An Unusual Case of Tricuspid Stenosis

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ABSTRACT

Tricuspid stenosis is an uncommon valvular abnormality commonly associated with other valvular lesions. Ebstein's anomaly is a rare congenital heart malformation characterized primarily by abnormalities of the tricuspid valve and right ventricle. Endomyocardial fibrosis is a restrictive cardiomyopathy observed in tropical and subtropical regions. It may cause right ventricular distortion with apparent apical displacement of the tricuspid valve, mimicking Ebstein's anomaly. Eosinophilia is the most commonly cited aetiological link in endomyocardial fibrosis. Here we report the case of 42-year-old male patient who presented with heart failure and severe tricuspid stenosis where a diagnosis of hypereosinophilic syndrome was also established. This case represented a diagnostic challenge in the search for the definitive cause of the tricuspid stenosis.

LEARNING POINTS

- Ebstein's anomaly is a rare congenital heart malformation characterized primarily by abnormalities of the tricuspid valve and right ventricle. The tricuspid valve is usually incompetent, and very rarely stenotic.
- Hypereosinophilic syndromes can be associated with heart damage. The fibrotic stage of eosinophil-mediated heart damage is characterized by altered cardiac function due to either compromise/entrapment of the cordae tendineae and/or restrictive cardiomyopathy.
- Endomyocardial fibrosis is a restrictive cardiomyopathy observed in tropical and subtropical regions that may be indistinguishable from the Loeffler's endocarditis observed in temperate climates. It may cause right ventricle distortion and apical displacement of the tricuspid valve, mimicking Ebstein's anomaly.

KEYWORDS

Tricuspid stenosis, hypereosinophilic syndrome, Ebstein´s anomaly, endomyocardial fibrosis

CASE DESCRIPTION

We present the case of a 42-year-old Portuguese male patient, born and living in Venezuela. He was asymptomatic until a year and a half before being admitted to our hospital, when he presented with progressive exertional dyspnoea, orthopnoea, paroxysmal nocturnal dyspnoea, increased abdominal circumference and lower limb oedema. He had a previous diagnosis of idiopathic thrombocytopenic purpura and a lower limb deep venous thrombosis when he was 35.

He had been recently hospitalized in Venezuela with right-sided heart failure. A transthoracic echocardiographic (TTE) study revealed a dilated right atrium and a apical implanted, severely stenotic tricuspid valve. A thoraco-abdomino-pelvic computed tomography (CT) scan

revealed right pleural effusion, a large volume of ascites and superior and inferior vena cava thrombosis. A diagnosis of antiphospholipid syndrome (APS) was made and treatment with warfarin was initiated. Cardiac catheterization showed absence of coronary disease. A percutaneous tricuspid balloon dilatation valvuloplasty was performed.

Five months later, symptoms recurred. TTE revealed a severely stenotic tricuspid valve. Surgical treatment was proposed, but the patient decided to travel to Portugal where he was admitted for investigation and treatment.

On examination, he was haemodynamically stable, had a diastolic murmur (grade II/IV) on the left sternal border, decreased breath sounds at the right lung base, a large volume of ascites and bilateral lower limb oedema.

Methods and Procedures

Laboratory tests (*Table 1*) revealed mild thrombocytopenia. Eosinophilia (2.03×10^9/l) was present for more than 6 months. Parasitological stool examination was negative. The serum immunoglobulins, tryptase, protein electrophoresis and immunofixation were normal. Immunophenotypic analysis of peripheral blood cells revealed no monoclonal population. The 24-hour urinary excretion of 5-hydroxyindoleacetic acid (5-HIAA) was normal. Urinalysis was unremarkable.

Variable	Reference range	Result
Haemoglobin (g/dl)	*13.0–18.0*	*17.0*
White cell count ($\times10^9$/l)	*4.0–11.0*	*9.61*
Eosinophils ($\times10^9$/l)	*0.02–0.5*	*2.02*
Platelet count ($\times10^9$/l)	*150–400*	*111*
Alanine aminotransferase (U/l)	*10–37*	*34*
Aspartate aminotransferase (U/l)	*10–37*	*13*
Alkaline phosphatase (U/l)	*30–120*	*128*
Gamma-glutamyltransferase (U/l)	*10–49*	*90*
Total bilirubin (mg/dl)	*<1.2*	*1.53*
Direct bilirubin (mg/dl)	*<0.4*	*0.32*
Creatine kinase (U/l)	*10–172*	*62*
Myoglobin	*<146.9*	*39.7*
Urea (mg/dl)	*10–50*	*56*
Creatinine (mg/dl)	*0.67–1.17*	*1.01*
Sodium (mEq/l)	*135–147*	*137*
Potassium (mEq/l)	*3.5–5.1*	*4.8*
C-reactive protein (mg/l)	*<3.0*	*7.4*
Brain natriuretic peptide (pg/ml)	*<100*	*210*
Thyroid-stimulating hormone (IU/ml)	*0.35–4.94*	*2.58*
Thyroxine (T4) (ng/dl)	*0.70–1.48*	*1.08*
Anti-cardiolipin antibodies IgG (GPL)	*<15*	*295.0*
Anti-cardiolipin antibodies IgM (MPL)	*<15*	*1.3*
Beta2 glycoprotein 1 IgG (SGU)	*<15*	*53.1*
Beta2 glycoprotein 1 IgM (SMU)	*<15*	*<1.0*
HIV (Ag+Ab HIV 1+2)	*–*	*Negative*
HCV Ab	*–*	*Negative*
HBs Ag	*–*	*Negative*
HBc Ab	*–*	*Negative*
HBs Ab (IU/l)	*–*	*0.29*

Table 1. Laboratory data

HBc Ab, hepatitis B virus core antibody; HBs Ab, hepatitis B virus surface antibody; HBs Ag, hepatitis B virus surface antigen; HCV ab, hepatitis C virus antibody; HIV, human immunodeficiency virus.

The electrocardiogram showed right atrial enlargement and right axis deviation (*Fig. 1*) and the chest X-ray a moderate right pleural effusion (*Fig. 2*). TTE (*Fig. 3*) revealed a severely dilated right atrium, a dysmorphic severely stenotic tricuspid valve (functional area of 0.9 cm^2) with extreme apical insertion of the septal leaflet (22 mm from the mitral valve plane) and a small right ventricle suggesting Ebstein's anomaly. Anticoagulation with enoxaparin was maintained during the hospital stay. Oral prednisolone (1 mg/kg/day) was introduced with normalization of eosinophil values. Diuretics were used to treat congestion.

Surgery revealed a severely dilated right atrium and no atrialization of the right ventricle. The tricuspid valve presented no commissures and had a small hole in the antero-septal commissure remnant (*Fig. 4*). The apical displacement of the septal leaflet was only apparent due to the fibrosis, with thickening and shortening, of the subvalvular apparatus. The valve was replaced with a mechanic prosthesis and the right atrial dilated portion was removed (*Fig. 4*).
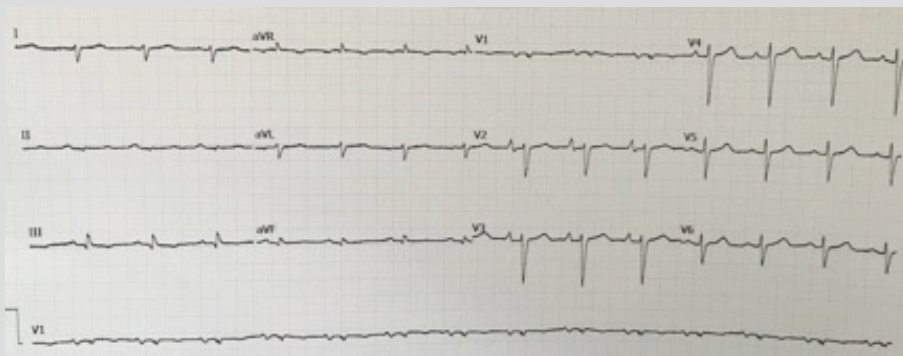

Figure 1. Electrocardiogram showing right atrial enlargement and right axis deviation

Figure 2. Chest X-ray showing right pleural effusion

Figure 3. Transthoracic echocardiogram (apical four chamber view) revealing a severely dilated right atrium, a dysmorphic and severely stenotic tricuspid valve with apical insertion of the septal leaflet (22 mm distance from the annulus) and a small right ventricle. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

The postoperative period was uneventful and the patient was discharged.

At follow-up, peripheral eosinophilia (2.5×10^9/l) was detected again despite glucocorticoids. The investigation of hypereosinophilia was extended. Serology for Strongyloides stercoralis and Trypanosoma cruzi were negative. A thoraco-abdomino-pelvic CT scan did not reveal suspicious lesions. Bone marrow examination showed no evidence of haematological neoplasia. BCR-ABL and Fip1like1platelet-derived growth factor receptor alpha (FIP1L1-PDGFRA) fusion products were negative. Karyotype analysis was normal. Upper and lower endoscopy with biopsies showed inflammatory activity, with eosinophils, in duodenal and colorectal mucosa. Gadolinium-enhanced cardiac
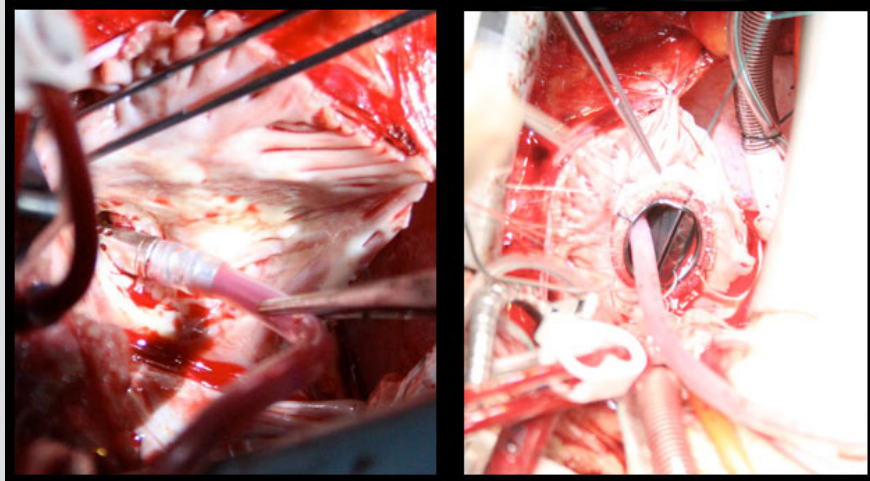
Figure 4. Photographs taken at the beginning of surgery (on the left) and after tricuspid valve replacement with a mechanical prosthesis (on the right). Note the small opening of the native tricuspid valve

magnetic resonance imaging (MRI) excluded areas of late enhancement (suggestive of fibrosis or abnormal infiltration). A heart biopsy showed scarce interstitial lymphohistiocytic inflammatory infiltrate with occasional eosinophils. A diagnosis of hypereosinophilic syndrome (HES) was established and azathioprine was started. The platelet and eosinophilic counts are being monitored and glucocorticoids tapered. The patient is also being treated with warfarin and acetylsalicylic acid.

DISCUSSION

Isolated tricuspid stenosis is a rare valvular abnormality, most commonly of rheumatic aetiology. The majority of cases of rheumatic disease present with tricuspid regurgitation or a combination of regurgitation and stenosis. Rheumatic tricuspid disease almost never occurs as an isolated lesion. Consequently, we considered this aetiology unlikely[1].

Carcinoid syndrome may also cause tricuspid stenosis. However, 24-hour urinary excretion of 5-HIAA, a sensitive and specific diagnostic test, was negative[2].

In this patient, echocardiographic findings suggested Ebstein's anomaly. This anomaly accounts for less than 1% of congenital heart disease. It is characterized by apical displacement of the septal and posterior tricuspid valve leaflets, leading to right ventricle atrialization, with a variable degree of malformation and displacement of the anterior leaflet. However, in most cases, these abnormalities cause tricuspid regurgitation[3] and, usually, it presents at an earlier age.

Endomyocardial fibrosis (EMF) is observed in the tropical/subtropical regions. It may be indistinguishable from the Loeffler's endocarditis (eosinophilic myocarditis) of temperate climates. EMF pathogenesis remains unknown, but eosinophilia is the most commonly cited aetiological link[4]. EMF may cause right ventricular distortion with apparent apical displacement of the tricuspid valve mimicking Ebstein's anomaly[5]. We found no evidence of a restrictive physiology or areas of endomyocardium apical fibrosis on cardiac MRI or heart biopsy. The only area where fibrosis was observed was in the valve.

HES is a known cause of cardiac disease. The fibrotic stage of eosinophil-mediated heart damage is characterized by altered cardiac function/heart failure due to either restrictive cardiomyopathy and/or compromise/entrapment of the cordae tendineae due to fibro-inflammatory remodelling (although this usually also leads to mitral/tricuspid regurgitation)[6].

Our main challenge was to identify a cause for tricuspid stenosis. The severity of valvular stenosis seemed excessive when presenting at such late age and secondary to Ebstein's anomaly. Epidemiological data supported EMF, but there was no evidence of fibrosis of the endomyocardium. However, extreme valvular fibrosis was found intraoperatively. As the patient presented with two uncontrolled autoimmune diseases (HES and APS), one of them known to cause cardiac involvement with valvular fibrosis, we hypothesized that the prolonged exposure to an increased inflammatory (and prothrombotic) response might have contributed to the fibrosis of a possibly previous slightly defective valve. We report this clinical case because of its rarity and its complexity. Several rare diagnoses were simultaneously present in this patient – an intriguing case of tricuspid stenosis, HES syndrome with gastrointestinal and heart involvement and APS – with an unusual interaction between them.

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