

# Hughes-Stovin Syndrome as an Outcome of Behçet Disease or as a Different Entity

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Hughes-Stovin syndrome is a rare disorder of unknown etiology. Although the association between multiple pulmonary artery aneurysms and venous thrombosis of the lower limbs was reported by Beattie and Hall in 1911, it was not until 1962 that the eponym “Hughes-Stovin syndrome” was formally introduced in the medical literature. We describe 2 patients with Hughes-Stovin syndrome who presented with pulmonary artery aneurysm, thrombophlebitis, hemoptysis, and oral ulcers, review the manifestations of the disease, and compare its similarities with and differences from Behçet disease.

**Key words:** 1. Hughes-Stovin syndrome  
2. Behçet disease  
3. Pulmonary artery aneurysms  
4. Thrombosis  
5. Oral ulcer

## Case reports

### 1) Case 1

A 37-year-old woman presented with recurrent oral aphthae (Fig. 1A). She received topical corticosteroid treatment for 8 years. During this period, the patient was investigated for the diagnostic criteria of Behçet disease (BD), but she did not satisfy all of them. The patient presented with hemoptysis, which was determined to be due to the bleeding of a pulmonary artery aneurysm. After 3 months, thrombophlebitis in the saphenous vein was detected. In these 3 months, she experienced hemoptysis twice due to a pulmonary artery aneurysm in her pulmonary artery, which was 25 mm in diameter (Fig. 1B). Both times, the bleeding stopped spontaneously. The results for perinuclear anti-neutrophil cytoplasmic antibody (P-ANCA) and circulating anti-neutrophil cy-

toplasmic antibody (C-ANCA) were negative. The causes of the pulmonary artery aneurysm were investigated, and no findings suggested any other factors relevant for the etiology of the disease. When thrombophlebitis manifested in the saphenous vein (Fig. 1C), she was diagnosed with Hughes-Stovin syndrome (HSS) and systemic steroid (100 mg prednisolone equivalent) and azathioprine therapy were started. After 45 days, systemic steroid therapy began to be reduced and was eventually discontinued. She is still on azathioprine therapy.

### 2) Case 2

A 33-year-old man presented with oral aphthae (Fig. 2A). He only received topical corticosteroid therapy and 1.5 mg per day of colchicine for 3 years. During this period, the patient was investigated for the diagnostic criteria of BD, but he did not satisfy

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Fig. 1. (A) Aphtae on the inferior labial mucosa. (B) Fusiform aneurysm in the right pulmonary artery (25 mm in diameter). (C) Thrombophlebitis in the saphenous vein detected with Doppler ultrasonography.

all of them. Later, thrombophlebitis was detected in the basilic vein. The patient received antibiotic and anti-inflammatory treatment. When the patient complained of hemoptysis, computed tomography indicated that it was connected to the bleeding of a pulmonary artery aneurysm (Fig. 2B). His P-ANCA and C-ANCA results were negative. The causes of the pulmonary artery aneurysm were investigated, and no findings suggested any other factors relevant for the etiology of the disease. Based on the findings of thrombophlebitis (Fig. 2C) and pulmonary artery aneurysm, he was diagnosed with HSS. His treatment started with systemic steroid therapy (100 mg prednisolone equivalent) and azathioprine (150 mg per day). After 45 days, the systemic steroid therapy began to be reduced and was eventually discontinued. He is still on azathioprine therapy.

## Discussion

In this report, we described 2 patients with HSS who presented with pulmonary artery aneurysm, thrombophlebitis, hemoptysis, and oral ulcers. In this section, we review the manifestations of HSS and compare its similarities and differences with BD.

HSS is a rare disorder of unknown etiology [1]. Although the association between multiple pulmonary artery aneurysms and venous thrombosis of the lower limbs was reported by Beattie and Hall in 1911, it was not until 1962 that the eponym “Hughes-Stovin syndrome” was formally introduced in the medical literature [1]. In 1959, Hughes and Stovin [2] reported 4 cases of deep venous thrombosis and multiple segmental pulmonary artery aneurysms. Since then, this association of multiple pulmonary aneurysms and peripheral venous thrombosis has been referred to as HSS [3]. It usually affects young adults



Fig. 2. (A) Aphthae on the inferior labial mucosa. (B) Aneurysm (26 mm in diameter) in the left pulmonary artery. (C) Thrombophlebitis of the cephalic vein in the right upper extremity.

aged from 12 to 48 years and has a strong male predilection [3-5].

The initial presentation of the disease is generally non-specific, and patients can present with cough, shortness of breath, fever, and chest pain. Hemoptysis may develop later or can be the initial finding [2,3]. There was a long history of oral aphthae in both of our patients, in whom hemoptysis was the initial symptom of HSS, while thrombophlebitis appeared later.

Various degrees of hemoptysis are the most frequent and severe symptom of pulmonary artery aneurysms in HSS. Hemoptysis may occur when the aneurysms ruptures, with erosion towards the bronchus, or via thrombosis due to active vasculitis [4]. Hemoptysis can occur through 3 mechanisms: (1) rupture of an aneurysm, which is a common cause of death in patients with HSS; in this mechanism, the ruptured aneurysm causes erosion towards the bron-

chus, resulting in hemoptysis [4]; (2) active vasculitis, which can lead to thrombosis and hemoptysis [4]; and (3) hypertrophy in the bronchial arteries secondary to ischemic pulmonary artery occlusion, which can cause hemoptysis [5].

Mahlo et al. [6] reported dilated bronchial arteries in patients with HSS; they suggested that hemoptysis more likely results from the rupture of angiodysplastic bronchial arteries than from the rupture of the pulmonary arteries.

Being an extremely rare disease, there are no formally described diagnostic criteria or pathognomonic laboratory investigations for HSS. Generally, the syndrome is characterized by the findings of thrombophlebitis and multiple pulmonary and/or bronchial aneurysms [7].

The clinical paradigm of HSS can be divided into 3 phases [5,7]: (1) symptoms of thrombophlebitis, (2) formation of large pulmonary and/or bronchial

**Table 1.** Similarities and differences between Hughes-Stovin syndrome and Behçet disease and the clinical characteristics of the 2 cases presented in this report

Feature	Hughes-Stovin syndrome	Behçet disease	Case 1	Case 2
Pulmonary aneurysm	Diagnostic criterion	Possible	Present	Present
Thrombophlebitis	Diagnostic criterion	Diagnostic criterion	Present	Present
Skin conditions (acneiform eruption, erythema nodosum-like lesions)	Possible	Diagnostic criterion	Absent	Absent
Oral ulcer	Possible	Diagnostic criterion	Present	Present
Genital ulcer	Possible	Diagnostic criterion	Absent	Absent
Pathergy test	Possible	Diagnostic criterion	Absent	Absent
Eye involvement	Possible	Diagnostic criterion	Absent	Absent
Arthritis	No information	Possible	Absent	Absent
Neurological manifestations	Possible	Possible	Absent	Absent
Gastrointestinal manifestations	No information	Possible	Absent	Absent

aneurysms, and (3)aneurysmal rupture, leading to massive hemoptysis and death.

The incidence of BD varies geographically. In North America and Europe, it is 0.38–7.5 per 100,000, in contrast to about 42 per 100,000 in Turkey [8]. Unlike BD, HSS does not have a geographic predilection. Cases of HSS have been reported in North America, Europe, Africa, and Asia [9-11].

Both conditions predominantly affect young adults, especially males [8]. However, there are examples of female patients with each of these conditions [12]. The medical treatment of both diseases involves a combination of immunosuppressive agents [13]. None of the case reports of HSS have reported familial histories or a history of consanguineous marriage. Unlike BD, for which a genetic predisposition has been shown and potentially relevant genes have been identified, no information exists regarding the genetic basis of HSS or any trend towards familial susceptibility.

Hepatitis A, B, C, and E, herpes simplex virus, parvovirus B19, *Helicobacter pylori*, *Chlamydia pneumonia*, *Streptococcus sanguinis*, *Streptococcus mitis*, *Streptococcus salivarius*, and *Saccharomyces cerevisiae* have been suggested as causative factors of BD, but their role has not been proven [12]. The pathogenesis of thrombi is unclear in both HSS and BD, although it is thought that thrombophilia is not a major factor [14].

The similarities and differences between HSS and BD and the clinical characteristics of the 2 patients we presented are shown in Table 1.

Some points in the diagnosis and management of HSS have yet to be sufficiently elucidated. Infectious agents have been suggested to be relevant, and this possibility could be clarified through electron microscopic investigations or siRNA studies. The possibility of a genetic basis of this condition and a familial predisposition must be investigated, with potential relevance for genetic counseling. Future studies should clarify whether there is a genetic proximity between HSS and BD by human leukocyte antigen typing. Finally, better treatment agents need to be developed in order to prevent pulmonary artery aneurysms, which are the main cause of mortality and morbidity in patients with HSS. The establishment of diagnostic criteria and management guidelines will lead to more standardization. Thus, differences in the geographic morbidity and mortality rates of HSS can be reduced.

### Conflict of interest

No potential conflict of interest relevant to this article was reported.

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