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ADVANCED

CASE REPORT: CLINICAL CASE

A Rare Case of Severe Nontropical Isolated Right Ventricular Endomyocardial Fibrosis



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ABSTRACT

We present a case of late presentation nontropical endomyocardial fibrosis isolated to the right ventricle and tricuspid valve (TV). In response to deteriorating hemodynamics, surgical debulking and TV removal were performed before initiation of centralized venoarterial extracorporeal membrane oxygenation support. Definitive endomyocardial resection with a TV prosthesis was then successfully completed. (**Level of Difficulty: Advanced.**)

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A 20-year-old man was urgently transferred for cardiovascular assessment after presenting with peripheral edema and progressive dyspnea. Born in Australia, he was of Fijian-Indian

heritage, had no pertinent family history, and was currently enrolled in tertiary education. There had been no international travel for more than 6 years. On physical examination he was afebrile, cachectic (body mass index 14 kg/m²), with gross peripheral edema and abdominal distention. Blood pressure was 97/56 mm Hg, heart rate was 115 beats/min, and respiratory rate was 19 breaths/min. Jugular venous pressure was elevated at 10 mm H₂O with prominent A waves. There was a short systolic murmur over the tricuspid area. Abdominal examination revealed massive ascites and a pulsatile liver edge.

LEARNING OBJECTIVES

- EMF is a rare condition with a high rate of mortality and morbidity.
- The natural history of EMF is of a progressive restrictive cardiomyopathy.
- Early diagnosis remains crucial to achieve favorable patient outcomes.
- CE-TTE with flash destruction replenishment imaging sequences provides an additional bedside modality to assess abnormal myocardial perfusion and aid in early diagnosis.
- Surgical intervention appears the only treatment option for advanced cases.

PAST MEDICAL HISTORY

He had a background of mild asthma rarely requiring salbutamol.

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DIFFERENTIAL DIAGNOSIS

The overall clinical presentation was consistent with symptomatic right-sided heart failure. Differential diagnoses, before investigations, included symptomatic heart failure with biventricular dysfunction, decompensated right-sided heart function secondary to primary pulmonary hypertension, severe tricuspid valve (TV) disease, and chronic pulmonary thromboembolic disease. Undiagnosed congenital heart disease and primary hepatic disease, with symptomatic portal hypertension, was also considered.

INVESTIGATIONS

Electrocardiography revealed a narrow complex sinus rhythm and diffuse T-wave inversion throughout precordial leads, most prominent in leads V₂ to V₄. There was evidence of both P-pulmonale and right-sided heart strain with right-axis deviation. Blood test results on presentation revealed the following: hemoglobin, 127 g/l; white cell count, 12.7 × 10⁹/l, and eosinophils 0.28 × 10⁹/l. His creatinine was 86 μmol/l and urea was 7.6 mmol/l. His aspartate aminotransferase was elevated at 1,000 U/l, albumin was reduced at 26 g/l, and international normalized ratio was raised at 1.6.

Transthoracic echocardiography (TTE) revealed normal left ventricular (LV) size and ejection fraction was 51%. Right ventricular (RV) function was severely impaired, and the RV cavity was restricted with nearly complete obliteration secondary to a homogeneous echo-reflective mass. The RV outflow tract (RVOT) was severely narrowed, with a flow velocity of 1.5 m/s and RVOT stroke volume of 11 ml. The right atrium had spontaneous echo contrast, associated with a 3.7 × 1.8 cm echo-dense mass against the right atrial (RA) free wall (Figure 1A). In addition, a smaller, pedunculated, spherical mass (12-mm diameter) was seen attached near the atrial surface of tricuspid annulus (Figures 2A to 2D). The TV was tethered to the RV mass with minimal mobility (Figures 1B to 1D). The inferior vena cava was dilated with no inspiratory collapse.

Supplementary multimodality imaging techniques were performed to further define the tissue characteristic of the RA and RV intracardiac masses and the underlying cardiac tissue: Contrast-enhanced (CE) TTE (CE-TTE) with flash destruction replenishment sequences revealed evidence of reduced myocardial perfusion (Figures 2A to 2D, Video 1). The RV mass was avascular, obliterating the RV apex with a line of absent perfusion along the length of the endocardium of the RV free wall consistent with endocardial scar.

Cardiac magnetic resonance (CMR) imaging confirmed a large triangular avascular mass in the right ventricle, consistent with a thrombus, with thickened RV myocardium and bright subendocardial late gadolinium enhancement, extending into the RA appendage, and large bilateral pleural effusions. The left ventricle was spared, with preserved systolic function and no regional wall motion abnormalities or late gadolinium enhancement (Figures 3A to 3D). CE computed tomography excluded: extension of the RA thrombus into inferior or superior vena cava, pulmonary arterial thrombus and hepatic or portal vein obstruction.

These findings were consistent with severe endomyocardial fibrosis (EMF) limited to the RV, complicated by severe subpulmonic RVOT obstruction and secondary RA thrombus resulting from stasis.

MANAGEMENT

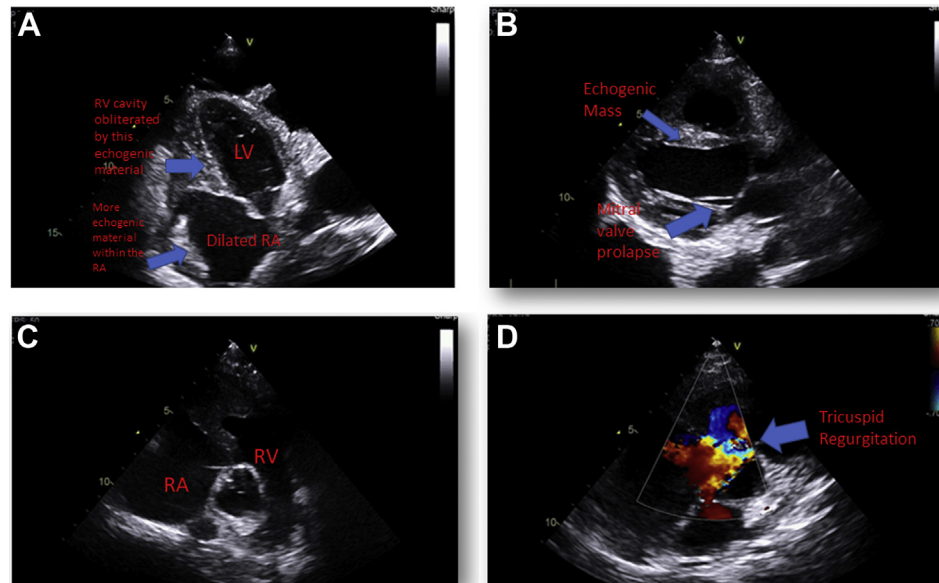
Surgical intervention with RA and RV thrombus resection, RV endocardial decortication, and repair or replacement of TV was recommended as his only long-term option. However, given the almost complete obliteration of the RV cavity, his cardiac output and organ perfusion were severely compromised. As part of pre-operative optimization, cautious diuresis and thrombolysis with alteplase (10 mg intravenous bolus followed by 60 mg over 2 h) were commenced in the intensive care unit, with the aims of improving RVOT obstruction and augmenting cardiac output. No discernable change in the RV thrombus volume were seen on TTE after thrombolysis.

On day 2 of the admission, he suddenly developed worsening hemodynamics and increasing oxygen requirements, thus expediting cardiac surgery. Intra-operative evaluation confirmed that extensive endocardial resection was required (Figure 4). The right ventricle was infiltrated with chronic, organized, and fibrin-rich thrombus, whereas the right atrium had evidence of fresh, red thrombus suggesting stasis (Figures 5A to 5D). Because of the marantic thrombus compromising the TV and subvalvular apparatus, TV replacement was required.

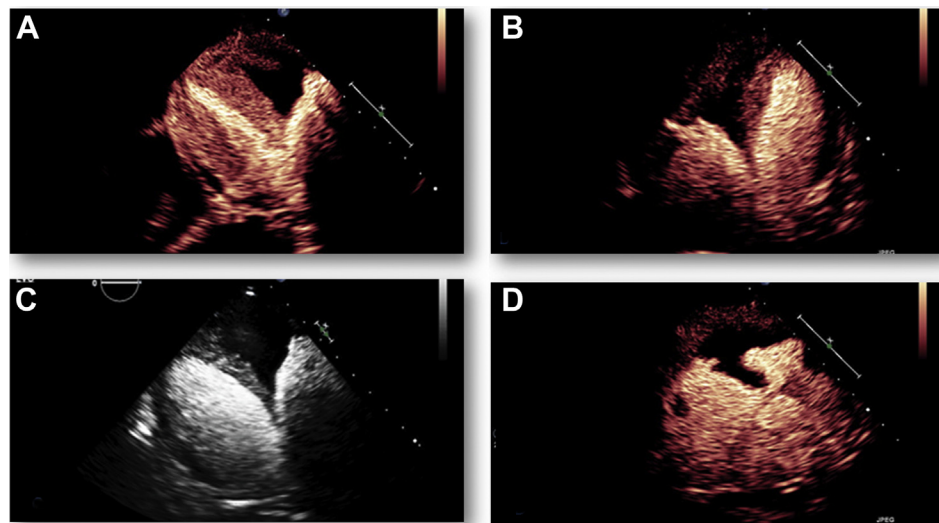
The decision was made to suspend surgery following excision of the TV and debulking of RV thrombus because of the underlying fluid overload with congested lungs, hepatic dysfunction, and borderline biventricular function. He was supported on central venoarterial (VA) extracorporeal membrane oxygenation (ECMO) with a 22 EOPA cannula

ABBREVIATIONS AND ACRONYMS

CMR	= cardiac magnetic resonance
CE	= contrast-enhanced
EMF	= endomyocardial fibrosis
ECMO	= extracorporeal membrane oxygenation
LV	= left ventricular
RA	= right atrial
RV	= right ventricular
RVOT	= right ventricular outflow tract
TTE	= Transthoracic echocardiogram
TV	= tricuspid valve

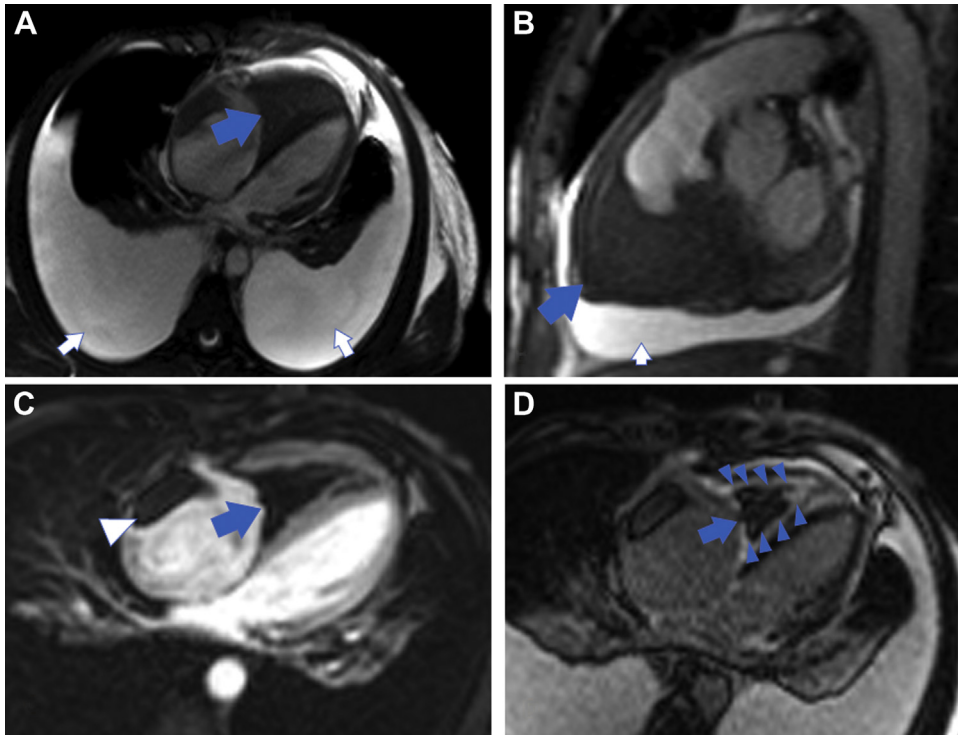
FIGURE 1 Transthoracic Echocardiography on Presentation

(A) Apical 4-chamber view showing obliteration of the right ventricular (RV) cavity (**upper arrow**) and an echogenic mass in the right atrial (RA) appendage (**lower arrow**). (B) Parasternal long-axis view showing echogenic mass filling the right ventricular cavity (**upper arrow**) with mitral valve prolapse (**lower arrow**). (C) Parasternal short-axis view showing the outline of the right ventricular cavity. (D) Midsystolic color Doppler imaging demonstrating severe tricuspid regurgitation (**arrow**). LV = left ventricle.

FIGURE 2 Contrast-Enhanced Transthoracic Echocardiography

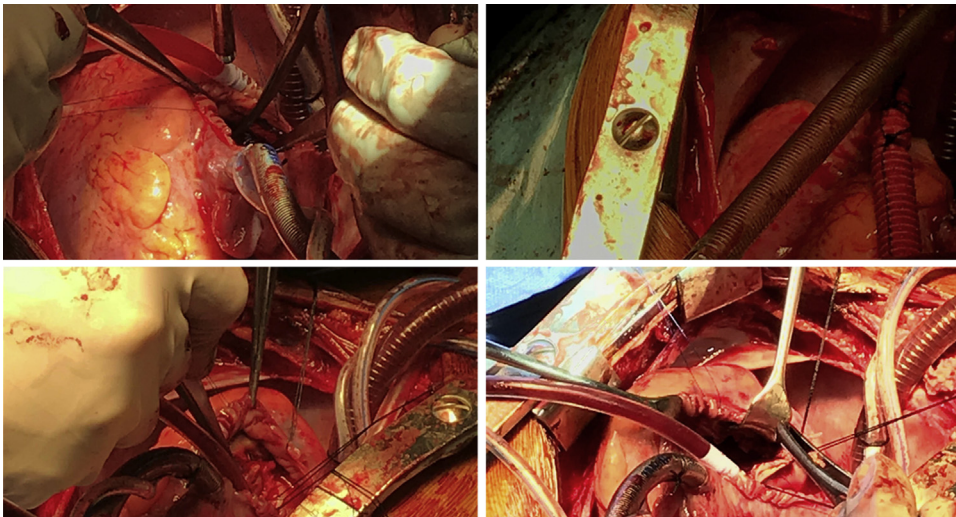
(A to D) Contrast-enhanced transthoracic echocardiography showing that the right ventricular cavity is nearly obliterated by a homogenous echo-dense mass. The mass displays well-defined endocardial tissue planes. The use of very low mechanical index myocardial contrast echocardiography with flash destruction replenishment sequences reveals abnormal myocardial perfusion and an avascular mass consistent with thrombus.

FIGURE 3 Cardiac Magnetic Resonance Imaging

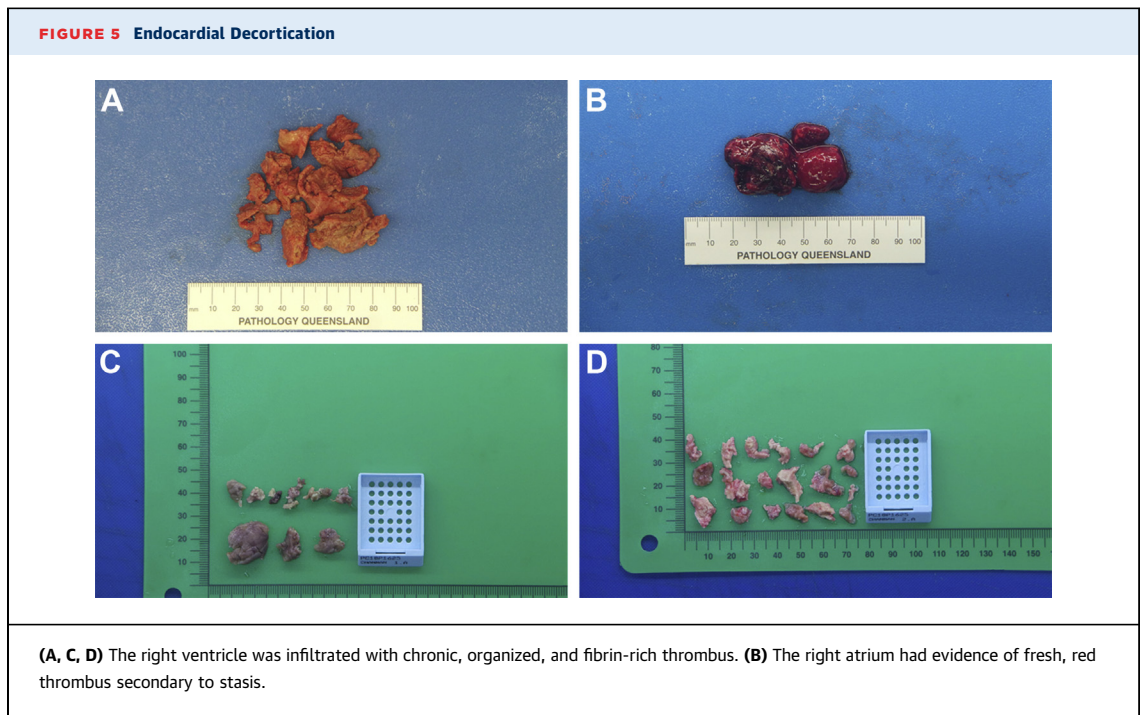


(A) A 4-chamber view demonstrating a dilated right ventricle with impaired contraction and cavity obliteration (**blue arrow**) and large bilateral pleural effusions (**white arrows**). (B) Right ventricular outflow tract view demonstrating obliteration of the right ventricular cavity (**blue arrow**) and pleural effusion (**white arrow**). (C) Immediate post-gadolinium enhancement image with large thrombi in the right atrial appendage (**white arrowhead**) and filling the right ventricular apex (**blue arrow**). (D) Late gadolinium enhancement image in the same plane as C and showing a triangular thrombus in the right ventricular apex (**blue arrow**) surrounded by bright subendocardial enhancement (**blue arrowheads**), confirming the diagnosis of endomyocardial fibrosis.

FIGURE 4 Surgical Resection



Images obtained during endocardial decortication.



(Medtronic, Minneapolis, Minnesota) in the ascending aorta and a 32 Bardic RA cannula (Bard, Billerica, Massachusetts). On initiating ECMO, LV systolic function was severely affected, with echocardiography revealing gross intraventricular septal deviation. With severely impaired RV function and no

TV, the right-sided chambers acted as a passive conduit interacting with VA-ECMO to affect intraventricular interdependence, thereby decreasing LV stroke volume. To augment the hemodynamics, LV and RV filling were optimized under transesophageal echocardiography guidance. VA-ECMO flows were

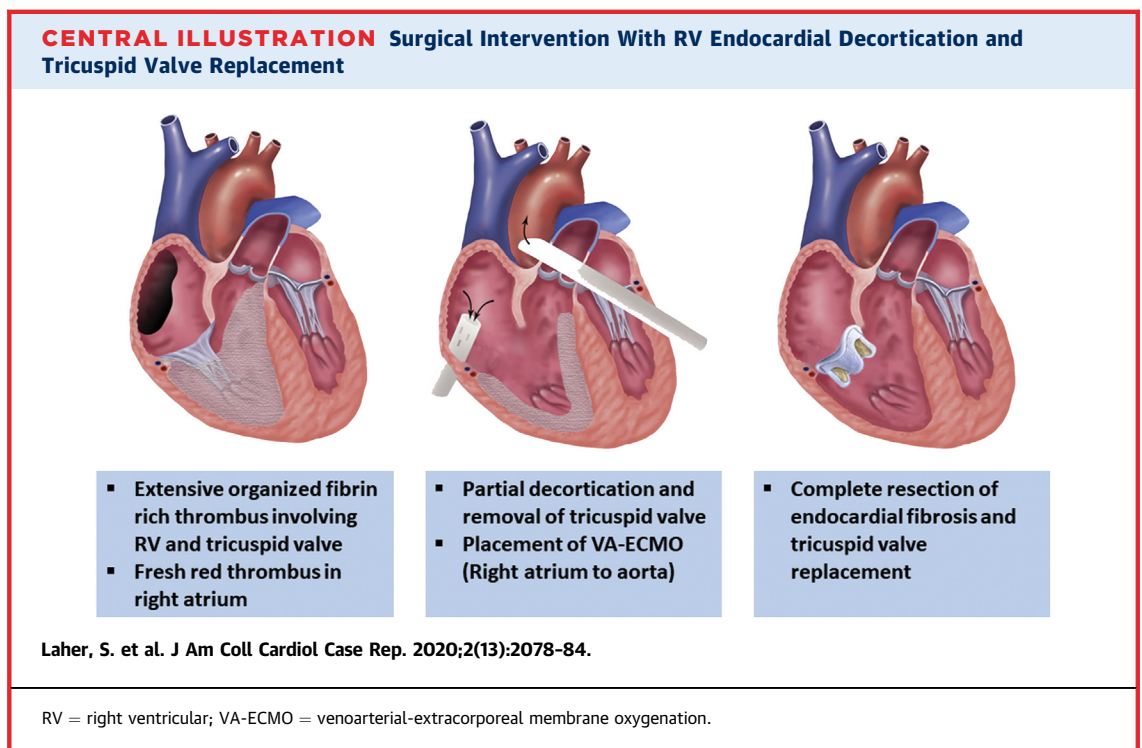
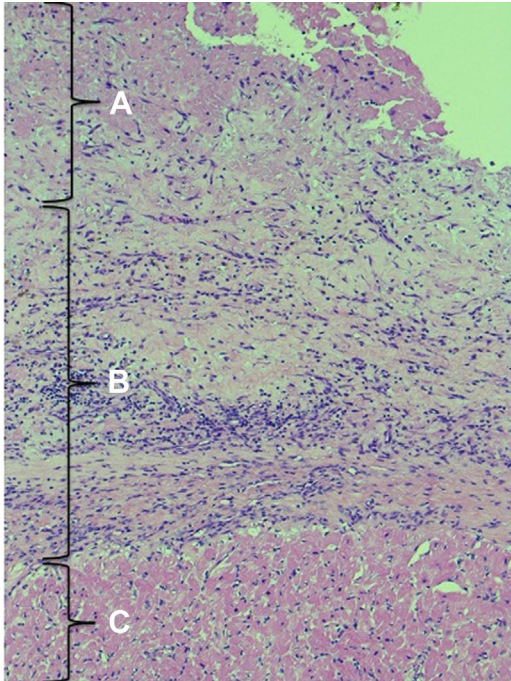


FIGURE 6 Endocardial fibrosis With Neovascularization, Mild Mixed Inflammatory Cell Infiltrate and Organizing Surface Fibrin Hematoxylin and Eosin, $\times 100$



The slide reveals a surface layer of fibrin (A) and neovascularized endocardium with fibrosis and mild mixed inflammatory cell infiltrate in the middle (B). The bottom layer shows myocardium (C).

reduced to 2.5 l, thus improving intraventricular interdependence; milrinone was initiated for both inotropic support and optimization of pulmonary vascular resistance. An intra-aortic balloon pump was inserted to facilitate LV recovery.

The patient returned to the operating room after 72 h with better fluid status, improved liver function, and optimized RV and LV afterload for the definitive decortication (Figures 5A to 5D). The fibrotic endocardium was resected, leaving underlying healthy muscle. Once completed, a 29-mm Mosaic tissue prosthesis was placed in the tricuspid position (Central Illustration). Post-operatively, complete heart block requiring a biventricular pacemaker developed.

Histological assessment revealed a surface layer of fibrin (Figure 6A) and a basal layer of myocardium (Figure 6C). In between these layers was neovascularized endocardium with fibrosis and mixed inflammatory cell infiltrate (Figure 6B). This finding was consistent with EMF and explained the abnormal perfusion observed with CE-TTE, as well as the 3

distinct tissue characteristics shown on post-late gadolinium enhancement CMR.

DISCUSSION

Despite first being described in 1948, EMF remains poorly understood, with only small case series to guide clinicians with its challenging and complex management. The natural history consists of rapidly progressive heart failure in 3 stages: necrosis, thrombosis, and finally deposition of fibrous tissue in the endomyocardium. Consequently, a restrictive physiology develops, and death usually results 2 years from the initial insult (1).

Typically described in tropical regions, EMF affects impoverished adolescents of lower socioeconomic status, and prognosis remains poor even with early diagnosis (1,2). Our patient was raised in Australia without any recent travel. The hyper-eosinophilic syndrome, Loeffler endocarditis, can have similar cardiac findings. We found no consistent myocardial or peripheral eosinophilia (eosinophil count $>1.5 \times 10^9/l$), but it is conceivable that transient eosinophilia may have been the culprit (3). Hypereosinophilic syndrome is important to consider because corticosteroids, if used early, may prevent disease progression and necrotizing myocarditis.

Isolated right-sided disease is rare, accounting for 7% to 28% of cases (4). It is associated with increased thrombus formation, pulmonary emboli, and subsequent pulmonary hypertension, thus increasing the risk of mortality. Echocardiography is the first-line imaging technique for diagnosis. The use of CE-TTE with microsphere ultrasound-enhancing agents may provide additional benefits, including improved delineation of the true endocardial border, clarification of apical thromboinflammatory material, and demonstration of reduced myocardial perfusion in associated segments. CMR is the reference standard for tissue characterization. However, it can be difficult to perform in unstable patients, and free-breathing motion-corrected and compressed-sense imaging may allow for accelerated image acquisition.

Although early post-operative mortality is between 10% and 30%, surgery improves survival and functional capacity over medical treatment (1). Complete endomyocardial decortication with TV replacement was the only durable option for our patient. Because of the late presentation and critical hemodynamics, we used a 2-stage surgical procedure with centralized VA-ECMO for organ support. Every effort should be made to preserve the native valve because replacing the valve can adversely affect the post-operative

course (5). Unfortunately, as in our case, this is generally not possible given the advanced stage of disease on presentation.

FOLLOW-UP

At 3 months our patient had returned to his university studies and achieved 452 m during a 6-min walk test. At 7 months, post-operative echocardiography and CMR (Video 2) revealed normal LV size and function (LV ejection fraction 68%). The right ventricle was of normal size and function (RV ejection fraction 57%). There was no residual thrombus noted and only minimal subendocardial enhancement in the right ventricle free wall and apex. The bioprosthetic TV replacement was well seated with good hemodynamics. Findings were consistent with fully resolved EMF.

CONCLUSIONS

This case highlights novel features in nontropical EMF presentation, diagnosis, and management. Prognosis

is extremely poor but can be improved with early diagnosis. Clinicians in developed countries should consider EMF in their differential diagnosis when patients present with these classic features. CE-TTE provides incremental benefit in morphological assessment and surgical planning and may reduce time to diagnosis. Similarly, CMR offers utility in diagnosis with the ability for tissue characterization. Surgery remains the only durable option and is recommended for all patients with EMF and heart failure.

AUTHOR DISCLOSURES

Dr. Platts is acting as a medical liaison for Lantheus Medical Imaging. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS contrast enhanced TTE, endomyocardial fibrosis, right ventricle

APPENDIX For supplemental videos, please see the online version of this article.