HERPES SIMPLEX – TRIGGER FACTOR FOR BEHCET DISEASE

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Summary

Introduction: *Behcet's disease is a multisystemic inflammatory condition, with unknown etiology. Most common clinical manifestations include painful oral mucosa ulcerations, painful genital mucosa ulcerations, cutaneous lesions and ocular lesions. Positive HLA-B51 antigen is a well-known risk factor. The etiopathogenesis of the disease includes bacterial, viral and environmental factors.*

Case report: *We report the case of a 24-year-old female patient, from urban area, who presented to our clinic for painful polymorphic cutaneo-mucosal lesions. Skin assessment revealed multiple painful oral and genital mucosa ulcerations, as well as upper chest pustules and pretybial bilateral subcutaneous nodules. Ophtalmological examination identified conjunctival hyperemia, right palpebral edema and photophobia. Laboratory findings revealed leukocytosis with neutrophilia, elevated erythrocite sedimentation rate (ESR) and positive rheumatoid factor (FR). Bacteriological and micological tests performed from the lesions were negative. Serological tests were performed and IgM anti herpes simplex virus type 1 (Ig M anti HSV-1) and IgM anti herpes simplex virus type 2 (IgM anti HSV-2) were identified. The patient followed systemic treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) and local treatment with a combination of steroidal and antibiotic cream. Clinical evolution was favorable, with complete resolution of lesions in approximatively 1 week.*

Conclusions: *The possible viral etiology of Behcet's disease is a long investigated topic. Complete evaluation and multidisciplinary follow-up of these patients is vital in the approach of these cases.*

Keywords: *Behcet, ulceration, erythema nodosum, anterior uveitis, herpes simplex.*

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Introduction

Behcet's disease is a multisystemic inflammatory condition, with unknown etiology. Most common clinical manifestations include painful ulcerations of the oral mucosa, painful ulcerations of the genital mucosa, cutaneous lesions (erythema nodosum, acneiform lesions, pustules, pseudofolliculitis, rarely cutaneous ulcerations) and ocular lesions (panuveitis, anterior uveitis). Uncommon symptoms of the disease include gastrointestinal (abdominal pains, nausea, vomiting), articular (arthralgias, arthritis, synovitis) and neurological problems (headache, dysarthria, ataxia). The clinical evolution is characterised by recurrent attacks and disease-free periods. The mean age of onset is in the 3rd decade of life, males being more prone to Behcet's disease than females [1]. Positive HLA-B51 antigen is a well-known risk factor. The ethiopathogenis of the disease is not completely known and involves genetical and environmental triggering factors. Bacterial agents (Streptococci, Helicobacter pylori), viral agents, some chemicals and heavy metals are linked to this disease [2]. This article aims to present a rare case of Behcet's disease in a young female patient triggered by a viral infection.

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Case report

We report the case of a 24 year-old female patient, from urban area, who was admitted to our clinic for painful polymorphic cutaneo-mucosal lesions.

Dermatological examination revealed oral mucosa ulcerations, genital mucosa ulcerations, subcutaneous pretybial nodules and upper chest pustules. Multiple painful oral ulcerations were identified on the buccal and gingival mucosa and were characterised by well-defined borders, perilesional erythema and white pseudo-membranes. Two genital ulcerations with under 1 cm in diameter and one larger than 1 cm in diameter were observed on the genital mucosa, characterised by punched-out aspect and yellow exudate covering the base of the ulcerations. On the upper chest, an erythematous plaque presenting with pustules was identified. Painful and tender bilateral erythematous subcutaneous nodules were found on pretybial areas. The lesions have been present for 5 days.

Clinical examination revelead slightly altered general condition, moderate weakeness in arms and legs muscles,conjunctival hyperemia and right palpebral edema. The patient complained of photophobia, ocular pain and slightly blurred vision. No lymphadenopathy or fever were detected.

Laboratory findings revealed leucocytosis with neutrophilia (14.26 x 10^3/μL, normal range: 4-10 x 103/μL; 81.28%, NR: 40-75%), lymphopenia (11.45%, NR: 20-45%), trombocitosis (504.70 x 103/μL, NR: 150-400 x 103/μL), elevated ESR (80 mm/h, NR: 0-12 mm/h) and positive rheumatoid factor (FR). Serological tests were performed and IgM anti HSV-1 (26.82 units U, NR: 0-9 U), as well as IgG anti HSV-1 (45.92 U, NR: 0-9 U) and IgM anti HSV-2 (12.76 U, NR: 0-9 U) were identified. Bacteriological and micological tests performed from the lesions were negative. Sexually transmited diseases were also excluded based on the laboratory tests performed. A suspicion of Behcet disease was raised.

The ophtalmology exam established the diagnosis of right eye anterior uveitis. Gyneco-

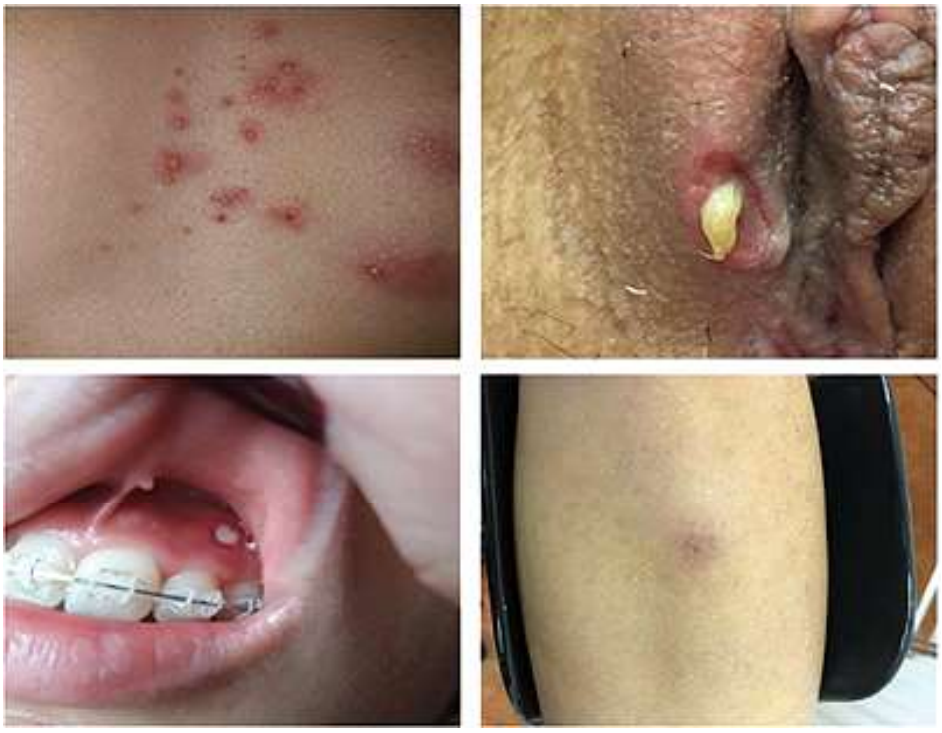

Figure 1. Lesions appearance before the treatment.

Figure 2. Lesions appearance after the treatment.

logical examination did not detect any pathological findings at the assessment of internal genitalia.

The International Criteria for Behcet's Disease (ICBD) from 2014 was used for positive diagnosis. Ocular lesions, genital mucosa ulcerations and oral mucosa ulcerations were each assigned 2 points, whereas 1 point was assigned to each of skin lesions (pustules, subcutaneous nodules). A final score of 8 points was calculated, which supports the diagnosis of Behcet's disease.

Disease activity was assessed using Behcet's Disease Current Activity Form. One point was given to each cutaneo-mucosal manifestation (genital ulcerations, oral ulcerations, erythema, pustules) and to the general signs, whereas the ocular involvement was assigned 1 point. A total score of 7 points was calculated and a transformed index score on interval scale of 11 points.

Taking into consideration the clinical and laboratory findings, as well as the total score of 8 points according to the ICBD criteria and after carefully considering the most likely differential diagnoses, we established the diagnosis of Behcet's disease triggered by HSV-1 reactivation and HSV-2 activation. The patient followed systemic treatment with NSAIDs 400 mg b.i.d and topical treatment with a combination of corticosteroid and antibiotic cream (hydrocortisone acetate + fusidic acid) b.i.d. Under treatment, general and local evolution were favorable, with complete remission of all cutaneo-mucosal lesions in one week.

Discussions

Behcet's disease, described in 1937 by the Turkish dermatologist Hulusi Behcet, represents a multsystemic inflammatory condition, whose ethipathogenesis is linked to genetical and environmental triggering factors. Characterised by oral mucosa ulcerations, genital mucosa ulcerations, cutaneous and ocular lesions, this pathology is more often found in the Middle and Far East, but sporadic cases are encountered in other regions as well. Its clinical evolution, with periods of relapse and remission distinguishes Behcet's disease from other vasculitides.

Clinical studies take into consideration the role of infectious and environmental factors in the pathogenesis of the disease. A possible viral etiology was first postulated by Behcet in 1937. Among the viruses, HSV-1 is the main virus for which an association has been observed. Other viral agents, such as Epstein-Barr virus [3], varicella zoster virus, parvovirus B19 [4] and hepatitis C virus [5] may have a role in triggering this disease. Bacterial agents, such as various species of Streptococcus [6,7], Mycobacteria, Helicobacter Pylori [8] and Escherichia Coli and organic chlorine compounds, organic phosphorus compunds and inorganic copper powder [9] are also mentioned as possible triggering factors.

Elevated levels of anti HSV-1 and anti HSV-2 antibodies have been described in several studies in a significantly higher proportion in patients with Behcet's disease compared to controls [10,11].

Experimental studies use laboratory mice to induce the symptoms of Behcet's disease. Cutaneous-mucosal ulcers, eye and joint lesions, and histopathological changes after HSV-1 inoculation were similar to those seen in patients with Behcet's disease [12].

Sugata et. al [13] reported in 2007 the case of a female patient who developed the incomplete form of Behcet's disease, triggered by the reactivation of HSV-1 virus. An increased number of HSV-1 viral copies was identified in samples collected from the lesions. A similar observation was made by Ju et al. [14] who noted the association between anti HSV-2 antibodies and the onset of Behcet's disease. In our case, we observed the association between IgM antibodies against HSV-1 and IgM antibodies against HSV-2 and the occurence of Behcet's disease symptoms.

The ICBD criteria [15], used since 2014 for the diagnosis of Behcet's disease, involve assigning a certain number of points for each manifestation of the disease. Thus, two points are given for ocular lesions, genital ulcerations and oral ulcerations, whereas one point is assigned for each type of skin lesions, as well as for neurological and vascular manifestation. If the patthergy test is conducted and the result is positive, an additional point is added. A total score higher or equal to 4 points is necessary to establish the diagnosis. The main advantage of these criteria is that they permit the early diagnosis and a positive pattergy test is no longer mandatory for diagnosis.

Existing data on the treatment of Behcet's disease with a triggering viral factor are limited. Acyclovir treatment does not affect the evolution of orogenital ulcerations [16], but famciclovir has proved to be effective in improving symptoms and preventing relapses [17]. Our patient responded favorably to treatment with NSAIDs.

Regarding the ocular damage, Tugal-Tuktun [18] mentions that although most patients present with nongranulomatous panuveitis and retinal vasculitis, a small number of patients, especially females, may develop strictly unilateral anterior uveitis. In addition, if the patient presents with strictly anterior uveitis, the prognosis of eye lesions is better and systemic therapy is not required. This observation is consistent with the lesions presented by our patient.

The clinical appearance, with the presence of oral and genital ulcerations, ocular and cutaneous lesions, and the ICBD score of 8 points allow the presented case to be classified as Behcet's disease. The increased titer of IgM and IgG anti HSV-1 antibodies, IgM anti HSV-2 antibodies, as well as the favorable outcome to the established treatment support the hypothesis that herpes simplex virus infection is a trigger of Behcet's disease in our case.

Conclusions

The viral etiology of Behcet's disease is a long-investigated topic. Treatment options for this condition are limited, therefore a better understanding of the pathogenesis could provide more effective therapeutic strategies.

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Conflict of interest
NONE DECLARED

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