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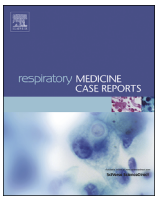

Case Report

Diagnosis of Behcet's disease in a young male patient with acute bilateral pulmonary embolism; A case report and literature review

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ABSTRACT

Behcet's disease (BD) is a chronic and inflammatory vasculitis characterized by recurrent oral and genital aphthous ulcers, uveitis, and skin lesions. Although there is a high rate of deep vein thrombosis in BD, pulmonary arterial thromboembolism (PTE) is a rare complication. We present a 30-year-old patient who was admitted with pleuritic chest pain, non-massive hemoptysis since 4 days ago and medical history of intermittent genial aphthous lesions, and skin lesions. During our evaluation, he had an S1Q3T3 pattern in the electrocardiogram, a high level of D-dimer, a low level of FDP and fibrinogen along with pulmonary emboli in lobar and segmental branches of the right pulmonary artery and segmental branches of left lower lobe pulmonary artery were detected in his pulmonary CT Angiography. Then, he was positive for HLA-B51. Based on his clinical condition and history of recurrent genital and skin lesions, a positive pathergy test. Therefore, the diagnosis of BD was confirmed for him. Diagnosis of PTE can be difficult due to the rarity of PTE in BD and nonspecific clinical symptoms; therefore, a high degree of suspicion and appropriate radiographic imaging is essential for the diagnosis.

1. Introduction

Behcet's disease (BD) is a chronic, multi-systemic inflammatory vasculitis disease introduced in 1937 by a Turkish dermatologist, Hulusi Behçet. It mainly presented with oral and genital ulcers, uveitis, cutaneous lesions, arthritis, and gastrointestinal and neurological involvement. The pathology and etiology of this disease are still unclear, but studies consider this disease as a combination of autoimmune and auto-inflammatory causes. In addition, recent genomic studies confirm the known role of HLA-b51 in BD [1–3].

It is typically prevalent in eastern Asia to the Mediterranean region, also called the famously ancient Silk Road. The prevalence in Turkey, Iran, and the United States is 420, 80, and 0.3 to 5.2 per 100,000. Previously, it was believed that this is more common in men, but the prevalence is equal in both gender; however, the severity is higher in males [3–7].

The diagnosis is usually based on International Study Group (ISG) criteria and includes recurrent oral aphthous ulcerations along with at least of the following, recurrent genital aphthous ulcerations, ocular lesions, skin lesions, and positive pathergy test [2,5,8–10].

BD involves all arteries and veins of any size. Although about 25% of patients experience deep vein thrombosis, pulmonary embolism (PTE) is an extremely rare complication and one of the main causes of morbidity and mortality in patients. It is majorly relevant to the essence of thrombosis in BD. Venous thrombosis is generated from the inflammatory process in the arteries; however,

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strong adherence of the thrombi to the arteries' walls in BD makes PTE development difficult and infrequent. Chest CT scan or MRI is more likely to diagnose pulmonary and intracardiac thromboembolism. In addition, investigating the progress and efficacy of treatment during follow-up can be done with echocardiography [1,3,6,11].

How to treat thromboembolic events in BD is debatable. Some suggest using anticoagulants, while others suggest giving immunosuppressive drugs to patients due to the inflammatory nature of the disease in treating patients. Some studies have also proposed the co-administration of immunosuppressive and anticoagulant drugs in these conditions [12–14].

In this case report, we report a young male patient with no medical history admitted with chest pain, fever, cough, hemoptysis, and dyspnea. During our investigation, we confirmed the diagnosis of PTE based on his current medical history, physical examination, S1Q3T3 pattern in the electrocardiogram, and CT angiography findings. Then, due to unprovoked PTE, only HLA-B5 was positive during our evaluation, along with his previous history of recurrence of genital aphthous lesions, skin lesions, and positive pathergy test. Overall, the diagnosis of DB was confirmed, which was extremely rare when presented with PTE.

2. Case presentation

A 30-year-old male was admitted to the emergency department at Sayyad Shirazi Hospital in Gorgan, Iran, with a chief complaint of chest pain four days ago. The chest pain was mainly at the right hemithorax and had a pleuritic nature, and was aggravated by breathing and physical activity. The pain has been continuous and has woken the patient up. He had a history of non-massive hemoptysis in the form of blood-streaked sputum in the past four days. Dyspnea started one month ago, which was progressive, and was at The New York Heart Association (NYHA) functional class III. In addition, he had a significant weight loss (10 kg) along with fever, chills, night sweats, and productive cough in the past month. He mentioned a history of frequent genital aphthous.

In his physical examination, his blood pressure was 115/85, Pulse rate 102/min, respiratory rate of 25/min, body temperature of 38C, and oxygen saturation level of 96% without oxygen supplementation therapy. The decreased sound was heard in the lower part of the right lung, along with bilateral crackles during auscultation. Scattered hyperpigmented lesions and pseudofolliculitis were also seen in bilateral lower limbs.

Based on his condition, Chest X-ray and laboratory was performed. Cardiomegaly without involvement in the lung parenchyma was seen in his Chest X-ray. On laboratory tests, complete blood counts were normal, the erythrocyte sedimentation rate (ESR) was 30 mm/s, and a c-reactive protein test (CRP) concentration was reported as +4. In echocardiogram (EKG), sinus tachycardia with S1Q3T3 pattern plus T invert in V1–V4 were observed.

Then, due to the clinical suspicion of pulmonary embolism, emergency cardiology and pulmonology consultations, pulmonary computed tomography (CT) scan, angiography, and diagnostic tests were requested, and he was transferred to the ICU unit. In cardiology consultation, an ejection fraction of 55% with no sign of pulmonary emboli was reported in echocardiography; further evaluation with CTA was suggested. Pulmonary emboli in the lobar and segmental branches of the right pulmonary artery and segmental branches of the left lower lobe pulmonary artery were visible. Peripheral mass-like alveolar densities and collapse consolidation in both lungs lower lobes were seen. Plural effusion on the right side (approximately 300 cc) and left side (approximately 100 cc) were noted (Figs. 1–3). In laboratory-specific tests, D-dimer and fibrin degradation product (FDP) levels were high, and a low fibrinogen level was reported. There was no evidence of limb deep vein thrombosis in Doppler sonography. As a result, treatment with heparin started.

Considering the diagnosis of pulmonary embolism for the patient and the lack of history of recent travel, immobility, recent surgery, and active cancer, further investigation was conducted for the underlying cause of PTE were conducted. In the laboratory investigation, P-ANCA, C-ANCA, CH50, C3, C4, ANA, Anti-dsDNA, Anti-phospholipid antibody (IgM, IgG), Anti-B2glycprotein (IgM, IgG), Anti-cardiolipin antibody (IgM, IgG), Lupus anticoagulant, Protein C, Protein S, Factor V Leiden, and prothrombin G20210A were negative; however, HLA-B5 was positive. Then, we performed a Pathergy test for the patient, which was positive as well.

Based on positive HLA-B5 and Pathergy test, frequent genital aphthous ulcer, hyperpigmented lesions, pseudofolliculitis, and venous thrombosis, the diagnosis of BD was confirmed, and also treatment with methylprednisolone started for him. After two weeks of treatment, his condition improved, and he was discharged with prednisolone 5mg daily, apixaban 5mg twice a day.

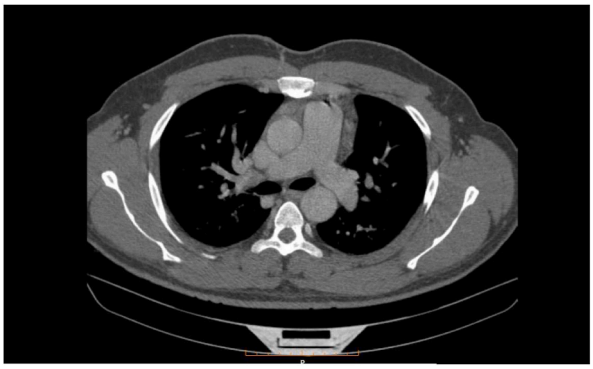

Fig. 1. A Pulmonary Computed Tomography Angiography shows pulmonary emboli in the lobar and segmental branches of the pulmonary arteries.

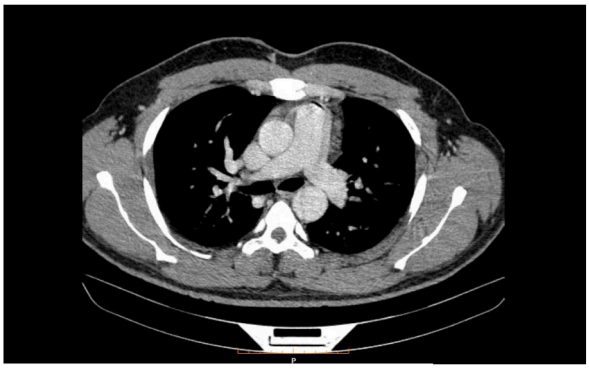

Fig. 2. A Pulmonary Computed Tomography Angiography shows pulmonary emboli in the lobar and segmental branches of the pulmonary arteries.

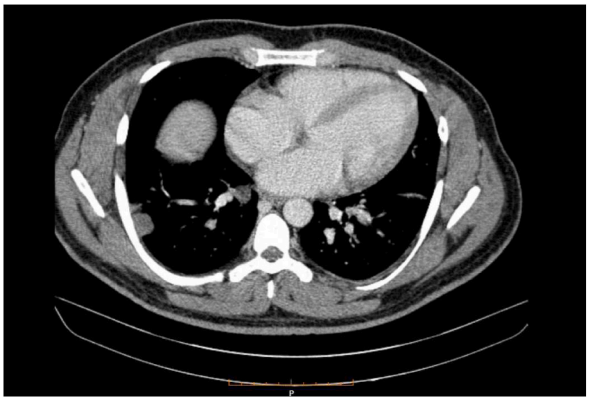

Fig. 3. A Pulmonary Computed Tomography Angiography shows peripheral mass-like alveolar densities and bilateral plural effusion.

3. Discussion

We admitted a 30-year-old patient with pleuritic chest pain, non-massive hemoptysis, and fever four days before hospitalization and a history of weight loss, nocturnal sweets, intermittent genial aphthous lesions, and skin lesions in the past month. During our evaluation, he had an S1Q3T3 pattern in EKG, a high level of D-dimer and FDP, a low level of fibrinogen along with pulmonary emboli in lobar and segmental branches of the right pulmonary artery and segmental branches of left lower lobe pulmonary artery were detected in his CTA. Then, in further evaluation, he was positive for HLA-B51. Based on his clinical condition and history of recurrent genital and skin lesions, a pathergy test was done, which was also positive. Therefore, the diagnosis of BD was confirmed for him.

BD is an inflammatory, relapsing, and remitting inconsistent vasculitis characterized by the recurrence of oral and genital ulcers and skin and ocular lesions. Young men are more likely to have vascular involvement, with a ratio of 4 to 1, compared to women. Due to the nature of this systemic inflammatory disease, other systems, including the vascular system, are also involved. It includes superficial and deep vein thrombosis, pulmonary embolism, peripheral artery aneurysms, aortitis, and arterial thrombosis. Among these, pulmonary embolism is mainly rare in these patients [1,5–8,12].

Pulmonary vascular involvement such as pulmonary artery aneurysm (PAA) and in situ pulmonary artery thrombosis (PAT), pulmonary hemorrhage, pulmonary infarction, PTE, arteriovenous shunt in the lung, and aneurysmal fistula, pleural effusion are the most frequent pulmonary complications in BD. According to the studies, clinical manifestations of PTE, in situ thrombosis, and pulmonary artery aneurysms include cough, fever, hemoptysis, pleuritic chest pain, and dyspnea. In line with our case, our patient was a 30-year-old male with no medical history admitted with systemic and respiratory manifestations and eventually diagnosed with PTE and BD [2–8].

The diagnosis of BD is based on clinical findings and diagnostic criteria. As mentioned, our patient was diagnosed with BD according to the ISG diagnostic criteria. The International Criteria for Behçet's Disease (ICBD) is also used to diagnose BD. According to that, eye lesions and oral and genital aphthous lesions are given 2 points. Skin lesions, nervous system involvement, vascular manifestations, and a positive pathergy test (optional) are each given one point. As stated in a study conducted by Davatchi F. et al., they evaluated both criteria in the training set and validation set. According to them, ISG had a higher specificity compared to ICBD (93.9% sensitivity and 92.1% specificity, compared with 81.2% sensitivity and 95.9% specificity for ISG); however, in the validation set, ICBD had a higher sensitivity (sensitivity of 94.8% vs. 85.0% and specificity (90.5%, vs. 96.0%). Our patient had a four score according to the ICBD, which also confirmed BD for him [6–12].

Angiography is the gold standard method for a patient with a suspected pulmonary embolism. In addition to the advantages of this method, which includes more accurate diagnosis and treatment if needed, Its disadvantages, which include being invasive and limited

in vasculitis patients, have led clinicians to use other non-invasive techniques such as MRI and CT angiography. Due to availability, practicability, high sensitivity (60–100%), and specificity (81–98%), diagnostic values make these modalities a suitable choice for PTE. Although a Ventilation-perfusion scan is a diagnostic method in PTE nevertheless, its accuracy in diagnosing pulmonary embolism in BD, considering that pulmonary artery obstruction in these patients often indicates thrombosis rather than embolism, questions the interpretation of pulmonary scintigraphy, therefore a simple mismatch is not to take into account as a PTE. Similar to our study, CTA revealed pulmonary emboli in the lobar and segmental branches of the right pulmonary artery and segmental branches of the left lower lobe pulmonary artery. Moreover, peripheral masslike alveolar densities, collapse consolidation in both lungs' lower lobes, and bilateral mild Plural effusion were observed [2,3,6–10,13,14].

The treatment of BD is different based on the type of involvement and its complications. For this reason, it is crucial to accurately identify the type of involvement and distinguish it from similar conditions. A high-dose diet of immunosuppressive drugs is recommended in PAA and PAT cases, and anticoagulants are not preferred due to the risk of increasing the possibility of active hemoptysis and mortality. In contrast, treatment with anticoagulants is necessary for patients with PTE. Our patient had a bilateral PTE, which is indicated for treatment with an anticoagulant. Similar to our study, Tekantapeh ST et al., 2018, reported a PTE in a known case of BD. Their patient was treated with methotrexate, prednisolone, and a monthly regime of cyclophosphamide due to refractory panuveitis. He was admitted with chest pain, dyspnea, hemoptysis, and edema of the left lower limb. Doppler ultrasound showed deep vein thrombosis, CTA, and a ventilation-perfusion scan confirmed the PTE in the patient, and anticoagulant treatment started for him [4–9,11,14].

The timely diagnosis of pulmonary embolism and its underlying cause, BD, is this study's main strength. A well-timed diagnosis of this disease led our patient to respond to treatment earlier and prevent morbidity and mortality. A limitation of our study was the lack of all laboratory diagnostic facilities in our center, which made us send patient samples to other centers.

4. Conclusion

BD is a multi-systemic chronic disease involving pulmonary, neurological, genitourinary, skin, and vascular systems. Pulmonary and cardiac involvement, such as PTE in BD, is rare but can cause life-threatening complications and is one of the leading causes of mortality and morbidity in this disease. Early diagnosis and treatment of PTE are essential for patients with large-vessel manifestations and BD, which should be considered in young patients with PTE who are not considered to have any risk factors for PTE.

Patient perspective

The patient was open to the idea of presenting and sharing his rare condition with all physicians around the world. Due to timely diagnosis, the patient was treated properly and there was no complications reported. All of the mentioned factors led to patient and family satisfaction with the process of diagnosis and treatment of the patient.

Ethics approval and consent to participate

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal. The purpose of this case report was completely explained to the patient and he was assured that his information would be keep confidential by the researchers. This case report was performed in line with principles of the declaration of Helsinki.

Consent for publication

The patient was fully informed about the purpose of this case report and assured that his information would be kept confidential by the researchers. Written consent was obtained from the patient to publish this case report and any accompanying images. The Editor-in-Chief of this journal can review a copy of the written consent.

Availability of data and material

The datasets used during the current study are available from the corresponding author on reasonable request. All data generated or analysed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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Authors' contributions

MH.TJ advised the case report study. M.M and N.L gathered patient's medical and health records. N.L and M.M wrote the first draft of the manuscript, and all authors commented on previous versions. All authors read and approved the final manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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