An atypical vascular case of Behçet’s disease and consequent treatment

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Behçet’s disease (BD) is a multisystem inflammatory disorder of unknown aetiology whose basic pathologic process consists of non-specific vasculitis of veins, arteries and capillaries in all affected organs. It is characterized by recurrent oral and genital aphthous ulcers, uveitis, skin lesions and other symptoms affecting the gastrointestinal tract, central nervous and respiratory systems, blood vessels (arterial aneurysm, arterial occlusion, thrombophlebitis, deep vein thrombosis) and kidneys. Since there is no pathognomonic diagnostic test, BD is ascertained through diagnostic criteria (Table 1) [1].

Although not included in the general BD diagnostic criteria, vascular BD occurs in 25% of patients [2]. When thrombosis is present, it is more commonly venous than arterial (88 vs 12%), and to date no overall agreement has been reached on the optimal treatment of venous thrombosis in BD.

We are reporting the following case of BD with venous vascular involvement to highlight two points:

1. the importance of a complete history and physical examination in order to ensure a correct diagnostic approach, especially to detect rare diseases;
2. a discussion of the correct treatment for superficial thrombophlebitis in BD, when two thrombophilic factors coexist.

In November 2006 a 24-year-old man presented with fever associated with pharyngotonsillitis, oral aphthae and genital ulcerations. Corticosteroids and amoxicillin/clavulanic acid were prescribed, and the symptoms apparently ceased. One month later the patient returned with ankle arthralgia, cutaneous erythematous-nodular lesions and bilateral superficial thrombophlebitis of the legs. An angiologist prescribed s.c. enoxaparin 6,000 IU o.d. for 20 days.

One month following the end of this treatment, the patient presented again with recurrence of superficial thrombophlebitis. Since thrombophilic screening showed factor V Leiden heterozygous mutation and hyperhomocysteinaemia (25 mmol/l), it was decided to prescribe warfarin in consideration of the presence of these two risk factors along with the recurrence of thrombophlebitis.

A few weeks later, fever recurred along with cutaneous lesions consistent with erythema nodosum, as a result of which the patient was admitted to our Department of Internal Medicine. Signs of inflammation were given by atypical findings (ESR 58 mm/h, CRP 5.8 mg/dl, fibrinogen 829 mg/dl) while other common blood tests were normal. Autoimmune diseases were excluded by ANA, ENA, Anti-dsDNA, ANCA, Ra-test, C3, C4, and circulating immune complex results. The serological and culture tests excluded significant infectious diseases (Streptococcus beta Haemolyticus, HIV, HBV, HCV, EBV, CMV, urethral and pharyngeus tampon, Ab. anti Yersinia, Salmonella, Campylobacter, Neisseria, Borrelia, Mycoplasma, Ureaplasm, and Shigella). The oral aphthae and superficial thrombophlebitis recurred while the patient was hospitalized.

This evidence led us to suspect Behçet’s disease, and was followed by a positive pathergy test and a dermatologic biopsy consistent with vasculitis. However, neither pathological ocular anomalies nor cerebral, thoracic or abdominal aneurysms were found.

Corticosteroid therapy (prednisone 25 mg) solved all clinical symptoms and reduced inflammatory signs;
however, upon reduction of the therapy, oral aphthae and superficial thrombophlebitis reappeared. Having established that the symptoms were prevalently muco-cutaneous and venous, we commenced immunosuppressive therapy with colchicine and topical corticosteroids in association with systemic corticosteroids. Once the disease was well under control, the systemic corticosteroids were suspended. Although the patient’s thrombosis was superficial rather than DVT, nevertheless there coexisted two thrombophilic factors (heterozygous V Leiden factor mutation and hyperhomocisteinemia).

Several studies propose ranking the differing thrombophilic factors contributing to the potential development of thrombosis in BD patients, yet few correlations have so far been found with the clinical occurrence of thrombosis [2]. In Italy no relationship has been established between V Leiden factor, prothrombin mutation G20210A and thrombosis in BD [3].

Hyperhomocysteinaemia, instead, is a documented independent risk factor for the development of thrombosis in BD [4] and correlates with BD activity [5], although it is true that this is a risk factor that can be kept under control. As such, hyperhomocysteinaemia may be able to assume a key role in explaining BD vascular damage, and open new approaches to thrombosis treatment.

Although treatment of DVT in BD is still being debated, nevertheless it is known that anticoagulants alone are ineffective and must be supported with anti-inflammatory and immunosuppressive therapy [6]. When the thrombophlebitis is superficial, oral anticoagulants are known to be unnecessary while the treatment of choice appears to be with LMWH since they have been proven to prevent VTE and spreading or recurrence of superficial thrombophlebitis [7].

Table 1

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<th>Manifestation</th>
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<td>Recurrent oral ulceration</td>
<td>Minor aphthous, major aphthous or herpetiform ulcers observed by a physician or reported reliably by patient, recurrent at least three times in one 12-month period</td>
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<td>Plus any two of the following findings:</td>
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<td>Recurrent genital ulceration</td>
<td>Recurrent genital aphthous ulceration or scarring, observed by a physician or reported reliably by patient</td>
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<td>Eye lesions</td>
<td>Anterior uveitis, posterior uveitis or cells in vitreous on slit-lamp examination; or retinal vasculitis observed by qualified physician (ophthalmologist)</td>
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<td>Skin lesions</td>
<td>Erythema nodosum-like lesions observed by a physician or reported reliably by patient, pseudofolliculitis, or papulopustular lesions; or acneform nodules observed by physician in postadolescent patients not receiving corticosteroids</td>
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<td>Positive Pathergy test</td>
<td>The interpreted as positive by a physician at 24–48 h, performed with oblique insertion of a 20-gauge or smaller needle under sterile conditions</td>
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On the basis of these considerations, warfarin therapy was withdrawn and replaced with enoxaparin for 20 days, with folic acid simultaneously administered to lower the patient’s hyperhomocysteinaemia.

One year later the patient continues to take colchicine and folic acid: he is currently asymptomatic, with blood indicators of inflammation and homocysteine levels normal and no further vascular complaints.

Conflict of interest statement  The authors declare that they have no conflict of interest related to the publication of this manuscript.

References