Cardiovascular Involvement in Behçet Disease

Abstract
Behçet’s disease is a disease with mixed vascular tropism: venous and arterial. Vasculo-Behçet or angio-Behçet presents a particular patient profile. Vascular involvement, especially pulmonary artery aneurysm, thoracic aortic aneurysm and Budd-Chiari syndrome are entities affiliated with the disease and strike the prognosis. Our series is predominantly male, with an average age of 36 years. Venous disease concerns the majority of patients: 40 patients. It is most often a deep vein thrombosis of the lower limbs. In the arterial system, the pulmonary artery aneurysm was found in 7 patients, the most common location of aneurysms. The association of venous and arterial involvement is more important. Corticosteroid therapy is prescribed in three out of four patients. Immunosuppressive treatment such as azathioprine or cyclophosphamide are prescribed in almost half of patients with venous involvement.

Introduction
Behçet’s disease (BD) is a systemic vascular disease distinguished from others by its involvement of arteries of varying calibers as well as veins. Vasculo-Behçet or angio-Behçet presents a distinct profile of patients in whom vascular manifestations dominate the clinical picture and tend to be recurrent. Vascular involvement, particularly pulmonary artery aneurysm, thoracic aorta aneurysm, and Budd-Chiari syndrome, represents a major prognostic factor as it directly accounts for 45% of patient deaths [1]. The objective of our study is to investigate the clinical, therapeutic, and prognostic characteristics of angio-Behçet in an internal medicine department.

Patients and Methods
This is a retrospective study involving 44 patients with cardiovascular involvement of BD, selected from among patients hospitalized in the internal medicine department of the university hospital center of Bab Eloued during a period from January 2010 to December 2018. The inclusion criteria were those of the International Study Group for BD [2]. The major criterion is recurrent oral aphthosis (at least 3 episodes over a period of 1 year). The minor criteria include recurrent genital aphthosis, ocular involvement (anterior uveitis or posterior retinal vasculitis), cutaneous manifestations (erythema nodosum, pseudo-folliculitis, papulopustular acneiform lesions...
outside the pubertal period and without corticosteroid treatment), and positive intradermal reaction to saline. The diagnosis of BD is established if the major criterion is fulfilled in association with at least 2 minor criteria.

**Results**

Table 1 records the clinical characteristics of the patients. The majority of patients in the series are male: 88.6% of cases. The mean age is 36 years. Among the extra-cardiovascular manifestations, cutaneous-mucosal manifestations are the most frequent: oral aphthosis 97.7%, genital ulcers 86.4%, and pseudofolliculitis 79.5%. Ocular involvement is present in 20.5% of cases.

The cardiovascular manifestations of BD are summarized in Table 2. Venous thromboembolic disease affects 40 patients (superficial in 5 patients and deep in 27 patients). The sites of venous thromboses include the lower limb in 25 patients, the inferior vena cava in 5 patients, cerebral veins in 7 patients, and the superior vena cava in 3 patients. Two patients have upper limb thromboses. One patient presents with thrombosis of the suprahepatic veins resulting in Budd-Chiari syndrome. Arterial involvement affects 12 patients, accounting for 27.2% of the population; 10 of them are male. The most frequent involvement is pulmonary artery aneurysm, thrombosed in 2 patients and non-thrombosed in 5 patients. Four cases involve stroke, and a single patient suffers from abdominal aortic aneurysm.

Intracardiac thrombus in the right ventricle is diagnosed in 3 patients, all of which were revealed by pulmonary embolism.

The treatment of Behçet’s disease with cardiovascular involvement is summarized in Table 3. Colchicine is prescribed for all patients. 80% received corticosteroid therapy, 34% received cyclophosphamide, with a switch to azathioprine in 32% of cases. Long-term anticoagulant therapy is prescribed for 28 patients, and...
low-dose aspirin is prescribed for 4 patients with arterial involvement. Three patients underwent embolization of pulmonary artery aneurysm. Recurrence of deep venous thrombosis occurred in 9 patients: All had never received immunosuppressive treatment, and 7 of them were on anticoagulant therapy at the time of recurrence. Three male patients died. The causes of death were cataclysmic hemoptysis due to rupture of pulmonary artery aneurysm, complicated cerebral venous thrombosis, and decompensated cirrhosis related to Budd-Chiari syndrome.

### Table 3: Behçet’s Disease with Cardiovascular Involvement Treatment

<table>
<thead>
<tr>
<th></th>
<th>our series (%)</th>
<th>Desbois (%)</th>
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</thead>
<tbody>
<tr>
<td><strong>Venous involvement</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>74,3</td>
<td>99</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>76,9</td>
<td>62,7</td>
</tr>
<tr>
<td>Immunosuppressants</td>
<td>43,6</td>
<td>46</td>
</tr>
<tr>
<td><strong>Arterial Involvement</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>33,3</td>
<td>47</td>
</tr>
<tr>
<td>Aspirin</td>
<td>16,7</td>
<td>44</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>100</td>
<td>88</td>
</tr>
<tr>
<td>Immunosuppressants</td>
<td>75</td>
<td>79</td>
</tr>
</tbody>
</table>

**Discussion**

Behçet’s disease often affects young individuals, typically under the age of 35. According to studies, 5 to 40% of Behçet’s disease cases exhibit vascular involvement [3]. A French cohort found 37% with venous involvement, 12% with arterial involvement, and 6% with cardiac manifestations [4]. This distribution of involvements aligns with our series, where venous involvement predominates in nine out of ten cases, followed by arterial involvement in almost a third of cases. When discussing the topographical aspect, the deep venous system is more frequently affected. Within this system, the lower limbs are involved in over half of the cases, followed by cerebral venous thrombosis. Budd-Chiari syndrome is found in one case. These results are comparable to French and North African series, where a similar frequency order is observed, with predominance of lower limb and cerebral vein involvement, and rarity of involvement of the suprahepatic and caval systems [3;5;6]. In the arterial system, pulmonary artery aneurysm is found in 7 patients, the most common location for aneurysms. There is a rarity of arterial thrombosis in our series [3;5;6]. The combination of venous and arterial involvement is more significant in our series compared to the North African series [6]: 2 cases of Hughes-Stovin syndrome, 4 patients have deep vein thrombosis and a pulmonary artery aneurysm. Pulmonary artery aneurysm without venous involvement is found in 3 patients, one of whom, a woman, suffered a stroke. Few pulmonary embolisms are observed in our series because venous thrombosis in Behçet’s disease is known to be less embolic [1;3]. Pulmonary embolism is most often related to intracavitary or in situ thrombus: In our series, it is associated with intracardiac thrombus in 3 patients.

Regarding cardiac involvement, 3 patients presented with intracardiac thrombus. Among them, endomyocardial fibrosis on cardiac MRI is observed. Intracardiac thrombosis is described in 29% of cardiac involvement, which represents 1.9% of angio-Behçet cases [1;3]. Corticosteroid therapy is prescribed in three-quarters of patients. Immunosuppressive treatment such as azathioprine or cyclophosphamide is prescribed in almost half of patients with venous involvement. Anticoagulation is prescribed in 75% of cases. The inferiority of anticoagulation compared to the French series [1;3] may be explained by its association with pulmonary artery aneurysm, which limits its use.

In arterial involvement, the use of antithrombotic treatment such as vitamin K antagonists or antiplatelet agents is not significant. In contrast, corticosteroid therapy is prescribed for all patients. The addition of an immunosuppressant is done in three out of four patients in accordance with the findings of the Desbois et al. series [1]. Immunosuppressive treatment is the cornerstone of therapy despite the lack of prospective studies [1]. EULAR recommends the use of azathioprine and cyclophosphamide in cases of deep vein thrombosis, peripheral and pulmonary aneurysms. Corticosteroid therapy is justified in cases of recurrent deep vein thrombosis or postoperative complications of aneurysms [1].

Anticoagulant therapy is not recommended due to the involvement of wall inflammation in thrombus genesis, the less embolic nature, and the hemorrhagic risk. However, we observe that the majority of patients are on anticoagulant therapy in the practices of published series [1;3]. Recurrence of deep vein thrombosis concerns 9 patients: 7 of them were on anticoagulant therapy and none received immunosuppressive treatment. Endovascular treatment by embolization is performed in 3 patients. The results of published studies encourage this type of procedure in cases of pulmonary artery aneurysm and massive hemoptysis. Interventional treatment would be more effective and safer than surgical treatment [1;3]. Three male patients
died from cataclysmic hemoptysis due to rupture of pulmonary artery aneurysm, complicated cerebral venous thrombosis, and complication of cirrhosis in a patient with Budd-Chiari syndrome. Pulmonary artery aneurysm and thrombosis of the suprahepatic veins are described as poor prognostic factors, unlike cerebral venous thrombosis. However, altered neurological status at diagnosis and relapses under treatment are considered as poor prognostic indicators [1;4;7].

Conclusion
Vascular involvement in Behçet's disease is common and serious, especially when a pulmonary artery aneurysm is present. Unfortunately, immunosuppressants remain underprescribed in angio-Behçet compared to anticoagulants. However, they are associated with reduced mortality and recurrence risk. Early diagnosis and management are crucial to reduce the risk of mortality.

References