



Arterial and venous involvement in Behçet's syndrome: a narrative review

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Abstract

Behçet syndrome (BS) is a unique type of vasculitis that affects veins and arteries of all sizes, leading to recurrent vascular events, mostly venous thrombosis. The prevalence of venous thromboembolism in BS patients ranges between 15 and 40%. Thrombosis is usually an early manifestation leading to diagnosis of BS in up to 40% of patients. BS is per se a model of inflammation-induced thrombosis. The primary autoimmune response activates lymphocytes that in turn produce a cytokine cascade that activates neutrophils, which modify the secondary structure of fibrinogen making it less susceptible to plasmin-induced lysis. This leads to endothelial dysfunction, platelet activation and overexpression of tissue factor leading to inflammatory thrombi, usually attached to the wall. The pathogenesis of thrombosis is especially relevant to direct the specific treatment, that is based on immunosuppression rather than anticoagulation. Superficial vein thrombosis (SVT) and deep vein thrombosis (DVT) are the most common form of thrombosis in BS, but thrombosis in atypical sites (cava vein, suprahepatic veins, intracardiac thrombus) and arterial involvement can also occur. We assessed the latest update of the European League Against Rheumatism recommendations for the management of BS. Vascular Behçet treatment is usually based on immunosuppressants, and the role of anticoagulation remains controversial. The use of interventional and surgical procedures should be carefully evaluated, due to the risk of triggering a vascular pathology phenomenon.

Keywords Behçet's syndrome · Venous thromboembolism · Venous thrombosis · Thrombosis

Highlights

- The importance of vascular involvement lies on its high frequency among BS patients (15–40%) and high rates of recurrences (30–50%).
- Vascular involvement is the main predictor of morbidity in BS.
- Vascular involvement is an early manifestation of the disease, emerging frequently before the diagnosis criteria have been fulfilled.
- Deep vein thrombosis should be treated with glucocorticoids and immunosuppressants in BS patients. The role of anticoagulation remains controversial.

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Introduction

Behçet's syndrome (BS) is a complex condition of unknown etiology that generally affects mucosa and skin but. However, the eyes, joints, blood vessels, central nervous system and gastrointestinal tract might also be affected [1]. BS has a peculiar geographic distribution in Mediterranean countries (Turkey has the highest prevalence, up to 42 per 10,000), Middle-East and Far-East [1]. The onset of BS usually occurs in third decade and both genders are equally affected, with more severe course among men [1–3].

Since a syndrome describes a collection of signs and symptoms that usually occur together and might not always have a definite cause, Behçet should be considered a syndrome rather than a disease [1, 4]. Based on the tendency of certain features to be associated, several phenotypes (or “clusters”) of BS might be distinguished [1, 5, 6], including skin-mucosa involvement alone, joint involvement, vascular involvement, eye involvement and parenchymal neurological involvement [1].

BS is a multifactorial condition with an unknown etiology. Previously considered an autoimmune disorder, BS shows no sex differences is not usually related with other autoimmune conditions. It seems reasonable to consider BS a polygenic autoinflammatory disease [6]. Pro-inflammatory IL-1 β levels are increased in patients with active BS; also, some variants of the Mediterranean Fever gene and genes encoding Toll-like receptors have been described [6]. An association with the Human Leukocyte Antigen (HLA) B51 has been described, and it is considered a risk factor present in 60% of cases of BS, suggesting a genetic predisposition in some cases [6, 7]. However, its presence alone cannot explain the pathophysiology of BS [6]. This led to the concept “MHC-opathy” [6, 8], which could explain some clusters of BS, but not all the spectrum of the syndrome. Classically, the prevalence of BS has been higher in the Silk Route, but due to migration it spread to other countries [6]. In that way, environmental factors might modify its clinical expression, due to environment-gene interaction [6]. Epigenetics have been proved to be important in BS, since some methylation patterns might be useful as biomarkers or therapeutic targets. The role of epigenetics in the geographical and environmental differences of BS needs to be clarified [6].

Diagnosis of BS is clinical and there are no laboratory, histological or imaging tests that might help [1]. Clinical criteria for the diagnosis have been established, including oral and genital aphthosis, ocular lesions, skin lesions, neurological and vascular manifestations. The course of the disease is characterized by frequent relapses and spontaneous remissions, which are usually more active during the first years of BS and tend to decrease over time [1]. BS can cause important morbidity, including physical disability, cognitive

impairment and blindness; besides, an increased mortality has been described, associated with vascular involvement [2].

Vascular tree involvement in BS occurs in a subgroup of patients who suffer from recurrent inflammatory thrombosis involving veins and, more rarely, arteries. Specific diagnostic and management strategies might be required in these patients [9]. Of note, vascular manifestations are the main predictor of mortality and morbidity in BS [10].

Epidemiology of vascular involvement in BS

Around 20–40% of venous involvement in BS patients has been reported [3], being more frequent in men [2], with a 14-fold increased risk of venous thrombosis [11]. Venous thrombosis in BS presents mainly as deep vein thrombosis (DVT) of lower extremities, but other vascular territories such as cerebral venous sinus, pulmonary artery and vena cava might also be affected [2, 7]. On the other hand, arterial involvement, although affecting only 3–5% of patients, represents a unique feature of BS, with aneurysms affecting peripheral, visceral and pulmonary territories [9].

Histological features and pathophysiology of vascular involvement in BS

BS is a unique vasculitis since the entire vascular tree might be compromised, including both veins and arteries of all sizes [12]. The vascular involvement includes neutrophil and lymphocyte infiltrates predominantly around the vessels, without granulomatous inflammatory lesions [9]. Fibrous thickening in all layers of the vessel wall and aneurysm formation (particularly in the pulmonary arteries) are often seen in biopsies of patients with vascular affection [13], and no increased risk of atherosclerosis compared to other inflammatory diseases has been reported [14].

The pathogenesis of vascular involvement (Fig. 1) consists of inflammatory thrombi formation that is usually attached to the inflamed vessel wall, a phenomenon also known as “thromboinflammation” [2]. Correlation between inflammatory response and thrombosis is the result of endothelial dysfunction, tissue factor overexpression and platelet activation mediated by cytokine production (Th1 phenotype: TNF (tumor necrosis factor) α , IL (interleukin)1, IL-6, and Th17 phenotype: IL-17), or by molecules that activate neutrophils chemotaxis (CXCL [chemokine ligand] 8 and G-CSF [granulocyte colony-stimulating factor]) and by the interaction of fibrinogen, thrombin, factor Xa and factor VIIa with immune cells through integrins, Toll like receptors and PARs (protease-activated receptor) 1,2,3,4 [9]. Neutrophils have an

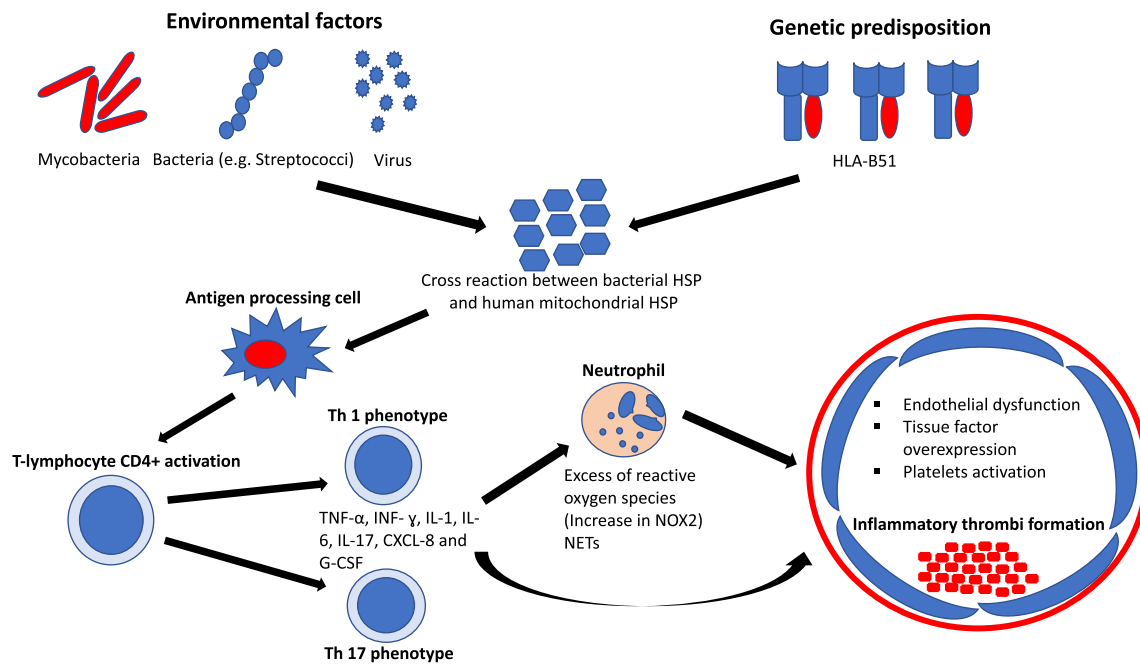


Fig. 1 Pathophysiology of vascular involvement in Behçet's syndrome. *HSP* heat shock protein; *TNF- α* tumor necrosis factor alpha; *INF- γ* interferon gamma; *IL-1* interleukin-1; *IL-6* interleukin-6; *IL-*

17 interleukin-17; *CXCL-8* chemokine ligand 8; *G-CSF* granulocyte colony-stimulating factor; *NOX2* NADPH oxidase 2; *NETs* neutrophil extracellular traps

important role in the pathogenesis of thrombosis, through NADPH oxidase (specifically NOX2), mediated by an excess of reactive oxygen species (ROS) that modify the secondary structure of fibrinogen making it less susceptible to plasmin-induced lysis [9, 15]. Programmed neutrophil death releases granules or structures that kill extracellular microorganisms such as adenylated chromatin, also called Neutrophils Extracellular Traps (NETs). NETs are implicated in maintaining inflammation and causing vascular damage seen in BS [16]. These findings suggest that BS is per se a model of inflammation-induced thrombosis [17].

Venous thrombosis

Vascular involvement includes venous and arterial territory. DVT and superficial venous thrombosis (SVT) of lower limbs are the most frequent manifestations of venous involvement [9]. VTE typically affects males in the fourth decade of life and it is usually an early manifestation (5 years within the disease onset) [2] leading to diagnosis of BS in up to 40% of patients [1, 7]. Erythema nodosum, fever and constitutional symptoms are associated with a higher risk of VTE [7]. Approximately 30–50% of patients with vascular BS have recurrent vascular episodes, with a mean of 1.1–2.2 episodes per patient [7, 18–20].

There are no tools to identify BS patients at higher risk for venous thrombosis. In a recent study [21], venous wall

thickness (VWT) was significantly higher in BS patients compared to ankylosing spondylitis patients and healthy controls, and the measures were higher in BS patients with vascular involvement. Seyahi et al. [22] demonstrated that VWT is increased in BS, with venous wall inflammation being a key feature. Therefore, VWT measurement might be useful to identify patients (mainly young males) presenting with a first idiopathic episode of VTE who are at risk of developing BS.

Here, we review both the typical venous involvement in BS (superficial and deep venous thrombosis) and the thrombosis in atypical sites. Figure 2 and Table 1 summarize the management of vascular involvement in BS.

Superficial and deep vein thrombosis

SVT and DVT are the most common vascular manifestation in BS, accounting for up to 70% of vascular Behçet [9]. SVT and DVT can affect superior or, most commonly, lower limbs. Long-term complications are frequent, leading to moderate or severe post thrombotic syndrome (PTS) in up to 25%, especially in patients with recurrent DVT [7, 9, 23, 24]. If anticoagulation is initiated in BS patients, a thoracic computed tomography should be performed to rule out pulmonary artery aneurysms due to the high risk of bleeding [23, 25].

In the latest update of the European League Against Rheumatism (EULAR), all the recommendations regarding

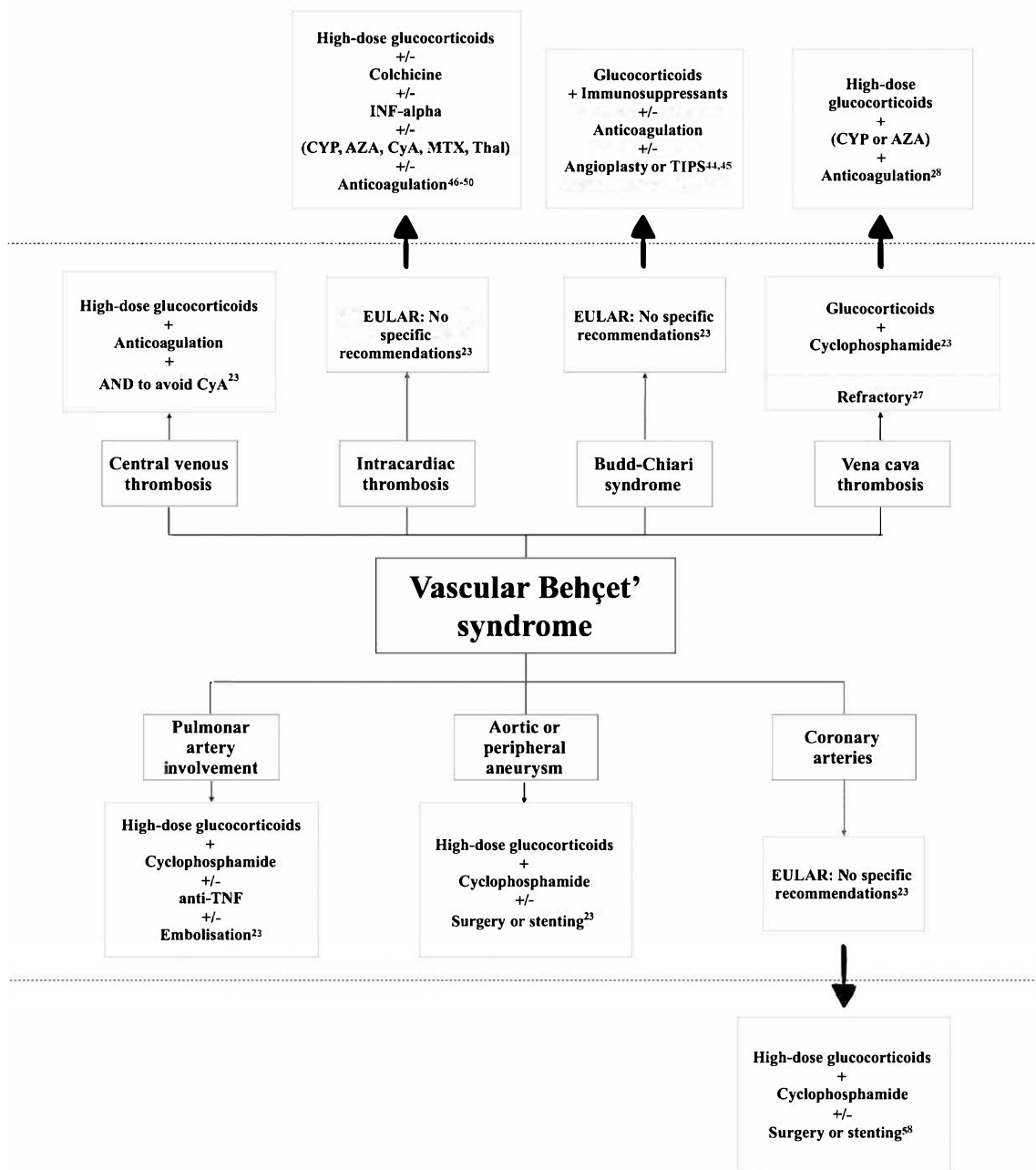


Fig. 2 Treatment of venous thromboembolism in atypical sites and arterial involvement in Behçet's syndrome [23]. *IFN* interferon; *CYP* cyclophosphamide; *AZA* azathioprine; *CyA* cyclosporine A; *MTX*

methotrexate; *Thal* thalidomide; *Anti-TNF* anti-tumor necrosis factor; *EULAR* European League Against Rheumatism

vascular Behçet (acute DVT, refractory venous thrombosis and arterial involvement) were based in scarce evidence (level of evidence III, strength of recommendation C) [23]. DVT in BS should be treated with glucocorticoids and immunosuppressants (IS) as azathioprine, cyclophosphamide or cyclosporine A, with no data to mandate the preference of one IS agent over the others [23].

DVT in BS is the result of inflammation of the vessel wall rather than hypercoagulability, which questions the role of anticoagulation in these patients [23]. A meta-analysis of three retrospective studies analyzed the efficacy of IS and/or anticoagulation for preventing DVT recurrences [9, 19, 26, 27]. The risk of VTE recurrence was higher in patients treated with anticoagulation alone compared to those treated with IS plus anticoagulation and compared to those with IS

Table 1 Treatment of vascular Behçet's syndrome

	SVT/DVT	VC thrombosis	BCS	ICT	CVST	PAI	Other arteries
<i>Medical treatment</i>							
Corticosteroids pulses [6, 23, 28, 42, 45, 49, 50, 52, 55, 61]	–	Methylprednisolone 1 g/day IV during 3 days	Methylprednisolone 0.5–1 g/day IV during 3 days	Methylprednisolone 1 g/day IV during 3 d Dexamethasone 40 mg/day during 3 d	Methylprednisolone 1 g/day IV during 5–7 d	Methylprednisolone 1 g/day IV during 3 d	Methylprednisolone 0.5–1 g/day IV during 3 d (prior and after surgery)
Corticosteroids [6, 19, 23, 27, 28, 41, 45, 49, 50, 52, 55, 61, 66]	0.5–1 mg/kg daily	1 mg/kg daily	0.5–1 mg/kg daily	1 mg/kg daily	1 mg/kg daily	1 mg/kg daily	1 mg/kg daily
Cyclophosphamide [6, 19, 23, 27, 28, 32, 39, 42, 45, 49]	500–1000 mg/monthly, 6–9 pulses IV	*500–1000 mg monthly 6–9 pulses IV	*500–1000 mg monthly 6–9 pulses IV	*500–1000 mg monthly 6–9 pulses IV	Not IS in first episode	*1000 mg monthly 6–9 pulses IV	1000 mg monthly 6–9 pulses IV [§]
Azathioprine [19, 21, 23, 26, 27, 32, 42, 45, 49, 57, 61, 64]	1–2.5 mg/kg/day	♦2–2.5 mg/kg/day	♦2–2.5 mg/kg/day	♦2–2.5 mg/kg/day	Not IS in first episode	♦2–2.5 mg/kg/day	2–2.5 mg/kg/day [§]
Methotrexate [19, 27, 42]	15–25 mg weekly	–	–	15 mg weekly	–	–	–
Cyclosporine A [26, 42, 49, 50]	3–5 mg/kg/day	–	–	3–5 mg/kg/day	Not recommended in CNS involvement	–	–
Interferon alpha [19, 27, 50]	3 MIU daily	–	–	9 MIU three times per week >> 5 MIU three times per week	–	–	–
Infliximab [19, 32]	*3–5 mg/kg every 8 weeks IV	*5 mg/kg/day every 8 weeks IV	*5 mg/kg/day every 8 weeks IV	*5 mg/kg/day every 8 weeks IV	–	*5 mg/kg/day every 8 weeks IV	–
Adalimumab [32, 34]	*40 mg every 14 days SC	*40 mg every 14 days SC	*40 mg every 14 days SC	*40 mg every 14 days SC	–	*40 mg every 14 days SC	–
Anticoagulation (always with IS) [23, 30, 42, 44, 45, 46, 49, 57]	May be added	May be added	May be added	May be added some positive results	Safe in short term, especially if other prothrombotic conditions	Contraindicated in PAA	May be added
<i>Other treatments</i>							
Surgery [23, 46, 59]	Not recommended	–	–	Only in life-threatening condition	–	Life-threatening condition	Possible* Surgeon choice
Endovascular procedures [23, 45, 68]	Not recommended	–	†TIPS †Angioplasty/stenting	–	–	If necessary preferred to surgery	Possible* Surgeon choice

Table 1 (continued)

SVT superficial vein thrombosis; DVT deep vein thrombosis; BCS Budd Chiari Syndrome; ICT intracardiac thrombosis; CVST cerebral venous sinus thrombosis; PAI pulmonary artery involvement; PAA pulmonary artery aneurysm; IV intravenously; SC subcutaneously; d; days; IS immunosuppressors; MIU million international units; AI arterial involvement; TIPS transjugular intrahepatic portosystemic shunt
*Induction treatment
◆Maintenance treatment
•Refractory cases
§Preferred cyclophosphamide to azathioprine
†Immunosuppressors before and after procedure
‡Selected refractory cases despite medical treatment
–Scarce evidence or no evidence

alone. Also, IS agents have shown a protective role for the development of a first VTE episode in BS patients [7]. In addition, a retrospective study reported good results with the use of combined treatment: corticosteroids, cyclosporine (CYP), azathioprine (AZA), and anticoagulation [28]. In these studies, all patients were treated with vitamin K antagonists, and there is no evidence regarding the role of direct oral anticoagulants in the treatment of venous thrombosis in BS. On the other hand, a study by Seyahi et al. [25] showed that the absence of anticoagulation could increase the risk of PTS, although Aksoy et al. could not demonstrate that in another retrospective study [29]. The role of anticoagulation in BS [30] remains an issue of debate, and more studies are required to clarify it.

DVT in BS patients is associated with less recanalization of the thrombi and more collateral circulation [31]. A prospective study [24] showed that the lack of recanalization of the thrombi is a risk factor predicting recurrence of DVT in lower limbs. IS decrease the risk of PTS, and interferon-alpha seems to increase recanalization rate, although it could not be compared to other IS [24, 29].

Monoclonal anti-tumor necrosis factor (anti-TNF) antibodies may be used in BS patients with refractory VTE. Anti-TNF agents showed benefits in arterial and venous involvement in retrospective studies [23, 32–34]. Anti-TNF agents could also be effective in BS with vascular involvement refractory to conventional IS and some data suggest they could also decrease the risk of VT recurrence [32]. In a retrospective study, adalimumab was effective inducing remission on venous thrombosis when compared to other IS [34].

To sum up, the mechanisms underlying thrombosis in BS are multifactorial including immune, inflammatory, tissue factor and impaired fibrinolysis. Accordingly, the question of management would not be immune modulation or anticoagulants, but probably a combination therapy for clearly defined periods of time. Thus, the optimal therapeutic strategy in terms of drugs and duration remains to be defined.

Venous thrombosis in atypical sites

Thrombosis in atypical sites, while uncommon, might be characteristic of vascular BS and its associated with a high morbidity and mortality. Figure 2 summarizes the treatment of thrombosis in atypical sites in BS patients.

Superior and inferior vena cava thrombosis

Involvement of the great veins in BS is rare (around 1–17%), affecting the inferior and superior vena cava equally [7, 19, 20, 27, 28, 35, 36]. Besides, BS is the main non-neoplastic cause of vena cava (VC) syndrome [28, 37], and

exceptionally might cause VC syndrome by inflammatory thickening of the vascular wall without the presence of thrombus [38].

The EULAR recommendations [23] for the management of VC thrombosis and lower limb DVT are similar. However, cyclophosphamide is reserved for cases of extensive thrombosis or VC involvement, due to potential adverse effects.

Budd–Chiari syndrome

BS is a frequent cause of Budd–Chiari syndrome (BCS) in countries with a high prevalence of BS, reaching up to 10–15% of the causes of BCS [39, 40]. On the other hand, BCS is a rare vascular complication of BS, even among patients of the “vascular Behçet” cluster, affecting about 1–5% of patients [39, 40]. BCS, pulmonary aneurysms, and neuro-behçet constitute the main burden of morbidity and mortality related to BS. BCS in BS may present in two different clinical pictures: acute or symptomatic BCS presents with abdominal pain, ascites, or hepatic failure whose mortality reaches up to 60%; and silent or chronic BCS which is often asymptomatic with efficient collateral formation, showing a better prognosis (10% mortality) [40, 41]. Also, thrombosis of the VC is usually associated [39, 42, 43]. Portal vein is rarely affected [40].

Due to this particularity, the management of BCS in BS is complex [44, 45]. The cornerstone of treatment is based on immunomodulatory therapy including corticosteroids, immunosuppressants (cyclophosphamide, cyclosporine-A or azathioprine), and biological therapy (infliximab) (level of recommendation III). Anticoagulation is still a matter of debate. On the other hand, interventional therapy is reserved for the chronic form, and it should be avoided in the acute phase due to the potential vascular inflammatory reactivity [40, 41, 46].

Intracardiac thrombosis

Only 100 cases of intracardiac thrombosis (ICT) in patients with BS have been reported, with a mean age of 30–40 years old and 87% males. ICT affects mainly the right chambers (right ventricle) with a low relapse rate [47, 48]. Importantly, in the presence of an intracardiac thrombus in the right chambers in a young male patient, BS should always be considered [47, 49]. ICT is usually associated with cardiac, pulmonary, or vascular involvement. Due to its high association, pulmonary aneurysms should be ruled out before considering anticoagulation [23, 47–50].

Recommendations for the management of ICT in BS patients are based on retrospective studies, and include colchicine [51], corticosteroids [42, 47, 49, 50], interferon-alpha [50], cyclophosphamide [42, 49], cyclosporine-A [42, 49, 50], azathioprine [42, 49], thalidomide [42], and

methotrexate [42]. Anticoagulant therapy alone is not recommended; however, positive results have been reported in combination therapy in individualized cases with low hemorrhagic risk [42, 46, 49]. In some refractory cases anti-TNF such as infliximab or adalimumab should be considered [32]. Surgical treatment might be considered in severe and refractory cases despite optimized medical treatment. However, surgery can trigger a vascular pathergy phenomenon consisting of venous thrombosis recurrence and early surgical complications, with high mortality [46, 48]. After treatment, resolution rates of 70–80% have been reported [42, 47–50].

Central venous thrombosis

Central nervous system (CNS) involvement in BS is rare (around 5–10% of vascular BS) and is more common in young men. Neuro-Behçet (NB) can affect the brain parenchyma, the vascular system, or both [52–54]. Simultaneous parenchymal and vascular involvement in the same patient is rare [55]. Central venous sinus thrombosis (CVST) varies according to the series from 2 to 40% of patients with NB [53, 54], and ranges from 0 to 13% in patients with vascular Behçet [7, 19, 20, 27, 36]. Shi et al. found that 52% of vascular-NB patients presented thrombosis in more than one location [55]. Hence, in the setting of CVST, screening for extracranial vascular involvement is strongly recommended [23, 52–54].

EULAR recommendations for vascular NB treatment include high doses of corticosteroids with slow tapering. IS are not recommended since no clear benefits have been reported. Furthermore, cyclosporine-A is recommended against in patients with acute or previous NB episode, due to potential neurological impairment [23]. Anticoagulant treatment seems relatively safe in retrospective studies [53–56].

Arterial involvement

Arterial involvement (AI) in BS represents a unique feature [6]. BS is probably the only chronic inflammatory disease that causes aneurysms that can affect peripheral, visceral and pulmonary arteries [9]. Aneurysms are the most common type of arterial lesion in BS but occlusions and stenosis can also occur [57, 58]. One-third of AI are multiple [57, 58]. Pathergy phenomenon, arterial stenosis or occlusion and arterial thrombosis are risk factors associated with aneurysm formation [58].

AI affects 1–7% of BS patients [9, 57] and is more common in males in the fourth decade of life [9, 57, 58]. It can be the first manifestation of the disease in some patients although it frequently appears few years after the diagnosis [57, 58]. AI can be consequence of traumatic injury including surgery, arterial puncture, arteriography or even lung

biopsy [57, 58]. Although fever is an uncommon symptom of BS, it is associated with AI [7, 57, 59], especially in aneurysm formation [57].

Long-term mortality and morbidity are increased if arterial manifestations are present, especially pulmonary aneurysms [9, 33, 58, 59]. The rate of mortality can reach up to 15% [58]. Hughes–Stovin syndrome, considered a cardiovascular subtype of BS, is defined by the presence of arterial pulmonary aneurysms and peripheral venous thrombosis [1, 9].

The main locations of AI are the aorta, femoral, pulmonary, and iliac arteries [57, 58, 60]. More uncommon locations include digestive, coronary and cerebral arteries [57]. Thoracic aorta and pulmonary arteries involvement have the highest mortality rate (up to 40% of deaths) [57].

IS are the cornerstone of treatment in AI [23]. The EULAR recommendation includes high-dose glucocorticoids and cyclophosphamide. Anti-TNF might be used in refractory cases, as they have shown efficacy in vascular BS in some retrospective studies [61]. Desbois et al. [32] demonstrated that anti-TNF led to remission in 89% of patients previously treated with IS and high dose glucocorticoids. The discontinuation of anti-TNF agents after initiated is still an unresolved question [61].

Pulmonary artery involvement

Two types of pulmonary artery involvement (PAI) have been described in BS: pulmonary artery aneurysms (PAA) and pulmonary artery thrombosis (PAT) [59]. The frequency of PAA in BS ranges from 1 to 18% and is more common in men [61, 62]. Pulmonary symptoms include hemoptysis, dyspnea, fever, cough or chest pain [59, 62]. By the time of diagnosis of PAI many patients have signs of active BS [59]. PAI is associated with venous thrombosis but not with peripheral artery disease [59, 63].

The first level of treatment of PAA are high-dose glucocorticoids and cyclophosphamide, followed by long-term azathioprine [6, 23, 61, 64]. With this treatment, 70% of patients achieve clinical and radiologic remission, but mortality rate and relapses remain high (26% mortality and 20% relapses during 7-year follow-up) [61]. Etanercept was superior to placebo in suppressing mucocutaneous lesions in the only randomized controlled trial developed with anti-TNF in BS [65], although it was not effective in suppressing the pathergy phenomenon. EULAR recommends the use of anti-TNF agents in refractory PAI cases. Except for life threatening situations, surgery is not recommended and endovascular treatment (embolization) is preferred [23, 61]. Anticoagulation is contraindicated due to high risk of bleeding [23, 25].

Aortic and peripheral involvement

The aorta is the most affected artery, especially abdominal aorta followed by coronary arteries, superficial femoral artery, subclavian artery and popliteal artery [58].

Treatment of aneurysmal lesions consists of glucocorticoids and immunosuppressants (cyclophosphamide) according to EULAR recommendations [23], and this treatment is necessary before intervention to decrease the risk of postoperative complications [23]. The choice of surgical intervention can be made according to aneurysm size and surgeon experience [23]. The risk of rupture is related to aneurysm diameter, but severe spontaneous rupture in BS is unusual [66].

Coronary arteries

Coronary arteries can be affected in BS, reaching up to 10% of all AI cases, with a mean age of 30 ± 11 years [58, 67]. Most patients with coronary artery involvement present with acute coronary syndrome [58]. Lesions can include stenosis, occlusion and pseudoaneurysm, with or without myocardial infarction. Patients with coronary involvement have poor prognosis compared with other patients with AI [67]. Treatment of coronary artery aneurysms agree with the AI medical recommendations and general recommendations of myocardial infarction.

In conclusion, the vascular involvement of Behçet syndrome can affect both veins and arteries of all sizes. Manifestations can include thrombosis and aneurysm formation. Vascular Behçet treatment is based on immunosuppressants and the role of anticoagulation is not clearly established.

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Data availability Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

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