mg/d. When the corticosteroid dose was reduced, there was an immediate outbreak of skin lesions. Other therapeutic alternatives were tried such as thalidomide, potassium iodide, colchicine, and dapsone with no improvement in the skin lesions.

In June 2001, while suffering a new outbreak of skin lesions, the patient presented with avascular necrosis of the femoral head and so was admitted to hospital once again. Laboratory tests during admission revealed a level of rheumatoid factor of 84 IU/L, polyclonal hypergammaglobulinemia, and a slight decrease in complement levels. Therapy was reinstated with prednisone at a dose of 15 mg/d, azathioprine at a dose of 100 mg/d, and colchicine at a dose of 1 mg/8 h with remission of the skin lesions.

In August 2001, he suffered severe recurrence of his skin lesions with generalized pustules, some of which were hemorrhagic. A serology test for the hepatitis C virus was



**Figure 2.** Low-magnification view of the skin biopsy showing severe edema of the papillary dermis. (Hematoxylin–eosin,  $\times 100$ .)



**Figure 3.** High-magnification view of massive neutrophilic infiltrate of the dermis. (Hematoxylin–eosin,  $\times 400$ .)

positive. As a consequence, the doses of prednisone and azathioprine were reduced.

In the following months, the patient developed progressive pancytopenia and coagulation disorders and died in June 2002.

Repeated studies of our patient during the 7 years of his illness never showed any evidence of solid or hematological cancer, active infection, or other findings that might help identify the cause of Sweet syndrome. Given the chronic nature and course of the condition, the disease was classified as an idiopathic chronic systemic inflammatory response syndrome.

## Discussion

Our patient was diagnosed with Sweet syndrome because he met 2 of the major criteria and 2 of the minor ones proposed by Su and Lui—acute onset of painful erythematous–edematous plaques, dermal edema accompanied by an infiltrate composed predominantly of neutrophils without leukocytoclastic vasculitis, prodromic symptoms such as fever, and good response to corticosteroid therapy.

The course of Sweet syndrome in this particular case was atypical in that it was chronic, spanning a long period of time, and extremely severe, and the patient died. The patient's condition deteriorated progressively because Sweet syndrome was accompanied by a chronic systemic inflammatory response syndrome. The etiology of these 2 conditions could not be determined despite the numerous studies done over the 7-year clinical course of the disease. An unknown antigen trigger was probably responsible for the chronic nature of Sweet syndrome and the chronic systemic inflammatory response.

The positive hepatitis C virus serology, which occurred late in the patient's history, might explain the clinical manifestations; however, several observations preclude a relationship between the 2 processes:

1. The prevalence of hepatitis C virus in the general population is high and it has rarely been associated with Sweet syndrome.<sup>19</sup>

2. Systemic inflammatory response syndrome has not been linked to the hepatitis C virus.

3. Although the patient was seropositive for hepatitis C, this does not mean the infection participated in the patient's clinical condition. In view of the patient's deterioration, a more extensive study to quantitate hepatitis C virus RNA copies was not undertaken.

No lesions characteristic of Sweet syndrome were reported during the nosocomial infection that necessitated the patient's admission to the intensive care unit. Subsequently, however, the lesions reappeared at the same time as the

patient's immune system recovered. Such an observation might be explained along similar lines to the inflammatory immune reconstitution syndrome that occurs in patients infected with the human immunodeficiency virus (HIV) after administration of highly-active antiretroviral therapy (HAART). A case of Sweet syndrome has already been described in an HIV-infected patient after HAART.<sup>20-22</sup>

Sweet syndrome has rarely been reported as a life-threatening dermatosis.<sup>6-13</sup> If we exclude cases in which Sweet syndrome was associated with serious life-threatening diseases, and hematological cancers in particular, the syndrome has rarely been fatal. When the syndrome does actually have a fatal outcome, death is due to neutrophilic infiltration of vital structures, such as the elastic fibers in the great arteries (Marshall syndrome), cardiac fibers, the myocardium, electrical conduits of the heart, or the liver.

There have been very few reports of Sweet syndrome associated with systemic inflammatory response syndrome,<sup>16-18</sup> and none of these associations were fatal. We therefore think that this case report is the first of Sweet syndrome associated with systemic inflammatory response syndrome with a fatal outcome.

## Conflicts of Interest

The authors declare no conflicts of interest.

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