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CASE REPORT

Right Ventricular *Thrombus* and Cerebral Artery Aneurysm in a Patient with Behçet's Disease

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جلطة في البطين الأيمن وتمدد الشريان الدماغي في مريضة بمرض بهجت

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ABSTRACT: We report a 35-year-old woman referred to the Imam Ali Hospital, Kermanshah, Iran, in July 2014 for evaluation of postoperative dyspnoea after neurosurgery performed seven days previously for a ruptured cerebral artery aneurysm. She was known to have Behçet's disease with a history of recurrent oral and genital aphthous ulcers and *uveitis*. At referral, her symptoms included *vertigo*, dysarthria, palpitations and chest pain. Transthoracic echocardiography (TTE) revealed a large *thrombus* in her right ventricle outflow tract and open-heart surgery was performed eight days after the previous surgery to remove the clot. The postoperative period was complicated by transient acute renal failure, which resolved spontaneously. The patient was discharged 13 days after the cardiac surgery on warfarin, prednisolone, azathioprine and cyclophosphamide. Cyclophosphamide and azathioprine were discontinued after three months as the symptoms had completely resolved; however, prednisolone was continued due to recurrent *uveitis*. A 10-month follow-up TTE scan revealed no *thrombus* recurrence and treatment with warfarin and prednisolone was continued.

Keywords: Behçet Disease; Thrombus; Fusiform Aneurysm; Case Report; Iran.

الملخص: هذا تقرير حالة لأمرأة تبلغ من العمر 35 عاما تم تحويلها إلى مستشفى الإمام علي، كرمانشاه، إيران، في يوليو 2014 لتقييم ضيق التنفس بعد إجراء جراحة لتمدد شرياني دماغي منفجر منذ سبعة أيام قبل التنويم. كانت المريضة مصابة بمرض بهجت مع تاريخ مرضي للقرح القلاعية المتكررة في الفم والأعضاء التناسلية والتهاب القزحية. عند التحويل كانت المريضة تعاني من دوار، تلعثم، وخفقان وألم في الصدر. كشف تخطيط صدى القلب عبر الصدر (TTE) عن وجود جلطة كبيرة في تدفق مجاري البطين الأيمن. تم إجراء جراحة قلب مفتوح بعد ثمانية أيام من الجراحة السابقة. تعقدت فترة ما بعد الجراحة بحدوث الفشل الكلوي الحاد، الذي شفي من تلقاء نفسه. غادرت المريضة بعد 13 يوما من عملية القلب المفتوح على عقاقير الوارفارين، البريدنيزولون، الآزوثيوبرين والسيكلوفوسفاميد. تم ايقاف عقاري السيكلوفوسفاميد والآزوثيوبرين بعد ثلاثة أشهر نتيجة لأختفاء كل الأعراض تماما. ومع ذلك، استمر عقار البريدنيزولون بسبب التهابات القزحية المتكررة. لم تكشف اعادة فحص ال TTE بعد عشرة شهور عن عودة الجلطات واستمر العلاج بالوارفارين والبريدنيزولون.

كلمات مفتاحية: مرض بهجت؛ جلطة؛ تمدد الأوعية الدموية المغزلي؛ تقرير حالة؛ إيران.

Behçet's disease is a chronic inflammatory disease diagnosed by recurrent aphthous ulcers, genital ulcers and eye involvement in the form of *uveitis*.[1] Cerebrovascular involvement with arterial aneurysm rupture is an exceedingly rare phenomenon in patients with Behçet's disease and is only found in 1.6–10% of all vascular lesions in these patients.[2,3] Cerebral artery aneurysms, brain parenchymal inflammatory disease, pseudotumour *cerebri*, intimal hyperplasia of the cerebral artery and vasculitis are the main symptoms of neuro-Behçet's disease.[4] Cardiac involvement leads to inflammatory endocardial disease, coronary artery *stenosis*, pericarditis, cardiomyopathy and *thrombus* formation.[4] However, the combination of an intracardiac *thrombus* with rupture of a cerebral artery aneurysm is a very rare occurrence.[5]

Case Report

A 35-year-old female known to have Behçet's disease was referred to the Imam Ali Hospital, Kermanshah, Iran, in July 2014 from the neurosurgery ward for evaluation of postoperative dyspnoea. Seven days previously, she had undergone a cranial surgery for a ruptured cerebral artery aneurysm and the removal of parenchymal haemorrhagic lesions. Upon admission to the neurosurgery ward, an initial diagnosis of a ruptured cerebral artery aneurysm was made based on the parenchymal changes observed on computed tomography [Figure 1]. Cerebral angiography confirmed haemorrhagic *sequelae* in the left cerebral artery branch due to the rupture of the aneurysm [Figure 2].

Seven days after the neurosurgery, the patient complained of *vertigo*, dysarthria, dyspnoea, fever,

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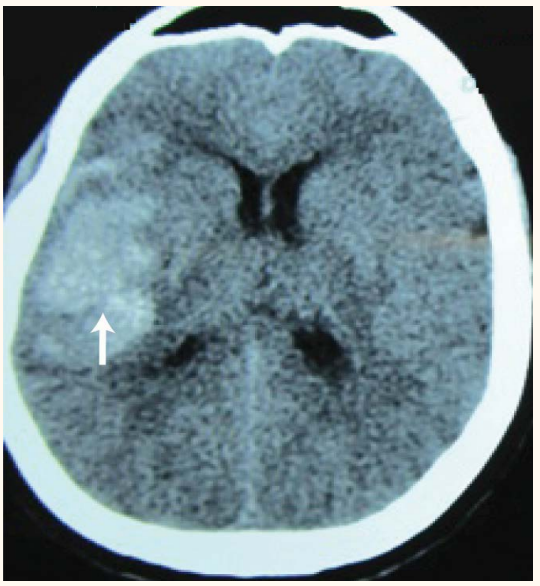

Figure 1: Preoperative computed tomography of a 35-year-old female patient with Behçet's disease showing a haemorrhagic mass in the right cranial hemisphere (arrow) indicative of a ruptured cerebral artery aneurysm.

heart palpitations and chest pain and was referred to the cardiac surgery ward. In the ward, her medical history revealed classic features of Behcet's disease, including four occurrences of mouth and genital ulcers in the previous year and ophthalmologist-confirmed *uveitis*. A physical examination revealed signs of the former cranial surgery, multiple aphthous mouth and genital ulcers and left *haemiparesis*. There were no signs of thrombophlebitis or lower limb oedema. Chest radiography was normal. The results of laboratory tests on admission were as follows: white blood cell count: 19,000/mm^{-3} (normal range [NR]: 4,300–10,800/mm^{-3})

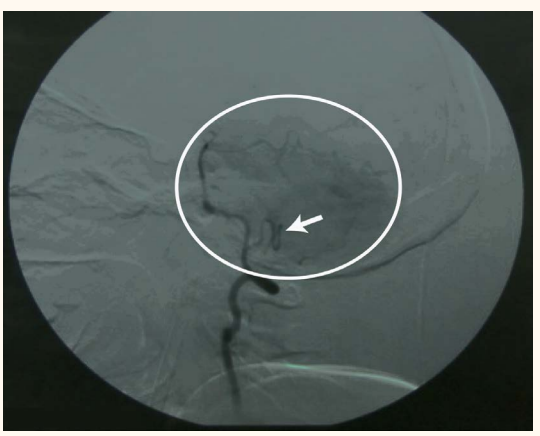

Figure 2: Postoperative cerebral angiography of a 35-year-old female patient with Behçet's disease with a ruptured cerebral artery aneurysm in the left middle cerebral artery branch (circle), with aneurysm clip *in situ* (arrow).

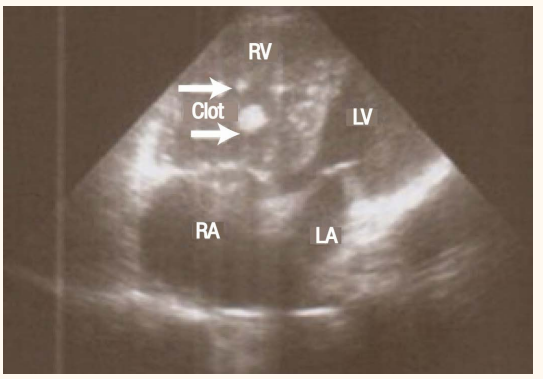

Figure 3: Transthoracic echocardiography of a 35-year-old female patient with Behçet's disease showing a large *thrombus* (arrows) in the right ventricular outflow tract.
LA = left atrium; RA = right atrium; LV = left ventricle; RV = right ventricle.

with 91% neutrophils; platelet count: 90,000/mm^{-3} (NR: 150,000–450,000/mm^{-3}); haemoglobin count: 10 g/dL (NR: 13–18 g/dL); C-reactive protein levels: 54 mg/dL (NR: ≤0.8 mg/dL); erythrocyte sedimentation rate: 80 mm/hour (NR: 0–20 mm/hour); blood urea nitrogen levels: 35 mg/dL (NR: 7–25 mg/dL); and creatinine levels: 2.9 mg/dL (NR: 0.6–1.2 mg/dL). The thrombocytopaenia was treated with prednisolone and her platelet levels had normalised when a repeat platelet count was performed three weeks later. Urinalysis revealed proteinuria without haematuria. Anti-nuclear, anti-neutrophil cytoplasmic, anti-double strand and anticardiolipin antibodies were negative, as were rheumatoid factor and *lupus* anticoagulants. Test results for other thrombophilia factors were normal, including hyperhomocysteinemia, antiphospholipid antibodies, protein S, protein C and antithrombin III levels and factor V Leiden.

Transthoracic echocardiography (TTE) revealed a mobile *thrombus* in the right ventricle outflow tract (RVOT) of the subtricuspid apparatus [Figure 3]; this was believed to have been the cause of the patient's respiratory symptoms. Eight days after the neurosurgery and one day after admission to the cardiac surgery ward, open cardiac surgery was performed to remove the clot. Intraoperatively, the *thrombus* was observed to be located in the RVOT with a single site of attachment to the perimembranous septum and septal tricuspid valve [Figure 4]. Surgical exploration of the pulmonary artery and its main branches revealed no other *thrombi*. A pulmonary thromboembolism was suspected; however, no facilities for lung perfusion scans were available and the patient could not be transferred to another centre due to her general condition.

Postoperatively, the patient suffered from acute renal dysfunction and nephrologists were consulted.

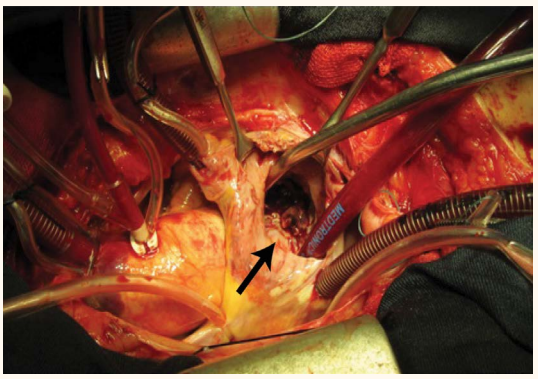

Figure 4: Intraoperative photograph of a *thrombus* in the right ventricular outflow tract of the subtricuspid apparatus (arrow) of a 35-year-old female with Behçet's disease.

However, the condition resolved spontaneously. A few days later, the patient was treated with immunosuppressive therapy for symptoms of Behcet's disease. Symptoms of oral and genital aphthous ulcers and *uveitis* were relieved using a combination of oral corticosteroids, prednisolone, azathioprine and cyclophosphamide. Nine days after the cardiac surgery, she was prescribed anticoagulation therapy (heparin and warfarin) to prevent further *thrombus* formation. The patient was discharged on the 13th postoperative day on warfarin, prednisolone, azathioprine and cyclophosphamide. After three months of treatment, the cyclophosphamide and azathioprine were discontinued due to resolution of the symptoms. At a 10-month follow-up, the patient's general condition was satisfactory and TTE indicated no *thrombus* recurrence. However, prednisolone was continued indefinitely due to recurrent eye involvement. Warfarin was also continued due to prolonged bedrest caused by *haemiparesis* which increases the risk of thromboemboli in the extremities.

Discussion

This report presents a patient with Behçet's disease with right ventricle *thrombus* formation after a previous cerebral artery aneurysm rupture. Cardiac involvement in Behçet's disease is very rare and consists mainly of *thrombus* formation. While any chamber of the heart may be involved in clot formation, the right atrium, with its unique haemodynamic characteristics, is the most commonly affected chamber.[5] All of the layers of the heart are involved in the inflammatory process of Behçet's disease.[6] Endothelial inflammation can cause luminal irregularities and thickening which is revealed as *thrombi*, Loeffler endocarditis and arterial aneurysm formation. *Thrombi* of the superior and inferior *vena cava* (IVC) may cause superior *vena cava* syndrome and Budd-Chiari syndrome. Systemic *lupus* erythematosus (SLE) can be associated with cardiac thrombosis and cerebral complications;[6] ruling out SLE as a diagnosis was therefore necessary in the current case.

Aneurysms of the large and medium arteries—such as the aorta, pulmonary and peripheral arteries including the femoral, popliteal, brachial and subclavian arteries—can form part of the vascular involvement in Behçet's disease.[6] One important medium-sized artery involved in aneurysm formation is the cerebral artery. Although vascular inflammatory disease is observed in only 25% of patients with Behçet's disease, it is nonetheless the most important predictive factor of Behçet's disease-related mortality.[6] The combination of cerebral and cardiac manifestations of Behçet's disease is a very uncommon phenomenon.[7] Intracardiac *thrombus* formation may be caused by cardiac endothelial inflammation or may arise from an extracardiac *thrombus* that has broken off from the thromboembolism source in a peripheral vein and dislodged into the cardiac chamber. However, emboli that originate from a cardiac chamber are a relatively uncommon occurrence.[7]

Mogulkoç *et al.* detected 13 cases of pulmonary emboli among 25 subjects with Behçet's disease; in approximately 50% of these cases, *thrombosis* in the inferior and superior *vena cavae* and deep lower extremity veins may have been the source of the embolism.[5] Most emboli in Behçet's disease patients begin in the cardiac chambers.[8] In patients without Behçet's disease, deep vein *thrombosis* in the lower extremities is usually associated with pulmonary emboli, as *thrombi* formed in the veins in the absence of inflammation can easily break off and travel to the heart and lungs. Contrary to conventional thromboemboli, the combination of a pulmonary thromboembolism with lower extremity phlebitis is a rare event in patients with Behçet's disease.[8] *Thrombi* formed in inflamed vessels are strongly adherent to the endothelium; therefore, these patients have a low risk of thromboembolism.[9,10] Houman *et al.* observed vascular involvement in 43.3% of 113 Behçet's disease cases; of those, 89.8% had deep vein *thrombosis*.[11] Involvement of the deep venous system is more common in men than women.[10] Luo *et al.* evaluated the clinical features of patients with Behçet's disease and cardiac chamber *thrombi*; they found that intracardiac *thrombus* formation frequently occurred in young male patients and usually involved the right cardiac chambers.[12]

In the present case report, the patient was treated with immunosuppressive and antithrombotic drugs following the surgical removal of the cardiac *thrombus*.

Cyclophosphamide, azathioprine and prednisolone were prescribed. Prior to starting treatment with cyclophosphamide and azathioprine, routine baseline assessments were performed, including a complete blood cell count and liver and renal function tests; regular monitoring continued throughout treatment. To prevent urinary toxicity such as haemorrhagic cystitis, patients need to be adequately hydrated and pass urine frequently. As such, patients should be instructed to increase their fluid intake 24 hours before, during and at least 24 hours after receiving cyclophosphamide.[12]

Conclusion

In the present case, a large intracardiac *thrombus* was detected in a patient with Behçet's disease who had previously undergone neurosurgery for a ruptured cerebral artery aneurysm. The patient underwent open-heart surgery for the removal of the *thrombus* before undergoing immune suppression and antithombotic therapy. At a 10-month follow-up, she was healthy with no evidence of further *thrombus* formation.

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