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## Case Report

# Diffuse alveolar Hemorrhage in a patient with Behcet's: immune or nonimmune?

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### ABSTRACT

Diffuse alveolar hemorrhage (DAH) is a rare, life-threatening condition often presenting with non-specific symptoms such as hemoptysis and cough, and can lead to respiratory failure. It is primarily associated with small-vessel vasculitides, like granulomatosis with polyangiitis. We report a 56-year-old male with a history of Behçet's disease who presented with cough, hemoptysis, and low oxygen saturation. Imaging studies and posterior bronchoscopy with bronchoalveolar lavage (BAL) confirmed DAH. This article discusses the probable causes of DAH in this patient.

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## Hemorragia alveolar difusa en un paciente con Behçet: ¿inmune o no inmune?

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### RESUMEN

La hemorragia alveolar difusa (HAD) es una condición rara y potencialmente mortal que generalmente se presenta con síntomas inespecíficos, como hemoptisis y tos, y puede llevar a la insuficiencia respiratoria. Está asociada principalmente con vasculitis de pequeños vasos, como la granulomatosis con poliangéitis. Se reporta el caso de un hombre de 56 años con antecedentes de enfermedad de Behçet que se presentó con tos, hemoptisis y baja saturación de oxígeno. Mediante estudios de imágenes y posteriormente broncoscopia con lavado broncoalveolar, se confirmó HAD. En este artículo discutimos las probables causas de DAH en este paciente.

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## 1. INTRODUCTION

Diffuse alveolar hemorrhage (DAH) is a rare, acute clinical syndrome that can result in respiratory failure. It is a life-threatening condition with nonspecific symptoms and, therefore, requires prompt evaluation to detect the cause and establish an appropriate course of therapy. Hemoptysis is the most common symptom, but it may be absent in up to one-third of patients [1, 2].

The underlying cause of DAH can be determined by the histopathologic pattern, which includes pulmonary capillaritis, bland pulmonary hemorrhage, and diffuse alveolar damage. The most common form of DAH is capillaritis, which is linked to systemic vasculitides and connective tissue diseases. Other potential causes include other rheumatic diseases, coagulation disorders, drug-induced effects, and infections [1-3].

Behçet's disease is distinctive among systemic vasculitides in that it causes arterial and venous inflammation, affecting vessels of all sizes, and additional recurrent, self-limiting skin and mucosa lesions that occur in almost all patients [4, 5].

This study aims to examine the potential causes of diffuse alveolar hemorrhage (DAH) in a patient with Behçet's disease, and to determine whether the DAH was of immune or nonimmune origin.

## 2. CASE REPORT

A 56-year-old male patient presented with a three-day history of cough, hemoptysis, and headaches. He reported a history of a persistent, productive cough with white-

yellowish sputum over the previous nine months, following a viral infection. Other symptoms, including fever, dyspnea, and thoracic pain, were not reported. The patient was diagnosed with Behçet's disease in 2007, with ocular and mucosal manifestations beginning as early as 2005. The patient was currently receiving colchicine at a dosage of 0.5 mg per day, but no systemic immunosuppressive therapy had yet been initiated. By questioning, the patient disclosed a one-week regimen of acetylsalicylic acid 500 mg (Aspirin®) and celecoxib 100 mg (Celebrex®) for the treatment of headaches. The patient has a history of heavy smoking, with an estimated 40 pack-years.

The clinical examination revealed bilateral basal coarse crackles, with a blood pressure of 130/80, a heart rate of 62 beats per minute, and an oxygen saturation of 91% on air. The laboratory findings were as follows: The patient's hemoglobin level was 15.4 g/dL. The leukocyte count was 12.4, and the C-reactive protein level was less than 5 mg/dL. Conventional radiography revealed bilateral peribronchial thickening but no evidence of infiltrates (Figure 1).

The patient was referred to the hospital for further assessment. A computed tomography scan of the thorax revealed bilateral, patchy ground-glass opacities, with a greater prevalence on the left upper lobe (Figure 2). Computed tomography pulmonary angiography showed no evidence of pulmonary embolism or pulmonary artery aneurysm. Bronchoscopy revealed the presence of diffuse alveolar hemorrhage upon lavage. The cytological examination revealed the presence of alveolar macrophages and siderophages. No increased count of inflammatory or malignant cells was identified.

Given the high suspicion of DAH, supportive treatment was initiated, and the patient received systemic glucocorticoid therapy with 125 mg of methylprednisolone intravenously

per day for four days. Subsequently, the patient began a tapering regimen of oral corticosteroids. Further investigations, including a respiratory pathogen panel and autoimmune serology for ANCA-vasculitis, yielded negative results. Renal function was normal, and urinalysis did not indicate glomerulonephritis. The hemoptysis resolved completely while the patient remained stable during the hospitalization period and was discharged a few days later.



**Figure 1:** Chest X-ray shows bilateral peribronchial thickening, without evidence of infiltrates or pulmonary nodules.

During monthly ambulatory follow-ups throughout one year, the patient remained free of further hemorrhagic manifestations or signs of inflammatory activity.

### 3. DISCUSSION

The patient, who had a known diagnosis of Behçet's syndrome and a longstanding smoking history, presented with hemoptysis, cough, low oxygen saturation, and diffuse radiographic changes. Although these symptoms lack specificity, they could indicate a severe underlying condition. Therefore, an urgent and comprehensive assessment is warranted. Following an initial tomographic evaluation, the diagnosis of DAH was considered and subsequently confirmed by bronchoalveolar lavage. Once a

diagnosis of DAH has been established, further tests are required to identify the underlying cause.

The majority of cases of DAH are caused by capillaritis, which is highly associated with systemic vasculitides. DAH is most frequently observed in small-vessel vasculitides, particularly granulomatosis with polyangiitis and microscopic polyangiitis. Although Behçet's disease is a vasculitis that can affect vessels of all sizes, it predominantly affects medium and large vessels [3, 6].

In addition, Behçet's involves mainly the venous system, with superficial thrombophlebitis and deep-vein thrombosis being the most common vascular manifestations of Behçet's [4, 5].

Arterial involvement in Behçet's disease is less common and tends to cause aneurysms. The aorta and peripheral arteries are the most affected. The involvement of the pulmonary artery is rarely observed. Pulmonary artery aneurysm (PAA) is a specific condition for Behçet's syndrome [7-9].

Therefore, DAH is a rare complication of Behçet's disease, presenting primarily because of the rupture of a pulmonary artery aneurysm (PAA), which represents the primary pulmonary manifestation of Behçet's disease. Studies have found that the occurrence of PAA in Behçet's is seen in less than 3% of patients [7-9].

To ascertain the presence of systemic vasculitides, specific serological tests, including ANCA, should be conducted. Moreover, an assessment of renal function and urinalysis is recommended for all patients with DAH to identify pulmonary-renal syndrome, which is highly suggestive of systemic vasculitides and less common in connective tissue diseases [3].



**Figure 2:** Chest computed tomography (CT) demonstrates bilateral, patchy ground-glass opacities, with a predominance in the left upper lobe, as indicated by the arrows.

Other potential etiologies of DAH include other rheumatic diseases, infections, tumor diseases, and certain drugs and toxins. In this case, there was no evidence of current infection or tumor [3].

The patient had been taking acetylsalicylic acid, a non-

selective non-steroidal anti-inflammatory drug (NSAID) with antiplatelet properties, and the selective NSAID celecoxib.

NSAIDs are generally understood to increase the risk of bleeding, with the majority of evidence indicating an association with gastrointestinal bleeding and a lesser degree of evidence suggesting a link with pulmonary bleeding. Selective NSAIDs, such as celecoxib, have been demonstrated to exhibit a reduced propensity for causing bleeding in comparison to non-selective drugs [10]. A review of the literature reveals only a small number of documented cases of non-selective NSAIDs being linked to DAH. The aforementioned cases are specifically associated with the use of ketorolac [10, 11]. To date, there have been no reports of DAH associated with celecoxib alone or in concomitant use with other drugs.

Antiplatelet agents have been observed to potentially induce DAH, although DAH is more commonly associated with anticoagulants. Only two cases have been reported in which acetylsalicylic acid use has been implicated in the development of DAH [2, 9, 13].

It is established that smoking causes damage to the lungs, which can increase the susceptibility to pulmonary bleeding. Individuals who smoke have an elevated risk of major bleeding and airway bleeding [3, 12]. Furthermore, there have been reports associating vaping with DAH. Although the majority of cases of vaping result in diffuse alveolar damage (DAD) and organizing pneumonia [14, 15].

A comprehensive workup was conducted in this case, leading to the exclusion of numerous potential causes of DAH. Given the temporal relationship between exposure to NSAIDs and the onset of symptoms, a diagnosis of DAH secondary to concomitant use of acetylsalicylic acid and celecoxib was postulated at hospital discharge.

## 4. CONCLUSIONS

As outlined above, the role of NSAIDs in DAH is rare and remains questionable in this case, however, the impact of these drugs, particularly in patients with predisposing conditions such as autoimmune vasculitis and a history of smoking, should be well considered.

Therefore, in this case of clinical presentation with hemoptysis and beginning respiratory failure, a rapid workup, including medication anamnesis, rheumatologic laboratory screening, and computed tomography, should be

conducted to rule out potentially life-threatening causes and warrant appropriate treatment.

## 5. CONFLICT OF INTERESTS

The authors have no conflict of interest to declare. The authors declared that this study has received no financial support.

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