Up-to date review and case report

Sweet’s syndrome revealed by oral pustulosis

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Abstract – Introduction: Neutrophilic dermatoses are conditions characterized by a dermal neutrophilic infiltration associated with variable leukocytoclasia. Oral involvement occurs but is rare and is of less importance than the cutaneous involvement. Observation: The case of a 71-year-old man with neutrophilic dermatoses in whom the major manifestations of the disease were recurrent oral ulcers associated with tongue pustulosis is reported. Oral and skin biopsies revealed a dense neutrophilic infiltrate in the lamina propria. Clinical symptoms were quickly resolved with colchicine treatment. The clinical course allowed us to diagnose Sweet’s syndrome associated with oral pustulosis. Discussion: The main differential diagnosis of Sweet’s syndrome is from Behçet’s disease. Overlap exists between the manifestations of the two diseases, so they must be differentiated. The recurrence of oral ulcers with little inflammatory halo and the quick resolution of ulcers associated with pustules, as well as the histological patterns, were not compatible with Behçet’s disease.

Introduction

Neutrophilic dermatoses (ND) are a collection of diseases characterized by the accumulation of neutrophils in the skin without an identifiable infectious agent [1]. Neutrophilic dermatoses, including Sweet’s syndrome (SS), pyoderma gangrenosum (PG), subcorneal pustular dermatosis (Sneddon-Wilkinson disease (SW)) and rheumatoid neutrophilic dermatitis, are inflammatory conditions of the skin often associated with underlying systemic disease [2]. Some deserve great attention due to major symptoms and the concept of reactive disease or for being a marker for other pathologies, especially neoplastic diseases. Common to all, there is a disorder of stimuli and proliferation of neutrophils, expressed by cellular skin infiltration [3]. A few cases of oral involvement have been reported in patients with ND and were mainly associated with SS [4-9].
The case of a patient presenting for evaluation of chronic and painful oral lesions is reported. The associated clinical symptoms allowed us to diagnose SS.

**Observation**

A 71-year-old male patient was hospitalized for painful oral ulcers associated with pruritic pustular lesions of the lower limbs. His past medical history revealed pneumonia three years before, oral ulcerations for which he had been hospitalized many years ago and Launois-Bensaude lipomatosis. More recently, he consulted a dermatologist for skin pustulosis, oral ulcers and diffuse scrotal erosions.

Physical examination revealed a slight fever of 37.8 °C. Pustular lesions were present on the four limbs, abdomen and upper back (Fig. 1). They were associated with painful oral ulcers of the tongue, lips, cheeks and pharynx, and pustules on the tongue (Figs. 2, 3 and 4). Axillary and inguinal lymph nodes were present.

The pathergy test was negative. Complete blood examination revealed leukocytosis (14,1x10^9/L) and an inflammatory syndrome with the C-reactive protein (CRP) concentration at 154 mg/L. The autoantibody profile was characterized by a positive anti-nuclear antibody at 1/100. Human leukocyte antigen (HLA) typing was negative for the B51 locus. EBV, CMV, HIV, HBV and HCV serologies were negative. A slight monoclonal peak was found on serum protein electrophoresis. The beta 2 microglobulin serum level and myelogram were normal. The monoclonal IgG/kappa gammopathy found in immunoelectrophoresis was classified as monoclonal gammopathy of undetermined significance (MGUS). A thoraco-abdominopelvic CT scan was done and ruled out underlying malignancy.

Histological study of oral biopsies showed a nonspecific infiltrate of neutrophils in the lamina propria with exocytosis and without leukocytoclastic vasculitis (Figs. 5, 6). The skin biopsy showed a subcorneal pustule (Fig. 7) and a marked neutrophilic infiltrate in the absence of vasculitis consistent with neutrophilic dermatosis. The oral and cutaneous immunofluorescence studies were negative.

Bacteriological samples from skin pustules were negative.

Treatment with colchicine (Colchimax®) led to regression of oral and skin lesions in one week. Within several days the formation of new skin lesions ceased, followed by a marked improvement of eruptions. After 1 month, only sequelar cutaneous pigmented lesions remained. There were neither mucosal lesions nor lymphadenopathy. Colchicine treatment was continued for 4 months. Five months after having the colchicine stopped, the patient was hospitalized for recurrence of erosive oral lesions, which were again treated with colchicine.

Because of the slight fever, the neutrophilic infiltrate with inflammatory syndrome, and the rapid resolution of both oral and skin lesions with colchicine, the final diagnosis was Sweet’s syndrome with oral involvement.

**Discussion**

Neutrophilic dermatoses are disorders of stimuli and proliferation of neutrophils expressed by cellular skin infiltration without an identifiable infectious agent. SS is the most common type of ND and is characterized by a constellation of findings which include pyrexia, elevated neutrophil count, tender erythematous skin lesions (papules, nodules, pustules and plaques), and on the skin biopsy a diffuse infiltrate of mature neutrophils typically located in the upper dermis. It can also present as a pustular dermatosis [10]. The symptoms and clinical
manifestations typically respond promptly after initiation of systemic corticosteroid therapy [10].

Our patient met the criteria for SS developed by Su and Liu and modified by von den Driesch [11-12]. In addition to the two major criteria (abrupt onset of tender or painful erythematous or violaceous plaques or nodules and neutrophilic infiltration of the dermis without leukocytoclastic vasculitis), he had three minor criteria (elevation of the CRP level, leukocytosis and preceding slight fever) [2]. Like our case report, cases of SS with recurrent oral ulcerations were reported [1,4-7]. They had tender erythematous nodular or vesicle-like papular skin eruptions on both forearms [5], over the face, neck, palms and legs [4], multicentric erythema and pustules progressing to ulcers on the legs, face, trunk and extremities [7],
and erythematous plaques on the legs [6]. Painful oral lesions were present on the mucous membrane and the lower lip [7], and on the palate and the lower labial mucosa [6], associated with genital ulcers [4]. All had an inflammatory syndrome with an elevated C-reactive protein level. Like in our case, direct immunofluorescence tests were negative, as well as HLA typing for the B51 locus [5]. In the same way, cervical, axillary and inguinal lymph nodes were swollen and bacterial cultures from pustules and peripheral blood were negative [7]. Histopathological examination of an oral lesion at biopsy revealed a dense, perivascular, neutrophilic infiltrate without leukocytoclasis in the lamina propria. Histological examination of the skin biopsy showed dense infiltration containing numerous neutrophils in the upper and middle dermis. Edema and aggregates of neutrophils were common in the epidermis and upper dermis, but there was no vasculitis. Treatment with systemic prednisolone only [6] or associated with oral cyclosporine [5], or colchicine [4], led to remission.

The main differential diagnosis of SS is from Behçet’s disease [5]. Moreover, overlap exists between the manifestations of Sweet’s syndrome and Behçet’s disease, so they must be differentiated [7]. Differences between Behçet’s disease and SS include predominant skin involvement in SS, with oral ulcers in only 3-30% of cases [13], and a distinctive clinical course [14]. Genital ulcers are exceedingly rare in Sweet’s syndrome [12]. Among the extra cutaneous manifestations of SS, joint involvement, which is found in 33-62% of cases, consists chiefly of asymmetric polyarthralgia without joint destruction [15]. This pattern is different from the asymmetric oligoarthritis typically seen in Behçet’s disease. Ocular involvement is a major source of morbidity in patients with Behçet’s disease, since over 90% of patients experience posterior uveitis, anterior uveitis or retinal vascular involvement at some point in the course of the disease [16]. Finally, Behçet’s disease is associated with high frequencies of HLA-B51 and HLA-DQW3, and SS with a high frequency of HLA-BW54 [14]. In our case, the lack of typical ocular and skin lesions (pseudofolliculitis), the absence of oral aphthous ulcers and the occurrence of pustules over the tongue ruled out the diagnosis of Behçet’s disease. In addition, the rapid resolution within 1 week of oral ulcers at the beginning of colchicine treatment without any scarring was not in favor of aphthous lesions. Our patient’s condition was unlike aphthous stomatitis, in which the ulcers typically begin in childhood and affect mobile mucosae such as the labial and buccal mucosae [17]. The recurrence of oral ulcers with little inflammatory halo associated with pustules, as well as the histological patterns, were not compatible with oral squamous cell carcinoma.

The other differential diagnosis also includes PG and SW. In our case, PG was considered as a differential diagnosis because of the involvement of the oral cavity, which has been reported [8,18-9]. As there are no diagnostic features on biopsy, PG diagnosis is primarily clinical and often a diagnosis of exclusion [8]. The oral lesions are painful, can be anywhere in the mouth, and may appear as irregular-shaped ulcers with rolled-out margins and a grayish-colored base [18-20]. The histopathology of the oral lesions shows necrosis, ulceration
with an overlying fibrinopurulent membrane and heavy infiltration of the lamina propria with neutrophils [18]. PG lesions tend to endure, lasting months to years, and heal with an atrophic cribriform scar [2, 21]. PG was excluded because oral and skin lesion healing was quick without cribriform scarring and without significant necrosis. Sneddon-Wilkinson disease (SW) was considered as a differential diagnosis because of the MGUS, the purulent eruption which merged to form annular patterns, the histological feature of the skin lesions, the oral pustule, and because direct and indirect immunofluorescence studies were negative [3, 23-25]. We did not find in our case the vesiculopustular lesions characterized by the presence of “half-half” content (the purulent portion located in the lower region and the clear portion in the upper region). SW was finally excluded because the infiltrate was mostly in the dermis, it is more common in women in the age group 40-50 years, and because the face and mucous membranes are almost never affected [26].

Conclusion

The interest of this case lies in the oral involvement. Not only was it the reason for consultation and the cause of major symptoms, but it was also responsible for the difficulty in diagnosing Sweet’s syndrome. Faced with recurrent oral ulcers with cutaneous lesions, not only Behçet’s disease but also neutrophilic dermatoses must be suspected.

Conflicts of interests: none declared

Bibliography