Recurrent venous thrombosis in a patient with Ebstein’s anomaly

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ABSTRACT

Herein, we report a case of a 27-year-old man with Ebstein’s anomaly and a history of unexplained recurrent venous thrombosis despite adequate anticoagulation. After surgical correction of the Ebstein’s anomaly, the venous thromboembolic events did not recur. This case demonstrates the possible etiopathogenesis of Ebstein’s anomaly in causing recurrent venous thromboembolism, which is likely caused through impedance of venous blood flow. Our objective in presenting this particular case is to highlight the possible association between Ebstein’s anomaly and venous thrombosis.

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The proposed mechanisms for the pathogenesis of venous thrombosis are explained by the Virchow’s triad, which consists of blood stasis, endothelial injury, and hypercoagulability. The causes of venous thrombosis can be classified as hereditary, acquired, or mixed. Factor V Leiden mutation, prothrombin gene mutation, and defects in protein S, protein C, and/or anti-thrombin III are known to be common inherited risk factors of venous thrombosis. The common acquired risk factors of venous thrombosis include recent surgery, malignancy, trauma, pregnancy, immobilization, and previous thrombotic episodes. Moreover, some vascular malformations are known to be risk factors for the development of deep vein thrombosis (DVT), such as Paget-Schroetter syndrome, May-Thurner syndrome, and Klippel-Trenaunay syndrome. Ebstein’s anomaly is a rare congenital heart disease that may be associated with right-to-left shunts that predispose to paradoxical embolization. Anticoagulant therapy is the initial treatment for venous thrombosis. Patients usually receive long-term anticoagulation therapy, such as warfarin or direct oral anticoagulants, which include dabigatran and rivaroxaban, to prevent recurrent thrombosis, embolism, and other late complications. Our objective in presenting this particular case is to highlight the possible association between Ebstein’s anomaly and venous thrombosis.
dural venous sinus thrombosis. Initial thrombophilia workup, including complete blood count, coagulation profile, proteins C and S, antithrombin III, factor V

Leiden, lupus anticoagulant antibodies, and cardiolipin antibodies, were all normal.

Thus, he was diagnosed with unprovoked cerebral sinus venous thrombosis and was treated with heparin followed by warfarin for 2 years due to the severity of the event. He was referred to King Faisal Specialist Hospital and Research Centre for further management.

**Clinical findings.** In 2005, despite maintaining a therapeutic international normalized ratio (INR) level (2.5–3.5), he developed deep vein thrombosis in the right leg. Warfarin was discontinued, and he was treated with enoxaparin (1 mg/kg b.i.d.). Repeated thrombophilia workup showed negative results.

In the course of his follow-up visits, he had a high platelet count that resolved on further follow-ups. Hence, bone marrow biopsy was carried out to determine any occult myeloproliferative neoplasms that can present with recurrent thrombosis. However, the result of the biopsy was normal. Eight months later, while on enoxaparin, he presented with abdominal distention and lower limb edema. Upon admission, his heart rate was 110 per minute. His blood pressure was
117/78 mmHg, and his oxygen saturation in room air was 97%. His jugular venous pressure was elevated, with a prominent V-wave. First and second heart sounds were normal, and there was a loud holosystolic murmur at the left sternal border. The abdomen was distended, with large ascites and hepatomegaly, measuring 6 cm below the right costal margin. The rest of the examination was unremarkable.

Laboratory investigations during his hospital stay showed the following: hemoglobin, 128 g/L; white blood cell count, 9.5 x 10^9 cells/L; platelets, 114 x 10^9/L; INR, 1.9; sodium, 134 mmol/L; albumin, 25 g/L; bilirubin, 89 umol/L; alanine aminotransferase, normal. The anti-Xa levels were not checked at the time because he had normal kidney function and was compliant with treatment.

**Diagnostic assessment.** He was diagnosed using Doppler ultrasound with Budd-Chiari syndrome. Moreover, because of the incidental finding of a murmur, he underwent echocardiographic evaluation and was diagnosed with Ebstein’s anomaly and severe tricuspid regurgitation, with no evidence of atrial septal defect or patent foramen ovale (Figure 1).

**Therapeutic intervention.** He was successfully treated by angioplasty of the inferior vena cava and right hepatic vein. Anticoagulation was resumed with 18 U/kg/h heparin IV, followed by warfarin (10 mg PO q.d.) and aspirin (100 mg PO q.d.). A multidisciplinary team decided to postpone any corrective cardiac surgery until the venous thromboembolic events (VTEs) were controlled.

A year later, he started complaining of shortness of breath and palpitations, which were affecting his daily activities. Consequently, he underwent tricuspid valve replacement with mechanical valve, which was complicated by complete heart block; thus, he underwent a permanent pacemaker insertion. The patient was maintained on warfarin (4 mg PO q.d.) and aspirin (100 mg PO q.d.) after discharge.

**Follow-up and outcomes.** Currently, 12 years after surgery, he remains asymptomatic and has no symptoms of recurrent VTE. He is maintained on warfarin (4 mg PO q.d.) and aspirin (100 mg PO q.d.) and undergoes regular follow-up for both cardiac and hematological conditions.

**Discussion.** Ebstein’s anomaly is a rare congenital heart disease characterized by the downward displacement of the tricuspid valve leaflets into the right ventricle of the heart, resulting in atrialization of the right ventricle. Clinical presentation usually varies depending on the severity of the disease, ranging from no symptoms to severe clinical manifestations. Common associations of Ebstein’s anomaly include interatrial communication, patent foramen ovale, ventricular septal defect, and distal right ventricle anomalies. It can be complicated by arrhythmias, severe cyanosis, heart failure, and death. A common complication of Ebstein’s anomaly in adults includes paradoxical embolism, which is an originally venous thrombus that transverses through a right-to-left shunt and enters the systemic circulation.

Our case demonstrates the rare association of Ebstein’s anomaly with pure, recurrent venous thrombosis in the absence of a right-to-left shunt. Despite the administration of different, full-dose anticoagulant therapy, this patient still had recurrent VTE. The fact that his recurrent VTE totally disappeared after the surgical repair of the Ebstein’s anomaly possibly suggests an association of the recurrent VTEs resulting from chronic venous stasis due to this cardiac anomaly. We reviewed the literature to try to identify this rare association; however, we only found one case in which Viallefont et al reported a case of retinal vein thrombosis in association with Ebstein’s anomaly.

Venous hepatic congestion can occur with Ebstein’s anomaly, leading to the development of Budd-Chiari syndrome. On the contrary, cerebral congestion and lower extremity venous congestion are not usually expected to occur in such patients.
In conclusion, Ebstein's anomaly is a rare disorder that can result in paradoxical embolisms when associated with right-to-left shunts. Venous stasis in patients with Ebstein's anomaly with tricuspid regurgitation may be a predisposing factor for VTE. Therefore, physicians caring for patients with such an anomaly should be aware of this rare association. In addition, patients presenting with recurrent unexplained thrombosis should have careful clinical evaluation and may require objective cardiac evaluation to rule out cardiovascular anomalies, as clinically indicated.

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**References**