JACC: CASE REPORTS VOL. 3, NO. 9, 2021

CASE REPORT

BEGINNER

HEART CARE TEAM/MULTIDISCIPLINARY TEAM LIVE

Follow the Lead

The Challenges of Cardiogenic Shock in Device-Related Infective Endocarditis

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ABSTRACT

We present the challenging case of a young man with congenital heart disease who survived severe device-related infective endocarditis and new pulmonary hypertension. He required prolonged mechanical circulatory support and had multiple significant complications. His case posed a management dilemma that was successfully resolved by effective multidisciplinary, tertiary center care. (**Level of Difficulty: Beginner.**) (J Am Coll Cardiol Case Rep 2021;3:1163–9)

HISTORY OF PRESENTATION

A 24-year-old man presented with an 18-month history of malaise, low-grade pyrexia, weight loss, intermittent coughing, and hemoptysis. He was investigated and treated with multiple courses of oral amoxicillin in the community for presumed chest infections. He had a past medical history of a left thoracotomy division of a double aortic arch, a spontaneously closed ventricular septal defect, and a single-lead pacemaker device for sinus node disease with significant pauses since childhood (Table 1). The lead had caused tricuspid valve regurgitation since implantation. Eventually, he was referred to the respiratory team because of nonresolving symptoms and staphylococcal growth on sputum culture.

He was admitted to his local intensive care unit (ICU) with worsening sepsis and started on empirical antibiotics for suspected infective endocarditis. He was transferred to our specialist center with a temperature higher than 38 °C, a heart rate of 66 beats/min, systolic blood pressure of 100 mm Hg, and high oxygen requirements. His chest was clear on auscultation, and he had no audible murmurs and no peripheral stigmata of infective endocarditis.

LEARNING OBJECTIVES

- DRE remains a diagnostic challenge, and a high index of suspicion in high-risk patients with nonspecific symptoms is essential.
- It is important to appreciate the expertise required to deal with challenges of prolonged mechanical respiratory and circulatory support in patients with congenital heart disease.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received April 30, 2021; accepted May 17, 2021.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2021.05.012

ABBREVIATIONS AND ACRONYMS

CT = computed tomography

DRE = device-related endocarditis

ECMO = extracorporeal membrane oxygenation

ICU = intensive care unit

MCS = mechanical circulatory support

MDT = multidisciplinary team

PET = positron emission tomography

PH = pulmonary hypertension

PPM = permanent pacemaker

RV = right ventricular

TEE = transesophageal echocardiography

TTE = transthoracic echocardiography

QUESTION 1: WHAT IS THE DIFFERENTIAL DIAGNOSIS AT THIS STAGE?

Given the chronicity of his symptoms, tuberculosis, HIV infection, and postviral fatigue syndrome were considered, in addition to suspected infective endocarditis of the pacemaker system.

QUESTION 2: WHAT INVESTIGATIONS ARE NEEDED AT THIS STAGE?

Routine blood tests (Table 2), 3 sets of blood cultures, and sputum cultures were taken; the results only showed *Candida* and *Stenotrophomonas maltophilia* in the sputum. The diagnosis of device-related endocarditis (DRE) can be challenging, with blood culture positivity being less common in native valve endocarditis (1). The lack of growth was likely the result of multiple courses of antibiotics in the community. Urine testing for hematuria should also be considered.

Following the European Society of Cardiology guidelines, we performed a transthoracic echocardiogram (TTE), which showed mildly reduced systolic right ventricular (RV) function and preserved left ventricular systolic function (Table 3) (1). Apart from previously seen fibrin material on the pacemaker lead, there were no obvious independently mobile masses (Figures 1A to 1C). There was associated moderate to severe tricuspid regurgitation with systolic flow reversal of the hepatic vein and evidence of ventricular septal flattening, indicative of elevated RV pressures. TTE can be normal or inconclusive in up to 30% of DRE cases, depending on expertise (2). Fibrin material is often seen on pacemaker leads; however, the relevance should be taken within the clinical context. Transesophageal echocardiography (TEE) is shown have superior specificity and sensitivity, although our patient was too ill, and his TEE was performed intraoperatively (2,3).

The patient also had a whole-body computed tomography; CT scan with contrast which revealed a large adherent structure to the pacemaker leads and confirmed the presence of large, bilateral central pulmonary emboli, alongside evidence of severely raised pulmonary arterial pressure: dilated pulmonary artery, right ventricle, and right atrium and associated enlarged liver with retrograde filling of contrast material (Figures 2A to 2C). He also had multiple enlarged mediastinal, subcarinal, and hilar lymph nodes and bilateral patchy ground-glass infiltrates and areas of consolidation that were believed to be infective. A subsequent abdominal ultrasound examination showed hepatic vein distention and congestive hepatitis with evidence of tricuspid regurgitation on hepatic vein Doppler images, in keeping with raised pulmonary pressures.

Coupling the patient's history with the investigations posed a further diagnostic dilemma: did he have septic emboli secondary to his endocarditis, or was this thromboembolic disease secondary to unremitting chronic infection causing the consolidation and associated lymphadenopathy? Peripheral venous thrombus was excluded by negative

TABLE 1 Timeline of Patient History Before Admission

Year	Events
2002	Implantation of single-lead permanent pacemaker (sinus node disease with significant pauses)
2008	New right ventricular lead placed and box change
2015	Laser lead extraction of single-chamber pacemaker Permanent pacemaker upgraded to dual-chamber device
2019	Multiple courses of oral amoxicillin for suspected recurrent chest infections Ongoing elevated inflammatory markers
2019	Catheter ablation for common atrial flutter
2019-2020	Nonspecific generalized symptoms Referral to respiratory physicians
2020	Acutely ill, with overwhelming sepsis and pulmonary emboli

TABLE 2 Blood Values on Admission

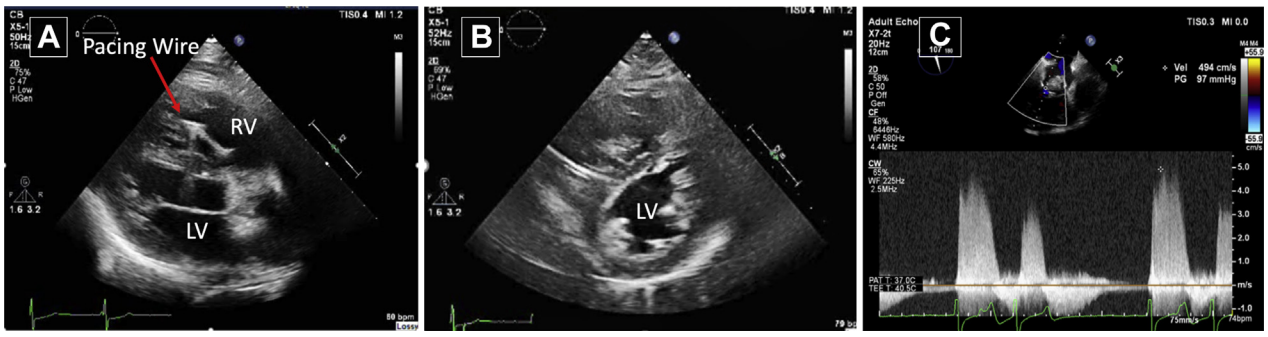
Serum Blood Results	Results	Normal Range
C-reactive protein (mg/L)	150	0-10
White blood cell count ($\times 10^9$/L)	16.6	4.4-10.1
Neutrophils ($\times 10^9$/L)	13.4	2.1-6.7
Hemoglobin (g/L)	95	134-166
Platelets ($\times 10^9$/L)	127	136-343
Urea (mmol/L)	5.1	2.5-7.8
Creatinine (μmol/L)	87	60-120
B-type natriuretic peptide (ng/L)	912	0-20

TABLE 3 Echocardiographic Parameters

	2019	August 2020: Intraoperative	Postoperative
LV function	Preserved	Preserved	Severe systolic impairment
Ejection fraction (%)	55	55	25
RVSP (mm Hg)	43	97	35
TAPSE (cm)	2.1	2	0.5
S′ (cm/s)	14	12	4
TR	Mild	Moderate to severe	Moderate

LV = left ventricular; RVSP = right ventricular systolic pressure; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation.

FIGURE 1 Admission Transthoracic Echocardiography



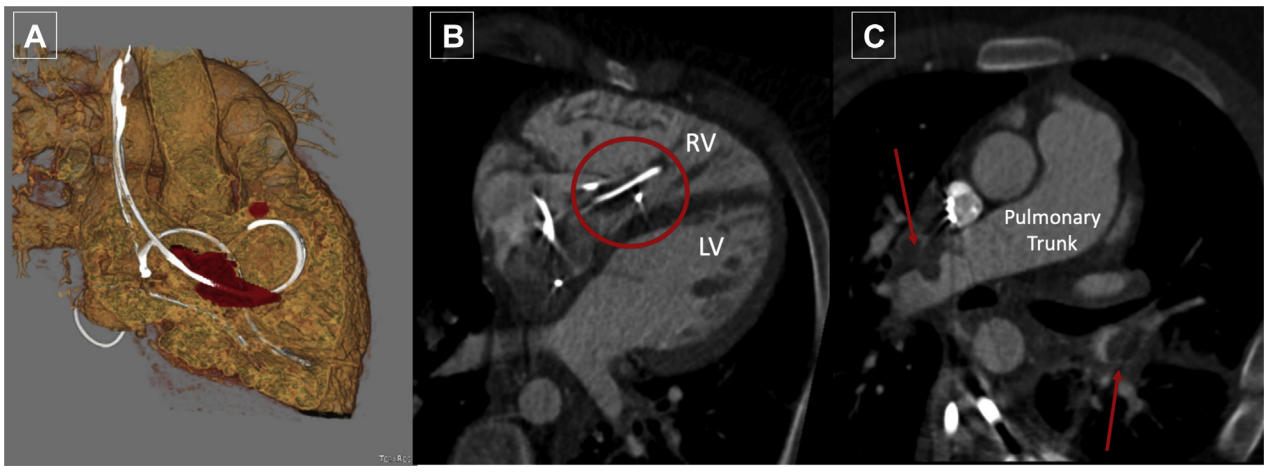
(A) Parasternal long-axis view. **(B)** Parasternal short-axis view with evidence of septal flattening. **(C)** Continuous-wave Doppler image with increased velocity and gradient across the tricuspid valve. RV = right ventricle; LV = left ventricle.

ultrasound examination of the lower extremities, thus making the theory of acute-on-chronic septic embolization in the context of fulminant sepsis more probable than thromboembolic disease.

QUESTION 3: WHAT IS THE IMMEDIATE MANAGEMENT PLAN?

DRE is a serious condition with high morbidity and mortality. Multiple endocardial leads, male sex, and younger age are reported risk factors that our patient had and that are known to play a role in the disease burden (4). Given these risk factors and ongoing sepsis despite multiple antibiotics, source control was considered the mainstay of treatment, and the patient was taken to a hybrid operating room for percutaneous lead extraction. Laser removal was not suitable because the RV lead was too adherent; therefore, the procedure was converted to an open sternotomy on bypass. Intraoperative TEE confirmed the presence of a large and elongated mass on his pacing lead (**Figures 3A to 3D,** Videos 1, 2, 3, 4, and 5). In addition to resection of the multiple cannon ball vegetations with the leads, his surgical procedure was complicated because the RV lead had eroded through the superior vena cava wall and was too adherent to

FIGURE 2 Initial Computed Tomography Scan



(A) Pacemaker leads with large adherent material **(red)** traversing the right atrioventricular valve and extending into the RV outflow tract. **(B)** Inferiormost vegetation traversing the right atrioventricular valve on the ventricular pacing lead **(red circle)**. **(C)** Bilateral pulmonary artery emboli **(red arrows)**. Abbreviations as in **Figure 1**.

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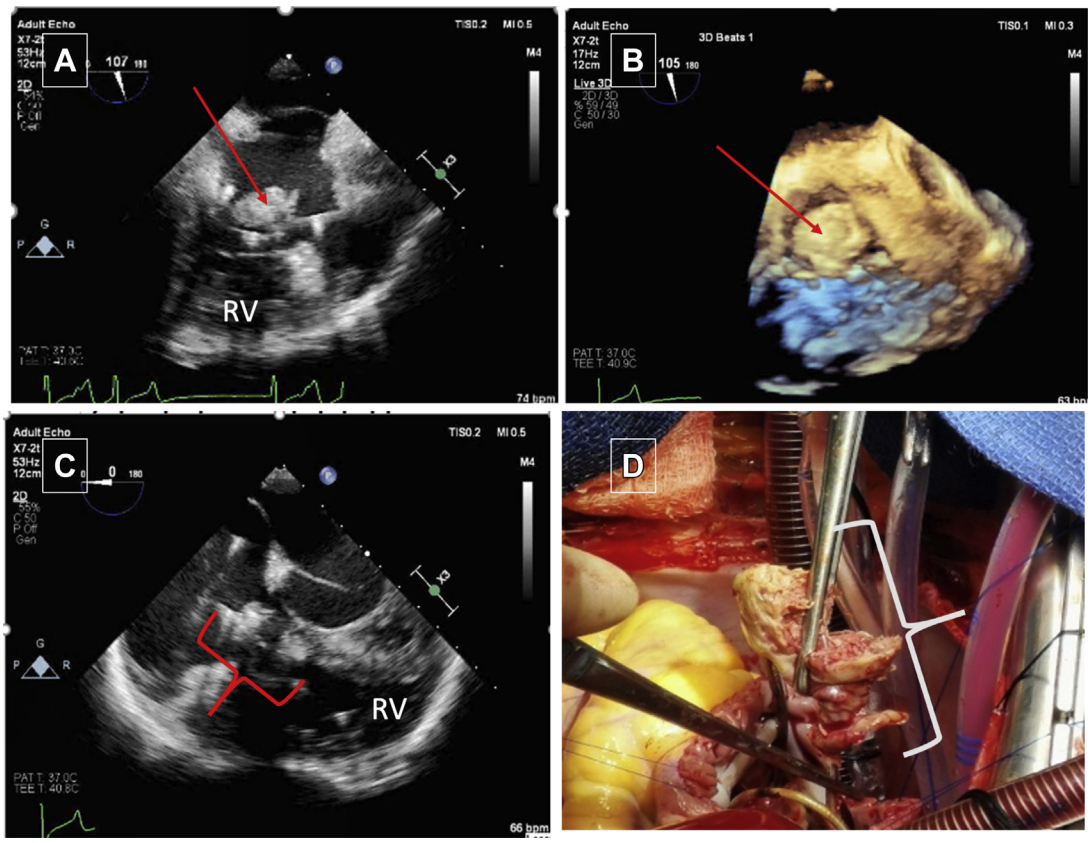
FIGURE 3 Intraoperative Images



Intraoperative transesophageal echocardiography. **(A)** Large vegetation obstructing the tricuspid valve **(red arrow). (B)** A 3-dimensional reconstruction showing vegetation obstructing the tricuspid outflow **(red arrow). (C)** Large, acorn-shaped vegetation over the right ventricular (RV) lead **(red bracket). (D)** Intraoperative photograph of the large vegetation wrapped around the pacemaker lead **(white bracket)**.

the innominate vein wall, thus resulting in resection and reconstruction with bovine pericardium of both vessels. He also required tricuspid valve repair because the RV lead was perforating the septal leaflet. Following resection of the pacing wires and battery, a temporary epicardial pacing system was inserted. Surgical embolectomy was considered for the management of his central pulmonary emboli, but he was deemed at very high risk because of his sepsis, raised pulmonary pressures, and additional prolongation of bypass time. In addition, it was regarded inappropriate to do so given the fragility of the acute emboli.

His immediate postoperative management was further complicated by cardiogenic shock secondary to deteriorating biventricular function refractory to optimal medical therapy. This was thought to be caused by toxins from the sepsis causing myocardial damage.

QUESTION 4: WHAT ARE THE NEXT STEPS IN THE MANAGEMENT OF CARDIOGENIC SHOCK?

Subsequent to weaning from cardiopulmonary bypass, he was observed for a short while but started to develop rising lactate (Table 4), which was initially managed with inotropes and vasopressors but with no improvement. A complex multidisciplinary team (MDT) discussion around the use of mechanical circulatory support (MCS) promptly occurred. He was considered an unsuitable transplant candidate because of the combination of ongoing sepsis and pulmonary hypertension (PH). Therefore, ventricular assist devices as bridging therapy were also believed to be unsuitable for him. Hence a decision was made to proceed with venoarterial extracorporeal membrane oxygenation (ECMO) to support the cardiac function by

TABLE 4 Postoperative Course

Postoperative Day	Events	Management
Day 0	Intubated F_{IO_2} 80%, PEEP 15, MV 7 On norepinephrine 0.2, epinephrine 0.15, milrinone 0.5	
Day 0 Immediate perioperative	Cardiogenic shock Low cardiac output Rising lactate (maximum was 9) Cool peripheries	Ionotropic support increased Initiated on VA ECMO (aortic arch and right femoral vein) Started at flow of 4.5 L/min and SGF 2 L/min Transfused 8× PRCs, 2× FFP, and 2× cryoprecipitate Chest stented and swabs kept inside
Day 2	Atrial fibrillation	Chemical cardioversion with amiodarone
Day 4	Multistage venous cannula placing pressure on interatrial septum Evidence of severe biventricular failure on TEE	Cannula withdrawn by 3 cm under real-time TEE guidance
Day 5	Poor response to heparin (low anti-Xa levels Severe acute kidney injury	Coronary angiogram: normal coronary arteries Discussion with hematologist and decision made to commence argatroban Change of urinary catheter Hemofiltration
Day 6	Palliative care input and MDT discussions	Replacement of arterial ECMO cannula from aortic arch to axillary artery Chest lavage Permanent pacing box placed in peritoneal space Temporary pacing wires removed Patient not suitable transplant candidate because of current ongoing infection
Day 7	*Candida* and *Stenotrophomonas maltophilia* in the sputum	Antifungal agents added (cotrimoxazole [Septrin], fluconazole) until negative culture results
Day 8	Ongoing high ionotropic requirement	Thoracic drains removed No weaning of ECMO Levosimendan started
Day 9	Ongoing fevers Worsening inflammatory markers and chest radiograph appearances	Antibiotics adjusted
Day 10	Weaning study with stable CVP, MAP, and LVOT VTI	Decannulated from VA ECMO
Day 11	Review by PH team because of elevated pulmonary pressures on PA catheter	Started on sildenafil 25 mg Continue with milrinone and nitric oxide Further CTPA
Day 12	Increased F_{IO_2} and nitric oxide Worsening bibasal consolidation New acute on chronic pulmonary emboli	Patient proning initially; unsuccessful Chest lavage and transition to V-V ECMO
Day 14	Discussion with local cardiothoracic surgery for potential embolectomy	Patient not suitable for embolectomy or pulmonary endarterectomy because of high burden of acute clot
Day 19	Failed attempt to wean from VV ECMO	Percutaneous tracheostomy inserted
Day 36	Bleeding in oropharynx and tracheostomy site	Regular tranexamic acid ENT review leading to scope
Day 52	Patient improved	Decannulated from VV ECMO Tracheostomy in situ And overnight CPAP Patient stepped down to ward-level care

CPAP = continuous positive airway pressure; CTPA = computed tomography pulmonary angiography; CVP = central venous pressure; ECMO = extracorporeal membrane oxygenation; ENT = ear, nose, and throat; FFP = fresh frozen plasma; F_{IO_2} = fraction of inspired oxygen; LVOT = left ventricular outflow tract; MAP = mean arterial pressure; MDT = multidisciplinary team; MV = mechanical ventilation; NO = nitric oxide; PA = pulmonary artery; PEEP = positive end-expiratory pressure; PH = pulmonary hypertension; PRCs = packed red cells; SGF = sweep gas flow; TEE = transesophageal echocardiography; VA = venoarterial; VTI = velocity time integral; VV = venovenous.

using the same bypass cannulas. His sternotomy wound was also left stented and packed for 10 days. Results of repeated blood cultures, β-D-glucan, and tissue cultures were all negative despite ongoing sepsis. We continued with aggressive medical management of his sepsis involving multiple courses of empirical antibiotics and antifungal agents, hemofiltration for acute renal failure, and intravenous amiodarone for new atrial tachycardia. He required treatment with enoxaparin 1.5 mg/kg once daily. Following a few days of intensive management, his cardiac function began to improve on TTE, and he was successfully weaned from venoarterial ECMO. Unfortunately, his condition suddenly deteriorated again, with worsening hypoxia despite maximum ventilation settings and improved biventricular function.

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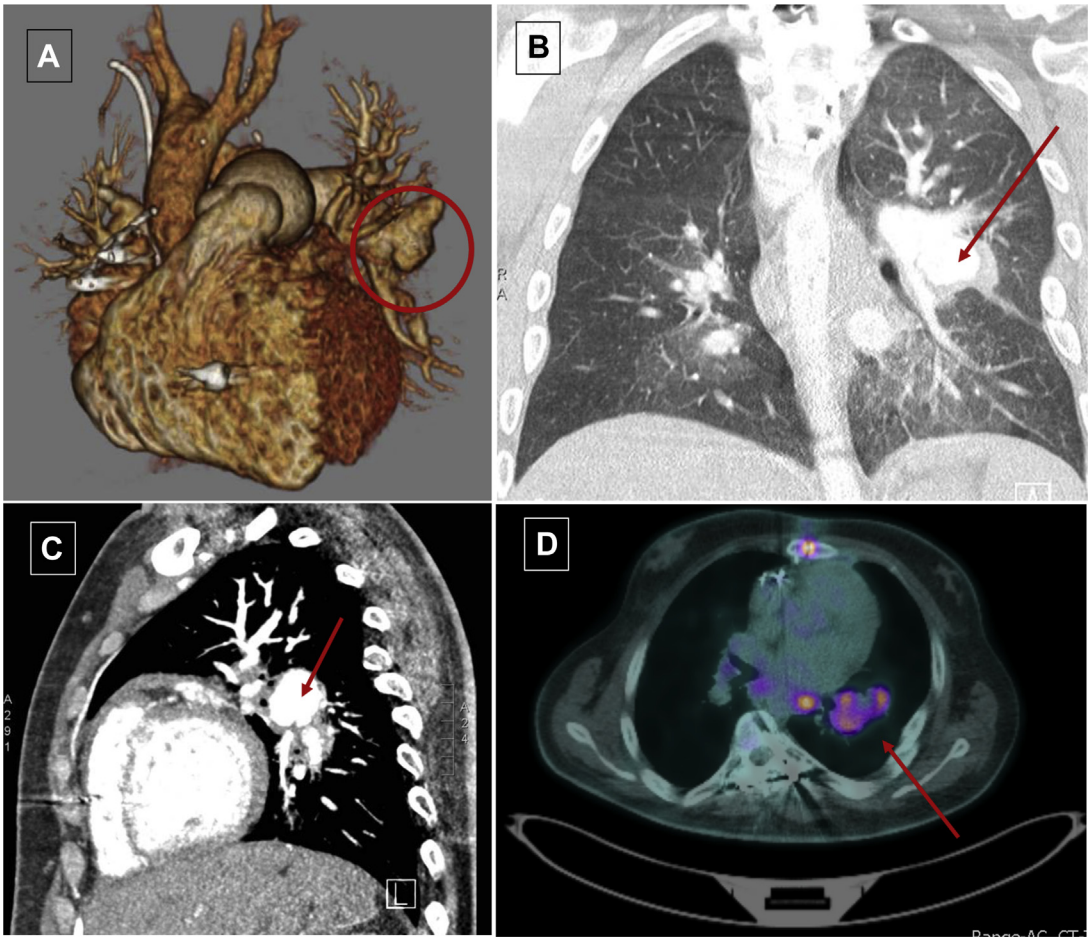
FIGURE 4 Follow-Up Computed Tomography and Computed Tomography-Positron Emission Tomography



Follow-up computed tomography showing a mycotic pulmonary artery aneurysm on **(A)** volume-rendered tomogram **(red circle), (B)** coronal view **(red arrow), (C)** sagittal view **(red arrow),** and **(D)** combined computed tomography and positron emission tomography showing active uptake **(red arrow).**

QUESTION 5: WHAT SHOULD BE THE NEXT STEPS IN MANAGEMENT?

We performed a CT pulmonary angiogram, which revealed a high burden of pulmonary emboli with worsening consolidation. Given his improved ventricular function and isolated significant hypoxia, he returned to the operating room for a chest lavage and cannulation to venovenous ECMO to support his lungs through peripheral cannulation. Echocardiography, CT, and pulmonary artery catheterization confirmed severe PH believed to be secondary to pulmonary emboli. Pulmonary endarterectomy was discussed, but he was deemed an unsuitable candidate because he was too acutely ill, and the septic emboli would be too friable to ensure good clearance. He was therefore started on pulmonary vasodilators (sildenafil 50 mg, 3 times a day) to reduce RV afterload. He remained critically ill, with ongoing mechanical and pharmacological support for 2 months. After protracted weaning, he was extubated and eventually stepped down to the ward. Further CT scans (including positron emission tomography [PET] scan) confirmed the development of a new, growing mycotic aneurysm of his left upper lobe pulmonary artery (Figures 4A to 4D). MDT discussion advised observation of the aneurysm, and he was subsequently discharged home.

QUESTION 6: WHAT WILL BE THE LONG-TERM MANAGEMENT FOR SUCH A PATIENT?

He was discharged home with an extended course of antibiotics. There is increasing use of PET scans for further assessing intracardiac and extracardiac involvement in DRE (5), and he therefore had serial imaging, which showed a reduction in size and uptake in his mycotic aneurysm (**Figures 4A to 4D**). He continues to be jointly followed up by the adult congenital heart disease and PH teams. Further discussions for later consideration of pulmonary endarterectomy will take place at a delayed stage to allow maturation of the embolic load.

CONCLUSIONS

DRE remains a diagnostic dilemma with high associated morbidity and mortality, especially in patients with congenital heart disease. The integration of a highly skilled ICU team with congenital heart disease surgeons, adult congenital cardiologists, and microbiologists played a vital role in this patient's care. Our center's experience with ECMO allowed for prompt decision making and appropriate adjustments in the presence of complications. Our case highlights challenges associated with use of MCS for biventricular failure secondary to overwhelming sepsis in this complex patient cohort.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS congenital, ECMO, infective endocarditis, mechanical circulatory support, mycotic aneurysm, pulmonary embolism, pulmonary hypertension

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

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