

CLINICAL NOTE

A continuous spectrum of neutrophilic dermatoses in Crohn's disease

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ABSTRACT

The inflammatory bowel disease is accompanied by cutaneous manifestations in approximately 10% of the cases. Neutrophilic dermatoses are located on the dermis and/or epidermis and are characterised on histological examination by the presence of an infiltrate that consists largely of neutrophils. The prototype of neutrophilic dermatoses is Sweet's syndrome; which is rarely associated with Crohn's disease.

Case report: A 63 year old woman was admitted to hospital with pyrexia, abdominal pain, episcleritis and skin lesions. She presented erythematous lesions on trunk, legs and arms, with tendency towards formation of plaques, nodules and vesicular pustular lesions. Both the colonoscopy and colonic biopsies confirmed the diagnosis of colonic Crohn's disease. Cutaneous biopsies revealed an infiltrate consisting mainly of neutrophils. These biopsies, together with clinical details led to the diagnosis of Sweet's syndrome. A methylprednisolone treatment rapidly improved the skin lesions and clinical symptoms.

The different clinical forms of neutrophilic dermatosis are an extra intestinal manifestation of Crohn's disease, and are sometimes found concurrently in the same patient, which would indicate a common pathogenesis with different clinical presentations (spectrum of neutrophilic dermatoses).

Key words: Crohn's disease. Sweet's syndrome. Neutrophilic dermatoses.

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INTRODUCTION

Crohn's disease is a process of unknown aetiology that can affect the digestive tract from the mouth to the anus. It is characterised by a clinical history of acute attacks alternated by remission periods. Crohn's has been associated with numerous extra intestinal manifestations. Some show a clear relationship between the activity of the intestinal disease, while others follow an independent course and are not altered by treatment of the underlying disease. Among the different extra intestinal manifestations, the dermatological disorders should be noted, such as Erythema nodosum, pyoderma gangrenosum, subcorneal pustular dermatosis and vesicular pustular eruptions which are of a continuous spectrum among the neutrophilic dermatoses (1). Sweet's syndrome is another clinical entity of unknown aetiology that is often associated with infectious, inflammatory and neoplastic diseases, but is rarely associated with Crohn's disease (2) and ulcerative colitis (3).

CLINICAL CASE

A 63 year old woman with a clinical history of hyperuricaemia, gout and hypercholesterolaemia. During approximately two months she suffered from asymmetrical migratory polyarthralgia in her small joints (wrists, knees and elbows). One month later she suffered a sudden onset of continuous pyrexia of up to 39 °C, cutaneous eruption consisting of erythematoviolaceous papules (Fig. 1) that changed into irregular plaques and subsequently vesicles developing into vesicular pustular lesions (Fig. 2) located on her neck, arms and legs, short-term hyperaemia in the right eye (Fig. 3) and mouth ulcers. Her haemogram showed leukocytosis with neutrophilia, slight anaemia, significantly raised acute phase reactants (VSG and C-reactive protein) and negative rheumatoid factor. One



Fig. 1.- Erythematoviolaceous papules developing into plaques of small diameters with irregular edges and a pseudo-vesicular pustular surface.

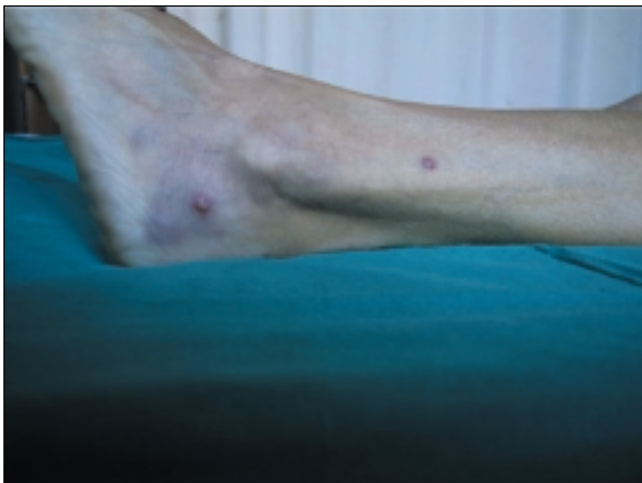


Fig. 2.- Vesicular lesions on legs.

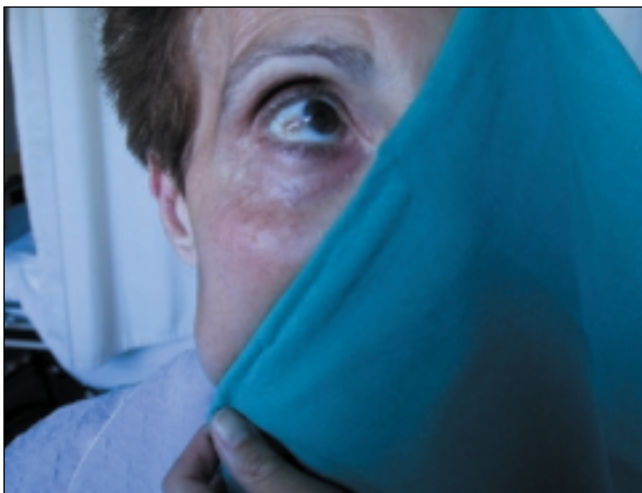


Fig. 3.- Episcleritis in right eye.

week prior to admission, she presented intermittent lower abdominal pain and 4-5 soft mucosal stool movements per day without blood or pus, and a weight loss of 8-9 kg throughout the last month. A colonoscopy was performed, which showed multiple deep, wide ulcers alternating with normal mucosal from the sigmoid colon and ascending 70 cm. Anatomopathological findings were compatible with chronic granulomatous colitis. Cutaneous lesion biopsies revealed inflammatory infiltration of neutrophils with necrotic keratinocytes and the subepidermal oedema was diagnosed as neutrophilic dermatitis without vasculitis (Fig. 4). The patient was started on a systemic treatment with methylprednisolone and her symptoms and cutaneous lesions disappeared one week later.

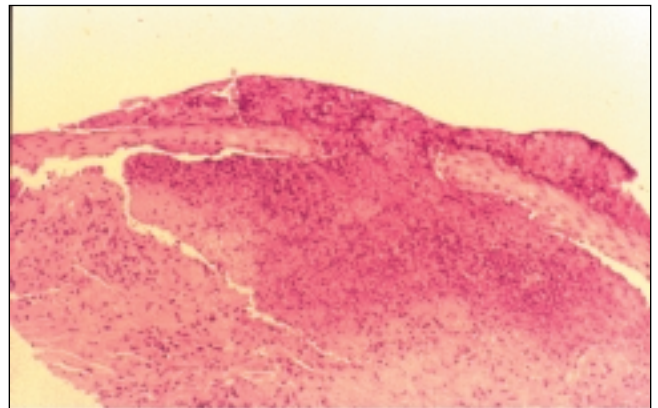


Fig. 4.- Skin biopsy showing papillary oedema and intense infiltrate of polymorphonuclears mixed with necrotic keratinocytes.

DIAGNOSIS

Outbreak of Crohn's (CDA 365) affecting the colon and end of ileum, associated with neutrophilic dermatitis (Sweet's syndrome and vesicular pustular eruption), episcleritis, stomatitis and colitis-dependent seronegative peripheral arthritis. The diagnosis of Sweet's syndrome is made when two major criteria and at least two minor criteria are met (4) (Table I). In this clinical case the accepted diagnostic criteria were met.

DISCUSSION

Sweet's syndrome is a rare process that was first described in 1964 (5). It is also known as acute febrile neutrophilic dermatitis. The term neutrophilic dermatitis covers a wide spectrum of skin lesions, characterised by the presence of an inflammatory infiltrate in the dermis and epidermis which mainly consists of neutrophils, without evidence of infection or vasculitis. However, recently there have been repeated suggestions that vasculitis is fre-

Table I. Diagnostic criteria for Sweet's syndrome (4)**Major criteria**

Sudden onset of typical skin lesions (erythematous nodules or plaques)

Histopathological findings compatible with infiltrate in dermis mainly consisting of neutrophils

Minor criteria

Pyrexia > 38 °C

Association with malignant haematological disease, inflammatory disease, pregnancy, or preceded by upper respiratory tract or digestive tract infection

Good response to systemic corticoids and no response to antibiotics

Altered laboratory parameters (3 out of 4): sedimentation rate > 20 mm, raised C-reactive protein, leukocytosis and neutrophilia

The two major criteria and at least two of the minor criteria must be met

quently found in biopsies of patients with Sweet's syndrome and these findings may be due to a cytotoxic action of substances freed by the neutrophils (6). The different types of neutrophilic dermatitis that have been related to inflammatory bowel diseases (IBD) are: pyoderma gangrenosum, Sweet's syndrome, subcorneal pustular dermatosis (Sneddon Wilkinson's disease), dermatitis-arthritis syndrome lesions associated with intestinal disease with or without intestinal by-pass and vesicular pustular eruptions frequently associated with ulcerative colitis and more rarely with Crohn's disease (1).

The pathogenesis of Crohn's is unknown. Suggested theories range from a hypersensitive reaction to an alteration in the neutrophil function and/or inappropriate function of the T-lymphocytes. However, what has indeed been proved is that there is an alteration in the regulation of certain cytokines and interleukins (IL), such as IL-1, IL-3, IL-5 and IL-8.

It has recently been suggested that Sweet's syndrome may be caused by an alteration in the immune system (particularly in neutrophilic response) and specifically in granulopoiesis (7, 8). There may be an alteration in the stimulation of production, activation, maturing and chemotaxis of neutrophils, caused by the endogenous granulocyte colony stimulating factor (G-CSF) (9). The most frequent drug-induced cause of Sweet's syndrome is due to the administration of recombinant G-CSF (6). Furthermore, it is believed that ANCA (anti-neutrophilic cytoplasmic antibodies) may play a pathogenic role in the activation of neutrophils in patients with IBS (10-13). The association with major histocompatibility complex antigens is not clear, but they are different from those found in Behçet's disease, which is occasionally found concurrently in patients with Sweet's syndrome (14, 15).

Sweet's syndrome is characterised by a sudden onset of erythematoviolaceous papules on the skin, which deve-

lop into plaques with diameters of a few centimetres and with a pseudo-vesicular surface (16). Actual pustules are occasionally formed. The most common systemic manifestations are: pyrexia in up to 80% of the cases, eye involvement (conjunctivitis, episcleritis, iridocyclitis) and up to a third part of the patients present arthralgia, myalgia and non-erosive inflammatory arthritis, mainly located in their wrists and knees, although elbows, ankles and fingers may also be affected (16). In 1988, Kemmett et al (17) were the first to describe the association of Sweet's syndrome with Crohn's disease and, in 1985, with ulcerative colitis. The association of Sweet's syndrome with IBS is very rare and when it occurs it is generally in women (87%), with affectation of the colon (100%) and is accompanied by other extra intestinal manifestations (77%). The presence of skin lesions is associated with IBS activity (67-87%), but may precede other digestive symptoms in up to 21% of the cases (16), even up to several years later. For this reason it is believed that the presence of skin lesions does not reflect activity of the disease itself. One case of Sweet's syndrome has even been reported in which it commenced three months after the patient had undergone a proctocolectomy due to ulcerative colitis, which suggests that this disease does not appear as a consequence of colon inflammation, although it is indeed associated with IBS (19). It is interesting to note that all reported cases of patients with Crohn's disease and Sweet's syndrome have colon affectation and/or perianal disease. No patients have affectation of the small intestine alone (2). This tallies with epidemiological studies that indicate that the extra intestinal manifestations of Crohn's disease are more frequent when the colon is affected than when the disease is confined to the small intestine (20, 21).

Some authors opinion is that (22), vesicular pustular eruptions associated with IBS are interpreted as a rare variation or even an abortive form of pyoderma gangrenosum.

In the case reported, there are two different forms of neutrophilic dermatitis: the onset of vesicular pustular lesions and a typical Sweet's syndrome, associated with an outbreak of Crohn's disease. The concurrence of different variants of neutrophilic dermatitis in the same patient has rarely been reported (23, 24). These circumstances support the idea that neutrophilic dermatitis is a unique entity with different forms of clinical manifestation.

The most commonly used treatment for Sweet's syndrome, when associated with IBS, is systemic corticoids, although good results have also been obtained with oral metronidazole and with a combination of both treatments (25). Colchicine, dapsone, ciclosporin, potassium iodide, indometacin, doxycycline, pentoxifylline and other immunosuppressive agents have also been used with poorer results (3). Spontaneous remission of lesions has even been reported (28). More recently, remission of skin lesions has been achieved with tacrolimus in a pa-

tient with ulcerative colitis refractory to corticoid treatment (27).

The association between Sweet's syndrome and Crohn's disease appears to be clearly based on three fundamental facts. The first is that Sweet's syndrome is a cutaneous indicator of systemic disease, fundamentally leukaemia and connective tissue disorders in over 50% of the cases, and it is now believed that it is the third most frequent association with IBS. The second factor is that Sweet's syndrome is a clinical form of neutrophilic dermatitis, in the same way that pyoderma gangrenosum is associated with IBS. And finally, patients with IBS and Sweet's syndrome often present other cutaneous alterations associated with IBS itself, such as pyoderma gangrenosum, erythema nodosum and vesicular pustular eruptions, indicating a common pathogenesis.

Due to the above mentioned, Sweet's syndrome is considered a rare extra intestinal manifestation of IBS, that is normally present in women with colon affection and is frequently associated to other skin manifestations. In addition to the different clinical forms of neutrophilic dermatitis, other dermatological manifestations, such as erythema nodosum and leukocytoclastic vasculitis, that are seen most frequently in Crohn's disease should also be considered in the differential diagnosis. With the onset of a dermatological pathology of these characteristics, a digestive study is recommendable, fundamentally a colonoscopy, despite no digestive symptoms at the outset.

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