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Case Reports and Series

Fusobacterium species cardiac device infective endocarditis diagnosed via molecular methods

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ABSTRACT

Background: Endocarditis of an implanted cardiac device is difficult to diagnose but has a high morbidity and mortality if left untreated. We present a case of culture negative endocarditis due to *Fusobacterium* species detected using molecular methods.
Case report: An 81-year-old female presents with chest pain and breathlessness two months after aortic valve replacement and permanent pacemaker implantation. Fevers, hypoxia, and a single splinter haemorrhage were noted. Transoesophageal echocardiography demonstrated a single vegetation. Blood cultures were negative, but 16S ribosomal RNA matching *Fusobacterium* species was detected in serum. Antimicrobials were rationalised and the patient made a complete recovery.
Conclusion: Infective endocarditis is a life-threatening condition which patients with cardiac devices in-situ are particularly susceptible to. There should be a low threshold for transoesophageal echocardiography when cardiac device endocarditis is suspected. Molecular methods such as polymerase chain reaction and serology are valuable when assessing culture negative endocarditis.

Background

We present a case of permanent pacemaker endocarditis due to Fusobacterium spp detected using molecular methods. We will discuss presentation and investigation of blood culture negative endocarditis, with a focus on cardiac devices.

Report

An 81-year-old female presented to the Emergency Department with a two-day history of dull central chest pain and breathlessness, exacerbated by lying flat and exertion and associated with palpitations. Approximately two months prior she had undergone an elective *trans*-catheter aortic valve implant for aortic stenosis, with a dual chamber permanent pacemaker insertion. On admission, the patient was tachycardic with an irregularly irregular pulse with no murmurs. A 12 lead ECG demonstrated atrial fibrillation with a fast ventricular response. Admission blood tests showed a haemoglobin of 12.9 g/dL, troponin I 50 ng/L (rising to 143 ng/L) and C-reactive protein 50 mg/L. Blood for culture was collected.

The patient was initially managed for a possible acute coronary syndrome with heart rate control using betablockers and the introduction of anticoagulation. A transthoracic echocardiogram demonstrated a small pericardial effusion as well as a left sided pleural effusion, which were initially managed conservatively. Her symptoms persisted and a repeat echocardiogram and chest radiograph demonstrated progression of pleural and pericardial effusions. These were drained with good symptomatic relief. The patient was diagnosed with post procedure pericarditis and after a long in-hospital stay was discharged with a course of colchicine.

Eight days later she was readmitted with worsening shortness of breath and blood oxygen saturation of 88%. She reported that since her discharge she began to feel more unwell with giddiness, fevers, shortness of breath on minimal exertion, lethargy, and weight loss. On examination, there was a single splinter haemorrhage and reduced air entry at both lung bases with fine crepitation. Femoral puncture and pacemaker site showed no signs of infection or inflammation. Blood tests showed haemoglobin of 14.4 g/dL and a C-Reactive protein of 76 mg/L, and a chest radiograph showed a re-accumulation of the left sided pleural effusion, which was drained. On this admission, there was a heightened

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clinical suspicion of infective endocarditis. Transoesophageal echocardiogram was performed which demonstrated no valvular vegetations but a 10 mm mobile mass on the right atrial pacemaker lead (Fig. 1).

Cardiac device infective endocarditis (CDIE) was diagnosed, with suspicions that there could be a fungal or atypical cause in view of repeatedly negative blood cultures. After discussion with the microbiology service, empirical treatment was starting with intravenous teicoplanin, intravenous caspofungin, and oral rifampicin. Blood was drawn for serum galactomannan, aspergillus antigen, fungal and bacterial polymerase chain reaction (PCR), and staphylococcal PCR. Repeat fungal and bacterial blood cultures were taken at this time. Bacterial 16S ribosomal ribonucleic acid (rRNA) was detected in EDTA blood matching *Fusobacterium* spp. The microbiology team recommended stopping caspofungin and commencing oral metronidazole, while continuing oral rifampicin and intravenous teicoplanin. The patient completed a six-week course of treatment with rapid resolution of symptoms and no clinical recurrence of endocarditis at follow-up.

Discussion

Epidemiology and presentation

Infective endocarditis (IE) is a rare condition with an incidence of up to 10 in 100,000 and a mortality of 30% in 30 days (Rajani and Klein, 2020). Patients with cardiac devices such as permanent pacemakers or implantable cardiac defibrillators are at increased risk of IE with an incidence of 190 per 100,000 device-years. The clinical presentation of CDIE is non-specific but fevers, night sweats, loss of weight and appetite, and fatigue are the usual presenting symptoms. A retrospective study found 80% of patients present with fever and 48% of patients with infective signs around the device pocket were later found to have CDIE (Sohail et al., 2008). CDIE is however more likely to present acutely with two thirds of patients having a history of less than 1 month (Athan et al., 2012). The modified Duke criteria are a standard clinical tool for diagnosing IE, however its sensitivity is lower for CDIE and there should be a low threshold for further investigation (particularly transoesophageal echocardiography) in patients with suspected CDIE (Athan et al., 2012).

Imaging

Echocardiography to identify vegetations and inspect valve function should be requested in patients under investigation for IE. Transthoracic echocardiography has a lower sensitivity than transoesophageal echocardiography, and patients with suspected CDIE should have a low threshold for transoesophageal echocardiography. In patients with suspected CDIE in whom baseline imaging remains normal, other techniques such as cardiac magnetic resonance imaging, positron emission tomography, or white blood cell scintigraphy can be valuable (Mahmood et al., 2019; Golzio et al., 2019).

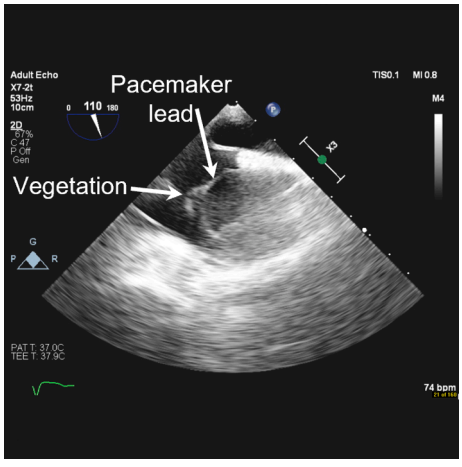

Fig. 1. Transoesophageal echocardiogram image showing vegetation on right atrial pacemaker lead.

Microbiology

Causative organisms in IE are usually gram-positive cocci and this is true for CDIE (Rajani and Klein, 2020). Other causes of IE include *Haemophilus* species, *Aggregatibacter* spp, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella* spp (the HACEK group). Gram negative organisms (such as *Fusobacterium* spp) are rare (Athan et al., 2012). A review of anaerobic IE found 39 cases of *Fusobacterium* spp IE published between 1970 and 2010, of which nearly all had a head and neck or oral source of infection (Brook, 2008). A 2021 case report and review of *Fusobacterium necrophorum* IE identified 10 cases, of which six had an upper respiratory tract or dental source (Sato et al., 2021). Although neither of these reviews included cases of CDIE, the lack of other source in the presented case strongly implies an occult oral or dental source.

Blood cultures are essential for the diagnosis and targeted management of endocarditis. All patients with suspected IE should have several sets of blood cultures collected before antibiotics are given (Habib et al., 2015). The predominant cause of culture negative endocarditis (35–40%) is prior antibiotic administration (Subedi et al., 2017). Other causes include fungal, fastidious bacteria, and non-infective endocarditis. Alternative laboratory investigations if blood cultures remain negative and IE continues to be suspected include serology, PCR on blood or extracted tissues, and histopathology of resected tissue (Fournier et al., 2010).

PCR can identify specific species or detect bacterial or fungal rRNA (also known as broad range PCR). Species specific PCR on EDTA blood is more sensitive than broad range PCR and multiplex PCR panels allows for parallel testing for multiple species at once (Fournier et al., 2017; Liesman et al., 2017). Species specific PCR is limited by the choice of species included in the panel and negative results should be confirmed with broad range PCR (Fournier et al., 2017). PCR conducted on explanted cardiac device leads is more sensitive than on EDTA blood and where available this should be used (Fournier et al., 2017; Liesman et al., 2017). PCR can detect non-viable genetic material present after successful management of infection and so positive results should be interpreted with caution, particularly in resected tissues, as they may be detecting residual material and not active infection (Liesman et al., 2017; Godfrey et al., 2020). If these investigations remain negative, then non-infective endocarditis should be considered (Subedi et al., 2017).

Management

IE and CDIE are treated with extended courses of intravenous antibiotics and empirical management should include gram-positive cover; for example, daptomycin, vancomycin, or teicoplanin in combination with other antibacterial therapies (Sławiński et al., 2019). Further management should be discussed with the local microbiology or infection service and guided by species identification and sensitivities (Sławiński et al., 2019). Cases of *Fusobacterium* IE treated successfully with metronidazole without valvular replacement have been reported (Brook, 2008), as have cases of medically managed CDIE (Uslan, 2008). However, the recurrence of CDIE is common in medically managed cases and improved survival is seen in CDIE if devices are explanted (Uslan, 2008). If devices are not explanted a six-week antimicrobial course is recommended, with careful follow-up for recurrence (Sławiński et al., 2019). When possible, cases should be discussed with the regional endocarditis multi-disciplinary team (Davierwala et al., 2019).

Conclusions

Patients with cardiac devices in-situ are at elevated risk of IE and

clinicians should have a low threshold for transoesophageal echocardiography in suspected CDIE. Molecular techniques such as PCR and serology can be used to investigate blood culture negative IE.

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Ethical approval statement

No ethical approval required for this work. Written consent for publication received from patient. Photographs of the patient are not included, nor are their initials, name, or hospital number.

CRediT authorship contribution statement

Oliver Galgut: Conceptualization, Writing – original draft, Writing – review & editing. **Andrew R.J. Mitchell:** Conceptualization, Writing – review & editing. **Pierre Le Page:** Conceptualization, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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