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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Table 1 - Progress of the patient case from initial presentation to diagnosis, treatment and follow-up.

| Dates               | Relevant past medical history and interventions | Diagnostic testing | Interventions                          |
|---------------------|-------------------------------------------------|--------------------|----------------------------------------|
| 8th November 2003   | Unprovoked cerebral sinus venous thrombosis diagnosed by brain MRI, managed with heparin followed by warfarin. | No other intervention |                                         |
| 24th July 2004      | Follow up visit                                 | Blood investigations for thrombophilia were negative (Table 2) |                                         |
| 20th February 2005  | DVT of the right leg                            | Doppler ultrasound  | Treated with enoxaparin (1 mg/kg b.i.d.) |
| 16th April 2005     | Follow up visit                                 | Blood investigations showed an elevated platelet count of 479 x 10^9/L. | No other intervention                   |
| 16th October 2005   | Presented with abdominal distention and lower limb edema. She was admitted for management. | He was admitted for an angioplasty (carried out on 18th October) of the inferior vena cava and right hepatic vein. |                                         |
| 16th October 2005   | Present with shortness of breath and palpitations. He was admitted for corrective surgery of his Ebstein’s anomaly. | He was admitted for tricuspid valve replacement with mechanical valve (carried out on 18th October) |                                         |
| 16th October 2006   | Routine pre-operative investigations            | Permanent pacemaker insertion (carried out on 30th October) | Discharged on warfarin (4 mg PO q.d.) and aspirin (100 mg PO q.d.) |

DVT - Deep vein thrombosis, PO - Oral, q.d. - Once daily, bid - Twice a day, IV - Intravenous, INR - International normalized ratio

Figure 1 - Transesophageal echocardiogram (TEE) (4-chamber view, apex down) Ebstein’s anomaly of the tricuspid valve is present. The septal leaflet is displaced apically, while the anterior tricuspid leaflet is elongated and tethered. (arrow) Absent posterior leaflet. ARV - atrialized right ventricle, RA - right atrium, LA - left atrium, LV - left ventricle

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 (Table 2).

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...
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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.8 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.5 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 al10 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.8 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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