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## Up-to date review and case report

# Sweet's syndrome revealed by oral pustulosis

Jean-Christophe Fricain[1,4,*], Vincent Sibaud[2], Sebastien Lepreux[3], Alain Taieb[4], Franck Boralevi[4], Jean-Marie d'Elbée[1]

[1] Department of Dentistry and Oral Health, University Hospital of Bordeaux, France
[2] Claudius Regaud institute, Toulouse, France
[3] Department of Pathology, University Hospital of Bordeaux, France
[4] Department of Dermatology, University Hospital of Bordeaux, France

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**Key words:** neutrophilic dermatosis / Sweet's syndrome / Behçet's disease / ulceration

**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.

**Mots clés :** dermatose neutrophilique / syndrome de Sweet / maladie de Behcet / ulcération

**Résumé – Introduction :** Les dermatoses neutrophiles sont caractérisées par une infiltration neutrophilique cutanée associée à une leucocytoclasie. Les manifestations orales sont rares et moins bruyantes qu'au niveau de la peau. **Observation :** Le cas d'un homme de 71 ans avec une dermatose neutrophile dont les principales manifestations de la maladie étaient des ulcères buccaux récurrents associés à une pustulose linguale est rapporté. Les biopsies buccales et cutanées ont révélé un infiltrat neutrophilique dense dans la *lamina propria*. Les symptômes cliniques ont été rapidement résolus avec de la colchicine. L'évolution clinique a permis de diagnostiquer un syndrome de Sweet associé à une pustulose orale. **Discussion :** Le principal diagnostic différentiel du syndrome de Sweet est la maladie de Behçet. Des chevauchements existent entre les manifestations cliniques des 2 entités. Mais celles-ci n'ont pas le même pronostic et doivent être différenciées. La récurrence des ulcères buccaux avec un discret halo inflammatoire, la résolution rapide des ulcères associés aux pustules ainsi que les aspects histologiques du cas décrit, n'étaient pas compatibles avec la maladie de Behçet.

## 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].

* Correspondence: jean-christophe.fricain@u-bordeaux2.fr





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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 (14,1x$10^9$/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.

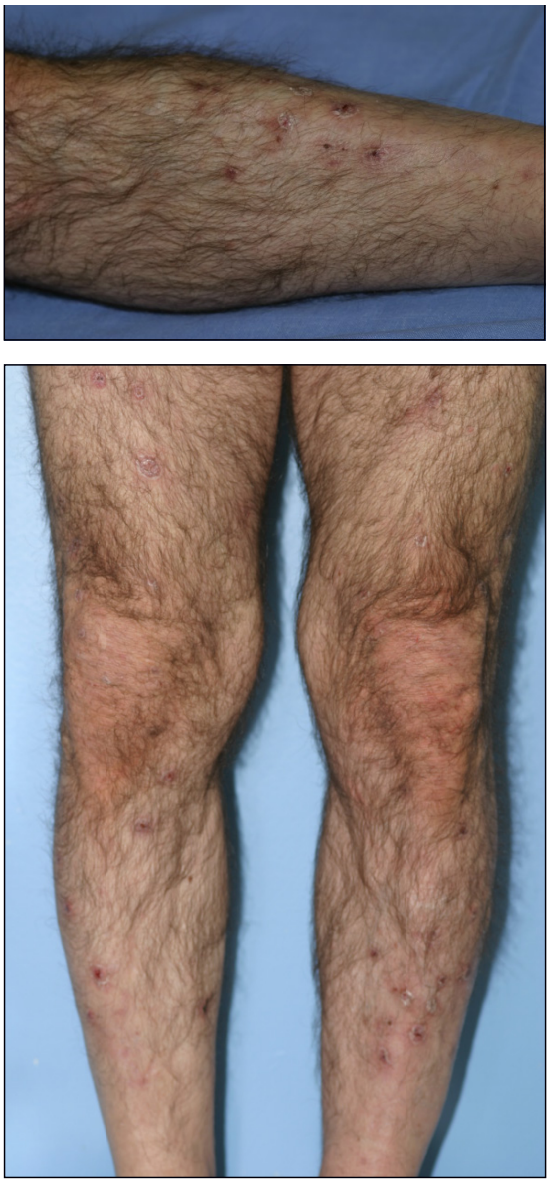

**Fig. 1.** Appearance of the skin lesions: diffuse pustulosis affecting the four limbs.
*Fig. 1. Pustulose affectant les 4 membres.*

## 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

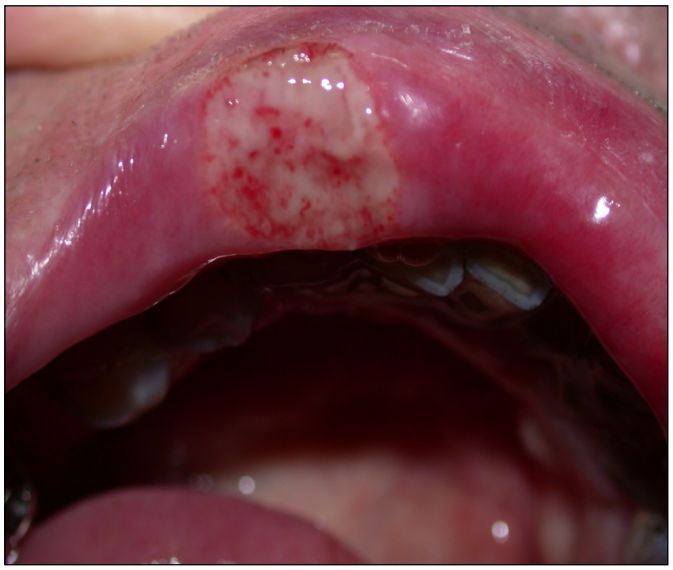

**Fig. 2.** Large and painful ulceration on the lower lip, with a white fibrinous base without a peripheral red halo.
*Fig. 2. Large ulcération de la lèvre inférieure sans halo érythémateux périphérique.*

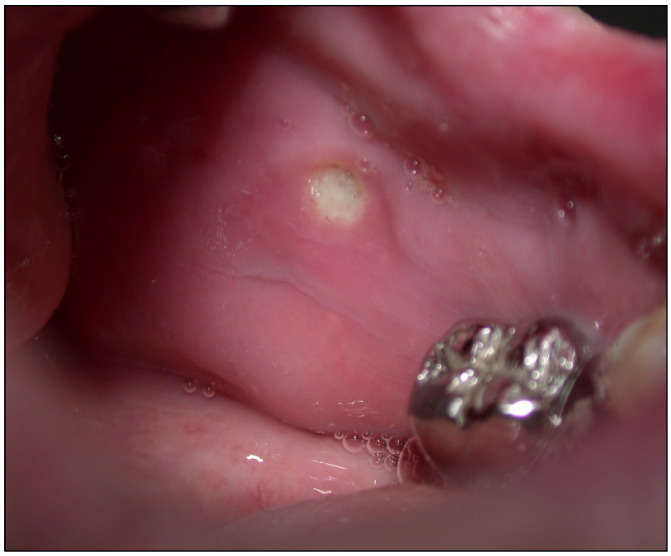

**Fig. 3.** Ulcerative lesion on the oral mucosae: a white-yellow fibrinous center without peripheral erythema.
*Fig. 3. Ulcération de la joue avec un fond fibrineux et une absence de halo périphérique.*

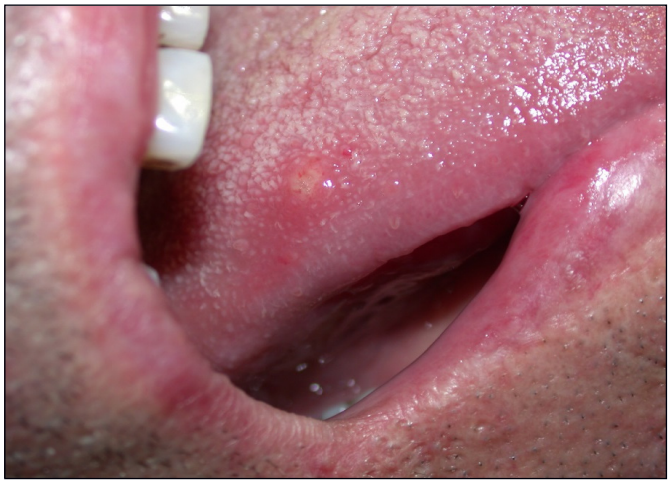

**Fig. 4.** Pustule on the tongue.
*Fig. 4. Pustule de la langue.*

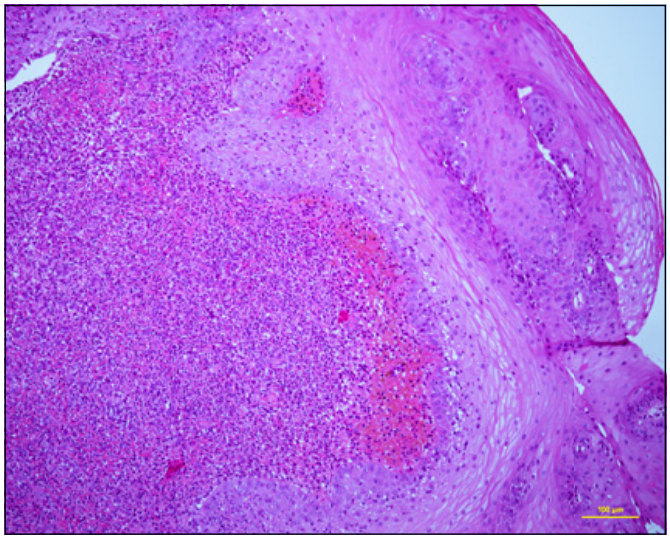

**Fig. 5.** Histological details of the mucosal biopsy of the pustule specimen revealing suppurative inflammatory infiltrate in the lamina propria (hematoxylin and eosin stain; magnification ×10).
*Fig. 5. Coupe histologique de la biopsie d'une pustule révélant l'infiltrat inflammatoire (coloration : hématoxyline et éosine, grandissement ×10).*

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],

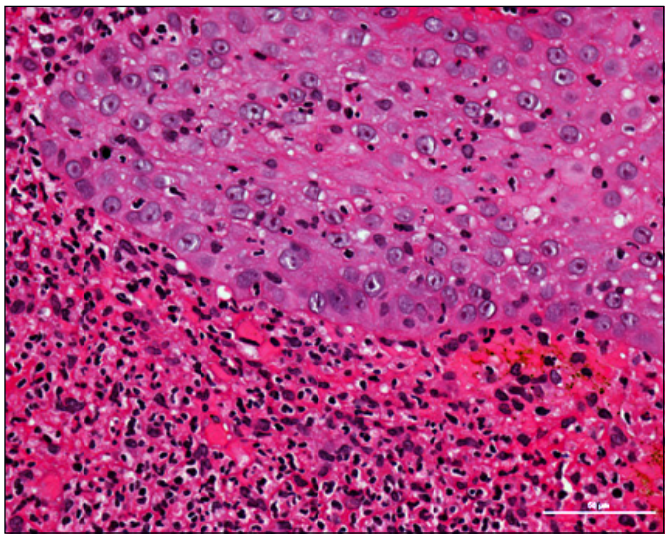

**Fig. 6.** Histological details of the mucosal biopsy specimen revealing neutrophilic infiltrate (hematoxylin and eosin stain; magnification ×40).
*Fig. 6. Détails histologiques révélant l'infiltrat neutrophilique (coloration : hématoxyline et éosine, grandissement ×40).*

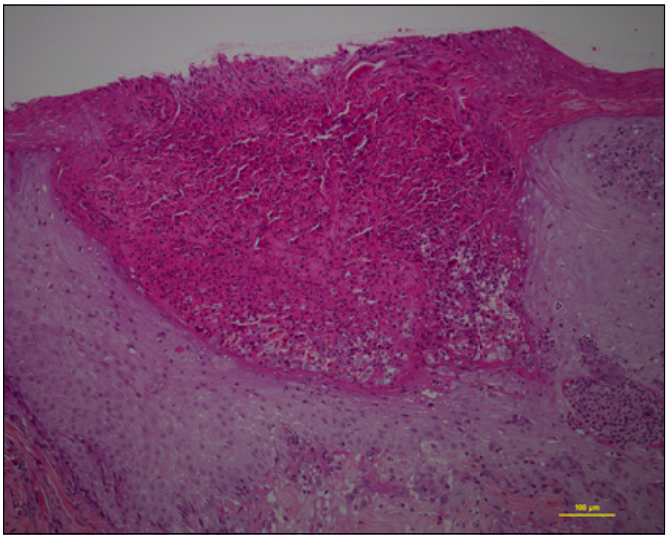

**Fig. 7.** Histological details of the skin biopsy revealing a subcorneal pustule (hematoxylin and eosin stain; magnification ×10).
*Fig 7. Coupe histologique révélant une pustule sous cornée (coloration : hématoxyline et éosine, grandissement ×10).*

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 leukocytoclastic vasculitis 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 pustular 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 dermatosis must be suspected.

**Conflicts of interests:** none declared

## Bibliography


1. Schadt CR, Callen JP. Management of neutrophilic dermatoses. Dermatol Ther 2012;25:158–72.
2. Dabade TS, Davis MD. Diagnosis and treatment of the neutrophilic dermatoses (pyoderma gangrenosum, Sweet's syndrome). Dermatol Ther 2011;24(2):273-84.
3. Razera F, Olm GS, Bonamigo RR. Neutrophilic dermatoses: part II. An Bras Dermatol 2011;86:195-209.
4. Hassikou H, Tabache F, Baaj M, Safi S, Hadri L. Sweet's syndrome in Behçet's disease. Joint Bone Spine 2007;74:495-6.
5. Femiano F, Gombos F, Scully C. Sweet's syndrome: Recurrent oral ulceration, pyrexia, thrombophlebitis, and cutaneous lesions. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2003;95:324-7.
6. Notani K, Kobayashi S, Kondoh K, Shindoh M, Ferguson MM, Fukuda H. A case of Sweet's syndrome (acute febrile neutrophilic dermatosis) with palatal ulceration. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2000;89:477-9.
7. Kato T, Kawana S, Takezaki S, Kikuchi S, Futagami A. A case of Sweet's syndrome with extensive necrosis and ulcers accompanied by myelodysplastic syndrome. J Nippon Med Sch 2008; 75:162-5.
8. Paramkusam G, Meduri V, Gangeshetty N. Pyoderma Gangrenosum with Oral Involvement – Case Report and Review of the Literature. Int J Oral Sci 2010;2:111-6.
9. Oguz O, Serdaroglu S, Tuzun Y, Erdogan N, Yazici H, Savaskan H. Acute febrile neutrophilic dermatosis (Sweet's syndrome) associated with Behçet's disease. Int J Dermatol 1992;31:645-6.
10. Cohen PR, Kurzrock R. Sweet's syndrome revisited: a review of disease concepts. Int J Dermatol 2003;42:761-78.
11. Su WPD, Liu HH. Diagnostic criteria for Sweet syndrome. Cutis 1986;37:167–74.
12. Von den Driesch P. Sweet's syndrome (acute febrile neutrophilic dermatosis). J Am Acad Dermatol 1994:31:535–56; quiz 557–60.
13. Roujeau JC. Dermatose aigüe febrile neutrophilique ou syndrome de Sweet. In: Kahn MF, Peltier A, Meyer O, Piette JC, Eds. Maladie et syndromes systémiques. Paris: Flammarion Medecine-Science, 2000, 1138-44.
14. Mizoguchi M, Chikakane K, Goh K, Asahina Y, Masuda K. Acute febrile neutrophilic dermatosis (Sweet's syndrome) in Behçet's disease. Br J Dermatol 1987;116:727-34.
15. Lee MS, Barnetson RS. Case report. Sweet's syndrome associated with Behcet's disease. Australas J Dermatol 1996;37:99-101.
16. Hamza M. Maladie de Behçet. In: Kahn MF, Peltier AP, Meyer O, Piette JC, Eds. Maladies et syndromes systémiques. 4e ed. Paris: Flammarion Médecine-Science, 2000, 882-924.
17. Porter SR, Hegarty A, Kaliakatsou F, Hodgson TA, Scully C. Recurrent aphthous stomatitis. Clin Dermatol 2000;18:569-78.
18. Setterfield JF, Shirlaw PJ, Challacombe SJ, Black MM. Pyoderma gangrenosum associated with severe oropharyngeal involvement and IgA paraproteinaemia. Br J Dermatol 2001;144:393-6.
19. Hiromi T. Case of pyoderma gangrenosum showing oral and genital ulcers, misdiagnosed as Behçet's disease at first medical examination. J Dermatol 2008;35:289-92.
20. Yusuf H, Ead RD. Pyoderma gangrenosum with involvement of the tongue. Br J Oral Maxillofac Surg 1985:23:247-50.
21. Bennett ML, Jackson JM, Jorizzo JL, Fleischer AB Jr, White WL, Callen JP. Pyoderma gangrenosum. A comparison of typical and atypical forms with an emphasis on time to remission. Case review of 86 patients from 2 institutions. Medicine 2000;79:37-46.
22. Su WP, Davis MD, Weenig RH, Powell FC, Perry HO. Pyoderma gangrenosum: clinicopathologic correlation and proposed diagnostic criteria. Int J Dermatol 2004:43:790-800.
23. Kasha EE, Epinette WW. Subcorneal pustular dermatosis in association with a monoclonal IgA gammopathy. A report and review of the literature. J Am Acad Dermatol 1988;19:854-8.
24. Lutz ME, Daoud MS, McEvoy MT, Gibson LE. Subcorneal pustular dermatosis: a clinical study of ten patients. Cutis 1998;61: 203-8.
25. Berk DR, Hurt MA, Mann C, Sheinbein D. Sneddon–Wilkinson disease treated with etanercept: report of two cases. Clin Exp Dermatol 2008;34:347–51.
26. Cheng S, Edmonds E, Ben-Gashir M, Yu RC. Subcorneal pustular dermatosis: 50 years on. Clin Exp Dermatol 2008;33:229–33.