

# Sweet's syndrome and inflammatory bowel disease – an uncommon association

Patricia Gonçalves, José Miranda, J. A. Mascarenhas Araújo

### Abstract

*Sweet's Syndrome (SSw) is a neutrophilic dermatosis characterized by fever, neutrophilia and skin lesions with a diffuse, neutrophilic and inflammatory infiltrate. Sweet's pathogenesis hasn't been entirely defined. It can be idiopathic or associated to other diseases (infectious, neoplastic, inflammatory) that's why this Syndrome should be primarily considered as a sign of underlying disease.*

The association between Sweet's Syndrome and Inflammatory Bowel Disease is not common and the first doesn't seem to reflect the activity of the last, but to share the same pathologic mechanism.

Key words: Sweet's syndrome, Crohn's disease, neutrophilic dermatosis, Gomm-Button disease.

### INTRODUCTION

Acute Febrile Neutrophilic Dermatitis was described for the first time in 1964, by the British dermatologist Robert Douglas Sweet.<sup>1</sup>

For 15 years, Sweet has identified eight women, with ages ranging from 32 to 55 years old, showing a clinical condition featured by fever, peripheral blood neutrophilic leukocytosis and maculopapular cutaneous lesions, purplish, increasing gradually in number and size, ending coalescing, often painful, defined histologically by the presence of dermic neutrophilic infiltrate, responding well to corticotherapy. Paying tribute to the first two patients described, Sweet's Syndrome (SwS) is also known as Gomm-Button's Disease.<sup>2</sup>

SwS pathogenesis remains unclear, it is thought to be multifactorial and associated to an immunologic mechanism not totally clarified. Cytokines, circulating auto-antibodies or immunocomplex seem to have an important role.<sup>1</sup>

Since it was first described, several other cases of SwS were reported in the literature, related with the most diverse causal factors, existing, also, records

of idiopathic cases. Drugs as Trimetoprim-sulphamethoxazole, the Granulocytes Colonies Stimulating Factor or even Furosemide, were associated to the development of SwS. Solid neoplasms (breast, genital-urinary or gastrointestinal tumors) and haematologic disorders, as well as rheumatology diseases (erythematous lupus, Sjögren's syndrome, Behcet's disease...), infections (mainly respiratory) and even the intestinal inflammatory disease, were related to the SwS development.<sup>1,3,4,5,6</sup>

Due to the severity of pathologies which might be associated with it, SwS must be primarily, considered as a systemic manifestation of an underlying disease.<sup>7</sup>

The association between the Sweet's Syndrome and Inflammatory Intestinal Disease is uncommon, having been described for the first time in 1988 by Kemmett et al.<sup>8</sup> Since then more similar cases were described, most in female gender patients, but also in male gender individuals.<sup>5,7,9,10</sup>

### CLINICAL CASE

We describe the case of a 36 years old patient, Caucasian, office worker, born and residing in Lisbon area, attending the Emergency Service of Hospital Fernando Fonseca due to a condition of arthralgias and cutaneous lesions evolving for about 3 weeks.

The patient, previously healthy, mentions the appearance of erythematous cutaneous lesions in the upper limbs, non painful, non pruriginous and initially non confluent, as well as a painful lesion on the cheek mucosa. Around 4 days after appearing the first cutaneous lesions, arthralgias of progressive



Initial papular lesions.

FIG. 1

worsening were associated with additive and symmetric involvement of the main joints, with mechanical rhythm, without edema or joint redness and abdominal pain of cholic type complaints, alleviated with defecation, without diarrhea or blood loss, or mucus or purulent.

On the following weeks, cutaneous lesions increased in number and pain complaints became more intense. Then on the anterior part of both lower limbs, erythematous and painful nodular lesions appeared. It was associated to a feeling of congestion and ocular pain of a bite type and bilateral, without photophobia or change on visual acuity. The patient never had fever and denied other symptoms.

The objective exam showed a patient in a good general condition, pink and hydrated, afebrile and haemodynamically stable. The skin was dry, with multiple papular and erythematous pseudovesicular lesions, of variable size (from 1 to 3 cm), in several stages of evolution, some confluent in a plaque, located preferentially in the dorsal part of the upper limbs, asymmetric, and in smaller number in the trunk and lower limbs (Fig. 1 to 3). In the anterior part of the lower limbs, it was also seen nodular purplish painful lesions. There was neither facial nor palm-sole involvement. Red eyes were observed bilaterally. On the cheek mucosa, a round lesion was seen, with around 1 cm diameter, well delimited, with a clear background and off white, the patient referred as painful. The remainder of the objective exam was normal.

Analytically, at the time of admission, hemoglobin



Pseudovesicular lesions.

FIG. 2

was 12.7 g/dL, with a Mean Corpuscular Volume of 87.3 fL, 11,100 Leukocytes/L (7,400 Neutrophils/L), 311,000 Platelets/L and CPR 13.6 mg/dL.

During admission, cutaneous lesions kept on increasing in number, reaching the palms, becoming scaling and confluent (Fig. 4). The patient has developed also, a condition of aqueous diarrhea, without blood, associated to a diffuse abdominal pain and multiple anal fissures.

Upper gastrointestinal endoscopy has shown a severe oesophagitis, ulcerated and a chronic gastritis, which has revealed itself positive to *Helicobacter pylori*. The colonoscopy has shown scarce ulcers surrounded by a normal mucosa all over the colon, that in the descending and sigmoid were excavated with off-white background and in the transversal, ascending and caecum showed aphthoid aspect. The biopsies carried out showed compatible changes with Crohn Disease in active stage. A positivity was detected for anti-Saccharomyces cerevisiae antibodies (ASCA). All other auto-antibodies have shown to be negative, including ANAs, dsDNA, rheumatoid factor, SM and ANCA.

Cutaneous biopsy has revealed a diffuse inflammatory infiltrate in the dermis, dense, perivascular in band, made essentially by neutrophils, without vasculitis, compatible with Sweet Syndrome.

The final diagnosis was then Crohn's disease with Sweet's syndrome as initial manifestation.

The treatment has included: Prednisolone 60mg/day, Mesalazine 500mg every 6 hours, Metronidazole



Coalescent lesions.

FIG. 3



Coalescent and scaling lesions.

FIG. 4

500mg every 8 hours, for the treatment of Crohn Disease (the Sweet's Syndrome can be administered with corticotherapy) and Omeprazole 40mg/day, Clarithromycin 500mg every 12 hours and Amoxicillin 1g every 8 hours to the eradication of *Helicobacter pylori*. As adjuvants were administered fluid therapy and analgesia.

The patient was discharged on the 23rd day of admission. Her evolution has been, so far, favorable, with remission of cutaneous lesions, arthralgias, diarrhea and anal fissure. The corticotherapy weaning off was started about a month after being discharged, without the exacerbation of the symptoms. The follow up is regularly made in the Internal Medicine outpatient service.

## DISCUSSION

This patient diagnosis path has shown to be a real challenge to the clinical reasoning due to the fact the cutaneous lesions appeared before the gastrointestinal manifestations of Crohn Disease (CD).

The cutaneous biopsy was essential to the diagnosis of Sweet's Syndrome, as its clinical manifestations can be confused with other pathologies, as multiform erythema, nodosum erythema (often following SwS), *Eritema elevatum diutinum*, Behcet's disease and even cutaneous CD. The SwS histologic features include the presence on the dermis of a diffuse neutrophilic inflammatory infiltrate, with a deep edema in the subepidermis range, without vasculitis.<sup>10,11</sup>

The Sweet's syndrome, does not reflect the activity of the intestinal inflammatory disease, seems to share the same pathophysiologic mechanism, not yet clarified.<sup>7</sup>

In most CD cases described associated to SwS, only the colon and/or perianal region were affected by CD, what is in agreement with the fact that individuals whose CD affects predominantly the colon and/or perianal region, are at higher risk of developing extraintestinal manifestations of inflammatory intestinal disease. In the case we described, there is also an esophagus involvement and the oral mucosa. Chronic gastritis would evolve from the *H. Pylori* infection, and it can not be excluded the gastric involvement for CD, that can affect all the digestive tract.<sup>12</sup>

The Sweet's Syndrome diagnosis, according to Su and Liu,<sup>9</sup> is made by the presence of two major criteria and at least two minor criteria. The major criteria are: (a) sudden appearance of plaque or purplish nodes, erythematous or painful and (b) dense dermic neutrophilic infiltrate without evidence of primary leukocytoclastic vasculitis. The minor criteria include: (a) Fever  $>38^{\circ}\text{C}$  (b) A good response to systemic corticoids, potassium iodate or colchicine (c) Laboratorial changes (3 out of 4): ESR $>20$  mm/h, positive CPR, Leukocytosis  $>8000/\text{mL}$ , Neutrophilia  $>70\%$  (d) Association with haematologic or visceral neoplasm, inflammatory disease or pregnancy or preceded by upper airway infection.<sup>9</sup>

In the case of SES associated to drug intake, items

(c) and (d) of the previous paragraph are not be applied, being necessary a coherent temporal rapport with the starting and ending the treatment with the suspected drug.<sup>1,3</sup>

The recommended treatment to SwS is corticotherapy (Prednisone or Methylprednisolone), that induces rapidly the cutaneous lesions remission. Other first line drugs are the colchicine and potassium iodate. Second line agents include indometacin, cyclosporin and dapsone.<sup>1,7</sup>

The SwS resolution will depend on the treatment of the underlying pathology, if identified or the drug withdrawal which has triggered it. If idiopathic, the remission of cutaneous lesions may occur, without treatment, in some weeks or months, without scars. The reoccurrence of cutaneous lesions in a patient with a known etiology and controlled previously, can mean a tumoral recurrence.<sup>1,3,7</sup>

This patient follow up should pass, first of all, through the education for the disease in a way to optimize the therapy compliance. She was made aware that the Crohn Disease was chronic and recurrent, and the possibility of emerging possible complications as fistulas, abscesses or nutritional deficits. Visits should be, initially more frequent to evaluate the efficacy of medication and start the corticotherapy gradual decrease (sensitivity period for the possibility of exacerbating the symptoms), being gradually less frequent. Due to the risk of developing colon rectal carcinoma, it should be carried out the colonoscopy in long lasting CD patients (>8 years of age).

## CONCLUSION

The association between the Crohn Disease and Sweet's Syndrome is uncommon. This fact, associated to the patient initial presentation just with extra-intestinal manifestations, made the CD diagnosis more complex.

Cutaneous biopsy is essential to the SwS diagnosis, and it is together with the typical cutaneous lesions, the *major* criteria described by Su and Liu. From the *minor* criteria, the patient shows laboratorial changes, good response to corticotherapy and finally association to an inflammatory disease, in this case, Crohn Disease.

Due to the severity of pathologies which might be associated to it, Sweet's syndrome should be considered as a systemic manifestation of an underlying disease. The histologic confirmation of this syndrome

should not be, for such reason, assumed as the end of the diagnostic path. ■

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