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Case report

Anticoagulation in Behçet related intrathoracic vasculitis

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ABSTRACT

Behçet disease is a rare multisystem condition associated with HLA-B51 positivity that commonly afflicts individuals of Turkish or Middle Eastern descent, less than 10% of whom have pulmonary involvement. Behçet-related pulmonary vasculitis is an uncommon and heterogeneous group of conditions, often with associated pulmonary artery thrombus formation. These microthrombi can result in a misdiagnosis of acute pulmonary embolism. Anticoagulation therapy can be difficult, as blood thinners increase the risk of pulmonary hemorrhage without affording the same benefits as in pulmonary embolism management. We present two cases of pulmonary vasculitis in the context of Behçet's syndrome, one in a Native American man with associated superior vena cava syndrome and pericarditis, with an increased risk of hemorrhagic pericardial effusion, and the other in an African American man with acute hypoxic respiratory failure with an increased risk of alveolar hemorrhage. We describe their management and the balancing act surrounding anticoagulation therapy in Behcet-related pulmonary vasculitis.

1. Introduction

Behçet disease is a rare multisystem condition associated with HLA-B51 positivity. The clinical triad of recurrent oral ulcers, scrotal ulcers and uveitis was initially described in 1937. Subsequently, Behçet disease has also been shown to affect the gastrointestinal tract, central nervous system and the pulmonary vasculature and parenchyma. The pulmonary manifestations are highly varied and typically present as non-specific opacities on chest radiography [1]. The clinical presentation of pulmonary Behçet disease can range from complete lack of symptoms to acute hypoxic respiratory failure, one of the most common reasons for admission to the ICU for these patients [2].

Acute hypoxic respiratory failure in pulmonary Behçet disease can result from alveolar hemorrhage, pulmonary embolism, or ventilation-perfusion mismatches in the context of pulmonary vasculitis. Early anticoagulation for pulmonary vasculature thromboembolism is typically avoided or delayed until the acute inflammatory changes have abated. However, in certain situations, the benefits of early anticoagulation may outweigh the risk of hemorrhage. We present two such cases that highlight this dilemma.

2. Case one

An 18-year-old Native American male presented with two days of pleuritic chest pain and shortness of breath. He was admitted to an outside hospital with similar symptoms one month prior where he was diagnosed with an acute pulmonary embolism with associated hemoptysis. He was started on apixaban and discharged after a brief hospital stay. He had no additional past medical history but had a family history notable for Behçet disease in his mother, complicated by oral, ocular, pulmonary, and central nervous system (CNS) involvement. He presented to our hospital as a direct admission with concern for the development of another pulmonary embolism. On admission, his oxygen saturation was in the high 90s on a simple face mask, blood pressure was in the low 100s/60s, and respiratory rate was in the low 20s. He was diaphoretic, clammy and uncomfortable appearing. His exam was notable for several small ulcerations at the base of the tongue as well as a 1cm painful, non-purulent ulcer on the scrotum. Pathergy testing was negative. Laboratory studies revealed a hemoglobin of 10.9 g/dL and a WBC count of 22 × 109/L. His CRP and ESR were elevated at 183 mg/L and 72 mm/h, respectively. HLA-B51 testing was positive. ANA, ENA, antiphospholipid antibody, DRVVT, and beta-2-

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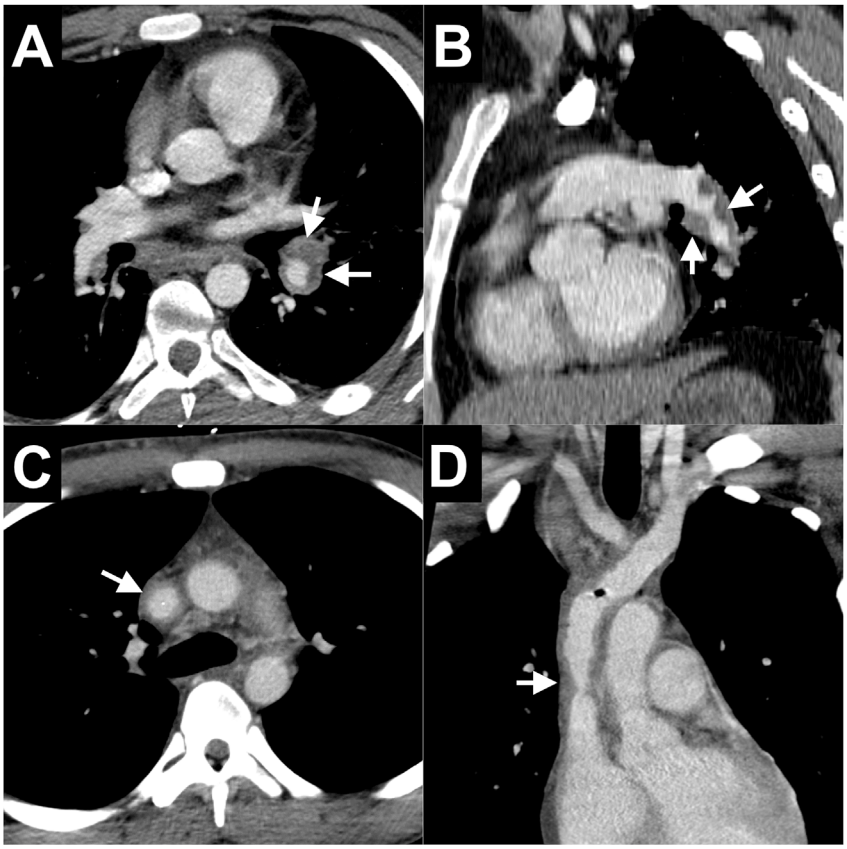

Fig. 1. Axial (A) and sagittal oblique (B) reconstructions from a contrast-enhanced chest CT of Patient 1 performed at an outside hospital. Images demonstrate irregular, eccentric filling defects within the peripheral aspects of the left lower lobe pulmonary artery which appear to distort the outer contours of the artery wall (circle). Initially interpreted as consistent with thromboembolic disease, in retrospect the findings are more suggestive of in-situ pulmonary artery thrombosis in the setting of Bechet's rather than thromboembolism from deep venous thrombosis. Axial (C) and coronal oblique (D) reconstructions from a contrast-enhanced chest CT of Patient 2 performed upon initial presentation. Images demonstrate soft tissue thickening of the wall of the central systemic veins, especially the superior vena cava (SVC), which is focally narrowed at its midpoint (circle).

glycoprotein 1 antibody and ANCA testing were all negative.

His CT chest revealed low-attenuation filling defects within and around his pulmonary arteries, presumed to be thrombosis. Multifocal airspace disease consisting of patchy consolidation and ground glass opacities probably reflected areas of hemorrhage and/or infarction related to his underlying vascular disease. No obvious pulmonary aneurysms were seen, although the pulmonary arteries had irregular contours in several areas (Fig. 1). He was started on IV methylprednisolone due to concern for pulmonary vasculitis. After steroid initiation his respiratory status improved. The following morning he underwent bronchoscopy, which was notable for scattered areas of hypervascularity and bland mucosa in the right upper lobe, but otherwise unremarkable without evidence of pulmonary hemorrhage. MRI of the head and neck were obtained but did not reveal any evidence of CNS vasculitis.

Over the following three days, his respiratory status improved, and he was discharged from the hospital on a 3-month prednisone taper. Given his significant respiratory distress, his apixaban was resumed with the goal of preventing microthrombi extension and further V/Q mismatch. At his 6 month follow-up visit after hospitalization, he had done well on the prednisone taper and apixaban, and started azathioprine under the supervision of his outside rheumatologist.

3. Case two

A 24-year-old African American male with a past medical history of recurrent oral and scrotal ulcers in the setting of presumed Behçet disease and chronic inhaled methamphetamine use presented to an outside hospital with dyspnea. He was determined to have a large pericardial effusion and 1L of serous fluid which was drained by pericardiocentesis. The patient subsequently developed a deep venous thrombosis associated with his peripherally-inserted central catheter line, which was further complicated by superior vena cava (SVC) syndrome. The etiology was believed to be related to his underlying Behçet disease rather than the PICC line itself. The patient was started on warfarin therapy.

He presented to our hospital one month later with symptoms of recurrent painful genital ulcerations. He had gone to several urgent care facilities in the weeks prior and had received various undisclosed antibiotics without any improvement. He also described an unintentional weight loss of approximately 20 pounds during this period.

On examination, he was hemodynamically stable, but uncomfortable appearing with a 2mm aphthous ulcer at the tip of the tongue as well as a painful non-purulent 15mm ulceration on the right side of the scrotum. Pathergy testing was negative. Laboratory testing revealed a hemoglobin of 8.5 with a leukocytosis of 14 × 109/L and a platelet count of 607 × 109/L. His CRP and ESR were elevated at 243 g/L and 93 mm/h, respectively. Liver function tests were within normal limits. HLA-B51 testing was positive. ANA, ENA, aldolase, antiphospholipid antibody, beta-2-glycoprotein 1 antibody, DRVVT, ANCA, CK, SPEP, HIV, HHV6, HHV8, CMV, EBV, histoplasma and RPR testing were all negative.

Compared to a prior CT from one month prior, repeat CT imaging of the chest, abdomen and pelvis revealed interval resolution of inflammatory-appearing soft tissue surrounding his SVC. However, there was now complete occlusion of the SVC with interval development of extensive venous collaterals within the anterior chest wall, along the internal mammary, azygos, hemiazygos systems, and paravertebral veins (Fig. 1C–D). No findings to suggest pulmonary aneurysm or embolism. The following day the patient underwent bronchoscopy which was entirely unremarkable. Biopsy of the scrotal ulcerations showed non-specific inflammatory infiltrates. Colchicine was initiated for his scrotal ulcerations and he was started on IV methylprednisolone which was transitioned to a 60mg prednisone taper contingent upon clinical response. For his expanding SVC thrombus, he was bridged to warfarin with enoxaparin. He was eventually started on azathioprine in the

outpatient setting.

4. Discussion

Behçet disease has variable clinical presentations with equally variable associated outcomes. This is especially true in the context of Behçet-related vasculitis, which occurs in roughly 30% of patients with Behçet disease [3]. The pulmonary manifestations of Behçet disease are typically vasculitis or pulmonary artery aneurysm [3]. Pulmonary artery aneurysms are both the most common and most feared pulmonary complications of Behçet disease with a reported 50% one-year mortality [3]. As such, all suspected pulmonary Behçet disease patients should have a CT of the chest for assessment of the pulmonary artery and lung parenchyma [3].

In these patients, anticoagulation in the context of pulmonary vasculature thromboembolism may precipitate pulmonary hemorrhage if not preceded by appropriate immunosuppression. As such, the European League Against Rheumatism recommends against routine anticoagulation in Behçet disease and instead recommends immunosuppression as the mainstay of therapy. Recent small retrospective studies investigating the treatment regimens in preventing relapse of vascular Behçet disease found that immunosuppression, but not anticoagulation, reduced relapse risk [4,5]. For this reason, rapid initiation of immunosuppression to minimize inflammation takes precedent over the decision to initiate anticoagulation therapy. Typical immunosuppressive therapy consists of intravenous corticosteroids, which is then transitioned to a prednisone taper followed by azathioprine.

Yet, in both of these cases, the decision to pursue early anticoagulation was based on significant respiratory distress in the first case and an expanding SVC thrombus in the second case. Importantly, neither of these patients had evidence of pulmonary artery aneurysm or intracranial vasculitis, both of which may be contraindications to anticoagulation. As such, we were able to anticoagulate safely even prior to adequate immunosuppression. It is not clear whether there is any benefit between the different types of anticoagulants, including the direct oral anticoagulants (DOACs), and here is no agreed upon duration of time for anticoagulation.

In conclusion, the presence of PE or DVT in the context of oral or genital ulcers should prompt the consideration of a diagnosis of pulmonary Behçet disease. As there are no available biomarkers, the diagnosis of Behçet disease is based largely on clinical findings. Clinicians and chest radiologists should maintain a low threshold for detection of pulmonary artery aneurysms as this carries the greatest risk for hemorrhage amongst all Behçet vasculitis manifestations. We successfully managed two patients with pulmonary Behçet disease using high dose steroids for three days before a prolonged steroid taper, with both warfarin and apixaban proving to be suitable anticoagulation options following three days of high dose steroids and clinical stabilization. With careful attention to detail and prompt initiation of immunosuppression, this rare disease manifestation can be managed without complication.

5. Learning points

The mainstay of treatment in Behçet-related pulmonary vasculitis is immunosuppression. In the appropriate clinical scenarios, anticoagulation may be safe potentially improve outcomes if immunosuppression has been started and clinical status is worsening. Despite the association of Behçet disease with HLA-B51 and individuals of Turkish or Middle Eastern descent, it can be seen across all ethnicities.

Financial disclosures

None.

Conflicts of interest

None.

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