Cardiology in the Young (2015), **25**, 563–565
doi:10.1017/S1047951114000432

Brief Report

Aspergillus endocarditis in a paediatric patient after a cardiac surgery, associated with septic pulmonary embolism and pulmonary hypertension

Joana O. Miranda,[1] António Rodrigues de Sousa,[2] José Monterroso[1]

[1]*Department of Paediatric Cardiology;* [2]*Department of Cardiothoracic Surgery, Centro Hospitalar São João, Porto, Portugal*

Abstract We report a rare case of pulmonary prosthetic valve endocarditis due to *Aspergillus fumigatus*, associated with septic pulmonary embolism and secondary pulmonary hypertension, in a 4-year-old boy with surgically corrected tetralogy of Fallot. The diagnosis and treatment of *Aspergillus* endocarditis remains highly challenging. The best therapeutic option for chronic thromboembolic pulmonary hypertension due to an infectious thromboembolic event is highly debatable and the results are poor.

Keywords: Endocarditis; *Aspergillus*; pulmonary hypertension; septic pulmonary embolism; congenital heart disease

Received: 13 November 2013; Accepted: 26 February 2014; First published online: 4 April 2014

ASPERGILLUS ENDOCARDITIS IS A RARE INFECTION often associated with significant morbidity and mortality. Several conditions predispose patients to Aspergillus infections, including underlying cardiac abnormalities, prosthetic heart valves, and immunodeficiency. Fungal endocarditis affects ~0.1% of all prosthetic valves, and the *Aspergillus* species contributes to ~25% of all cases of fungal endocarditis.[1,2]

We report a case of a pulmonary prosthetic monocusp valve endocarditis due to *Aspergillus fumigatus*, associated with septic pulmonary embolism and secondary pulmonary hypertension, in a 4-year-old boy with surgically corrected tetralogy of Fallot.

Case report

The patient was diagnosed antenatally with tetralogy of Fallot and no genetic anomalies were detected, including 22q11.2 microdelection. In the first year of life he had multiple respiratory tract infections. After a neonatal modified Blalock–Taussig anastomosis, at 2 years of age, he underwent complete cardiac surgical correction; a transannular patch and a Gore-Tex® monocusp valve were used to reconstruct the right ventricular outflow tract. The postoperative period was complicated by a fistulous tract from the mediastinum to the left hypochondrium, probably related to the pacemaker leads' retention. The leads were extracted surgically and antibiotics were administered; cultures of the retained leads were negative. At the follow-up, the patient developed moderate pulmonary stenosis and moderate pulmonary valve regurgitation. The study for immunodeficiencies was negative, including normal full blood count, immunoglobulin levels, CD4 and CD8 count, and T cell function tests.

At 4 years of age, he presented with low-grade evening fever, weight loss, asthenia, and a month-long anorexia and was diagnosed with a lower respiratory tract infection. Empiric intravenous antibiotics were started – ampicillin plus claritromicin and latter ceftriaxone. A thoracic CT scan was performed 12 days later as the patient became clinically worse, revealing thrombus in the right ventricle and pulmonary trunk and its branches and multiple ischaemic lesions in the lungs.

The patient was then transferred to our paediatric cardiology department and, at admission, the echocardiogram showed a large and pedunculated mass on the monocusp, causing a turbulent flow in the right ventricular outflow tract, and a hyperechogenic tubular

Correspondence to: J. O. Miranda, Department of Paediatric Cardiology, Centro Hospitalar São João, Porto, Portugal. Tel: +351 225512100; Fax: +351 225512273; E-mail: joanam@gmail.com

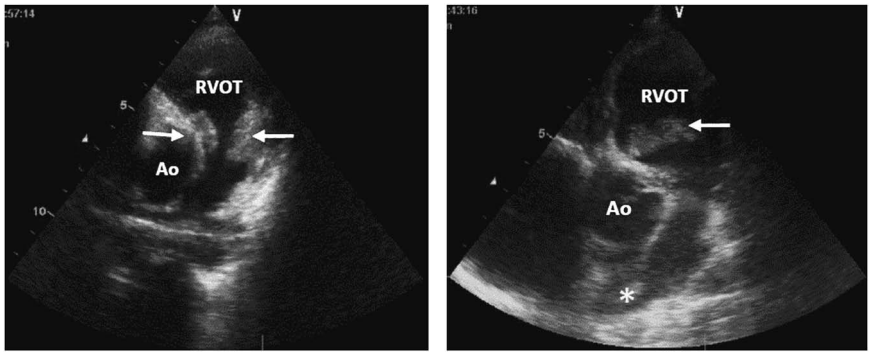

Figure 1.
2D-echocardiography at admission: parasternal short-axis showing a large and pedunculated mass on the pulmonary monocusp (arrow) and a hiperecogenic tubular mass inside the right pulmonary artery (*), corresponding to vegetations. Ao = aorta valve; RVOT = right ventricle outflow tract.

mass inside the right pulmonary artery (Fig 1). The diagnosis of probable infectious endocarditis and bilateral septic pulmonary embolism was established. Multiple sets of blood cultures were obtained and treatment with vancomycin and gentamicin was started. Hypocoagulation was initiated but stopped 1 week later after a significant lower gastrointestinal bleeding.

Despite treatment, the patient became septic and liposomal amphotericin B, 5 mg/kg/day, intravenous, was associated, even with negative blood cultures and negative galactomannan antigen assay. Nevertheless, the patient presented an overwhelming course refractory to broad-spectrum antibiotics, and a surgical debridement was performed 9 days after the diagnosis of probable infectious endocarditis. The vegetations and the monocusp were excised and replaced by a biological pulmonary prosthesis, with good surgical outcome and a rapid haemodynamic and analytical improvement. On the sixth postoperative day, the diagnosis of *A. fumigatus* endocarditis was confirmed, with the identification of the fungus in histologic specimen and in tissue culture of the resected vegetations and a positive polymerase chain reaction in blood. Voriconazole, 7 mg/kg twice per day, oral, was given. The patient underwent 6 weeks of inpatient treatment with liposomal amphotericin B and was then discharged home with voriconazole and endocarditis prophylaxis recommendations. The plan was to maintain voriconazole indefinitely.

At the eight-month follow-up, the patient presented with dyspnoea, orthopnoea, desaturation, and severe weight loss – 20% of body mass. The echocardiogram was suggestive of pulmonary hypertension, with no significant residual lesions or vegetations. The thoracic CT-angiography and the ventilation/perfusion scan were compatible with pulmonary thromboembolism. A cardiac catheterisation confirmed severe pulmonary hypertension with severe dilatation of the right ventricle and main pulmonary artery and its branches, and severe amputation of pulmonary peripheral vascularisation. Warfarin was started. The patient remained symptomatic, and thus a pulmonary vasodilator – inhaled iloprost, 10 mcg dose, 4 times a day – was added. Pulmonary thromboendarterectomy or heart–lung transplant were discussed as an end-stage invasive intervention. The patient was readmitted for massive pulmonary haemorrhage 2 weeks later. Unfortunately, the clinical course was overwhelming and the patient died subsequently to a pulmonary hypertensive crisis refractory to aggressive medical treatment. An autopsy was not carried out.

Discussion

The most critical step in the treatment of *Aspergillus* endocarditis is establishing the diagnosis in a timely manner. The diagnosis of *Aspergillus* endocarditis is usually very difficult and requires a high index of suspicion.

The diagnosis of *Aspergillus* endocarditis should be suspected in the presence of a predisposing condition and large vegetations.[1] Clinical presentation is typically insidious, with embolic complications often representing the first manifestation of the disease.[1,3] Besides several risk factors for *Aspergillus* endocarditis, namely male gender, congenital heart disease, prosthetic valve, and prolonged antibiotic exposure, our patient presented critically ill, with large vegetations on a prosthetic valve and with evidence of septic pulmonary embolism. The combination of these factors led us to establish the probable diagnosis of fungal endocarditis and treat him accordingly, despite several negative blood cultures. In fact, blood cultures for *Aspergillus* are almost always negative, even fungal blood cultures. In a recent review on 53 patients, identified in the literature from 1950 to 2010, the diagnosis was established postmortem in 21% of the patients and blood cultures were negative in 96% of the patients.[2] *Aspergillus*

https://doi.org/10.1017/S1047951114000432 Published online by Cambridge University Press

endocarditis diagnosis ultimately requires confirmation by tissue histology and culture, which typically only occurs with samples obtained intraoperatively.[2]

Data regarding treatment are scarce due to the relative infrequency of cardiac aspergillosis. Surgical debridement combined with antifungal treatment is imperative for the survival of almost all patients.[1,2,3] The mortality of medically managed patients without surgery approaches 100%.[2] In the Guidelines of European Society of Cardiology, treatment of *Aspergillus* endocarditis is poorly detailed.[4] The Guidelines of the Infectious Diseases Society of America state aggressive medical treatment and surgical intervention as mandatory.[3] Voriconazole is recommended as the first-line agent and amphotericin B should be continued for a minimum of 6 weeks after surgical intervention. In the guidelines deoxycholate amphotericin B is still recommended for *Aspergillus* endocarditis; however, the more recent studies support the use of liposomal forms as they have equal efficacy and less nephrotoxicity.[2] An extended course of antifungal therapy postoperatively with an antifungal triazole, possibly lifelong, is recommended because of the potential for recurrent infections following replacement of an infected prosthetic valve.

Septic pulmonary embolism complicated with secondary pulmonary hypertension in a patient with fungal valve endocarditis is extremely rare, and the scientific literature addressing treatment options is sparse, especially in paediatric patients. Previous attempts to perform pulmonary embolectomy/endarterectomy in infectious thromboembolic disease are very discouraging.[5] The authors point out technical difficulties related to the absence of resection plane due to fibrosis and formation of collagen into the media layer of the vessel wall. Of note, in this particular case, our patient presented with a disseminated microembolic event, which also precludes this surgical intervention. A heart–lung transplant was considered; however, the patient had a very poor clinical condition and, unfortunately, he died subsequently to a pulmonary hypertensive crisis not responsive to aggressive medical management.

Conflicts of Interest

None.

References

1. El-Hamamsy I, Dürrleman N, Stevens LM, Perrault LP, Carrier M. Aspergillus endocarditis after cardiac surgery. Ann Thorac Surg **2005**; 80: 359–364.
2. Kalokhe AS, Rouphael N, El Chami MF, Workowski KA, Ganesh G, Jacob JT. Aspergillus endocarditis: a review of the literature. Int J Infect Dis **2010**; 14: e1040–e1047.
3. Walsh TJ, Anaissie EJ, Denning DW, et al. Treatment of aspergillosis: clinical practice guidelines of the Infectious Diseases Society of America. Clin Infect Dis **2008**; 46: 327–360.
4. Habib G, Hoen B, Tornos P, et al. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009). The Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC) Endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and by the International Society of Chemotherapy (ISC) for Infection and Cancer. Eur Heart J **2009**; 30: 2369–2413.
5. Heiberg J, Ilkjær LB. Pulmonary endarterectomy after pulmonary infectious embolisms. Interact Cardiovasc Thorac Surg **2013**; 16: 556–557.