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CASE REPORT

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Aggregatibacter actinomycetemcomitans pacemaker lead infection—A case report and literature review

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Key Clinical Message

Aggregatibacter spp. is a rare cause for cardiac device infections. Due to limited data, the management of *Aggregatibacter* spp. device infections is not clearly defined but should always involve device removal and prolonged intravenous antibiotics.

KEYWORDS

Aggregatibacter actinomycetemcomitans, cardiac implantable electronic device, endocarditis, pacemaker

1 | INTRODUCTION

Aggregatibacter actinomycetemcomitans is a fastidious gram-negative coccobacillus that forms part of the HACEK group, which also includes *Haemophilus* spp., *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella* spp.[1] It is considered to be normal flora when found in the human oral cavity, but in certain circumstances can cause disease, namely periodontitis and infective endocarditis.[2] The HACEK organisms were historically grouped together due to their perceived tendency to cause infective endocarditis; however, more recent studies have shown this to be relatively rare.[3] As opposed to valvular endocarditis, there is significantly less literature describing infection of cardiac implantable electronic devices (CIED) with HACEK organisms like *A. actinomycetemcomitans*. In this case report, we present a case of *A. actinomycetemcomitans* CIED infection that required device extraction and perform a review of recent literature.

2 | CASE HISTORY/EXAMINATION

An 83-year-old gentleman presented to a metropolitan Sydney Hospital with a one-month history of multiple symptoms, including fatigue, nausea, and abdominal bloating. He denied having any fevers. His background

history included ischemic heart disease, atrial fibrillation with pacemaker inserted in 2020, pulmonary hypertension with severe tricuspid regurgitation, type 2 diabetes mellitus, stage 3B chronic kidney disease, and Childs Pugh B liver cirrhosis secondary to congestive hepatopathy. He was normally independent and lived at home with his family. He denied smoking or drinking any alcohol. His initial observations revealed a temperature of 36.7°C, heart rate of 86 beats per minute, blood pressure of 110/63 mmHg, and respiratory rate of 16 breaths per minute. His physical examination was significant for an ejection systolic murmur and moderate abdominal ascites.

3 | METHODS

Bloods on admission showed a white cell count of 6.6×10^9/L, and C-reactive protein of 54 mg/L. His liver function tests were stable, with ALT 54, AST 45, GGT 82, and ALP 103, and synthetic markers showed albumin 27 g/L, INR 1.6 and platelet count of 148×10^9/L. Computed tomography imaging revealed a known 9 mm lung nodule that was stable, and ascites. He was admitted for treatment of presumed liver cirrhosis-related symptoms with dietary salt restriction, diuretics, and anti-emetics. On Day 5 of hospital admission, he spiked a low-grade fever to 37.8°C, and a set of blood cultures were collected. An ascitic tap was performed, which demonstrated an exudative ascites with serum ascites albumin gradient of 0.4 g/L, but no evidence of spontaneous bacterial peritonitis or malignancy, with a leukocyte count of 1350×10^6/L that was primarily monocytic and normal cytology. On Day 9 of admission, he spiked another fever to 38.4°C. Blood cultures were again collected, and he was commenced on intravenous ceftriaxone 2 g 24-hourly to presumptively treat for spontaneous bacterial peritonitis. He defervesced and improved clinically.

The above two consecutive sets of blood cultures obtained within a 5-day interval exhibited positive signals, yet microscopic examination via gram staining revealed no discernible organisms. Both sets flagged positive on Day 5 of incubation. There were no organisms seen on gram stain. Following standard laboratory protocols, despite the absence of visible organisms on gram staining, cultures were inoculated onto 5% horse blood agar, chocolate agar, and Brilliance UTI clarity agar (Thermo Fisher, Australia). These plates were placed in an incubator set at 37°C with 5% CO_2 and monitored daily. Colonies grew within 3 days, and their identification was confirmed using the MALDI Biotyper® (Bruker Daltonics, Bremen, Germany) as *Aggregatibacter actinomycetemcomitans* in both sets of blood culture bottles. Despite the lack of defined European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints, antibiotic gradient strips (0.5 McFarland, Mueller Hinton Fastidious Agar) were performed to provide guidance for treatment strategies. Values generated are represented in Table 1 below. Further physical examination revealed poor oral hygiene with notable periodontitis. Ceftriaxone was continued, and subsequent repeat blood cultures remained negative, however, concern was raised for potential endocarditis. Transthoracic echocardiography revealed moderate mitral regurgitation and tricuspid regurgitation with pulmonary hypertension, but no evidence of infective endocarditis. Given the risk with his CIED, a transesophageal echocardiography was performed, which revealed a 0.9 × 0.4 cm vegetation on the distal pacing wire within the right atrial cavity with moderate tricuspid regurgitation (Figure 1). A positron emission tomography (PET) scan performed incidentally for characterization of the previously noted lung nodule revealed non-uniform activity along the cardiac device lead (Figure 2), reaffirming the concern for lead infection.

TABLE 1 Minimum inhibitory concentration (MIC) using antibiotic gradient strips.

Antimicrobial	MIC (mg/L)
Ceftriaxone	0.032
Ciprofloxacin	0.016
Rifampicin	0.5
Tetracycline	0.125

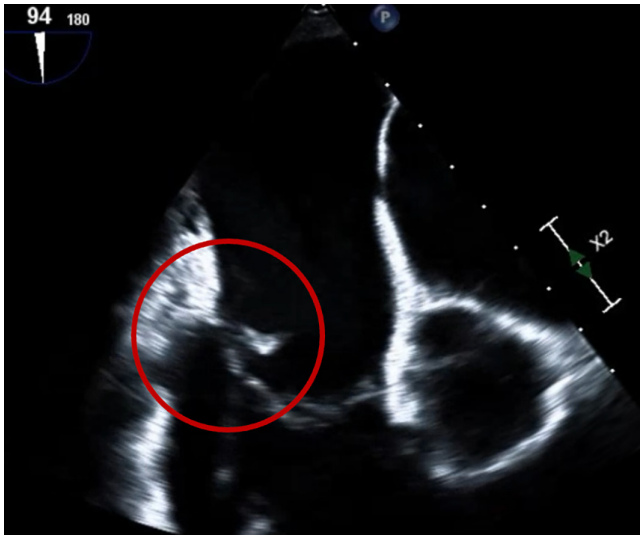

FIGURE 1 Transoesophageal echocardiography demonstrating a 0.9 × 0.4 cm vegetation on right atrial lead.

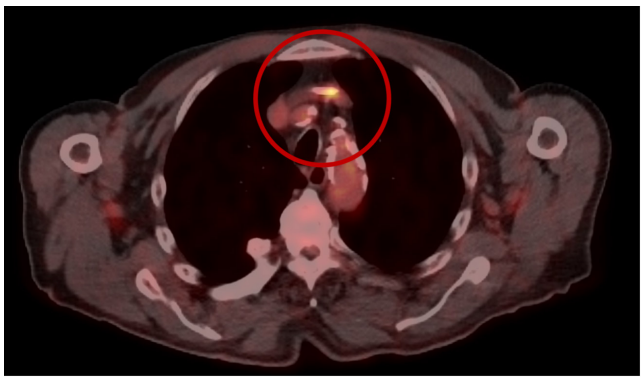

FIGURE 2 Positron emission tomography demonstrating avid uptake along venous pacing lead.

4 | CONCLUSION AND RESULTS

Ceftriaxone was continued. His teeth were reviewed by the maxillofacial team and were deemed unsalvageable; all were removed in preparation for cardiothoracic intervention. Cardiac device check revealed a high ventricular pacing burden of 96%. A transvenous lead was considered; however, decision was made to not pursue this as it would have delayed implantation of a permanent pacing system, and potential risks of worsening tricuspid regurgitation and right ventricular failure. Four weeks after commencement of ceftriaxone, he proceeded to have an epicardial pacemaker insertion, followed by complete removal of the previous CIED system. The pacemaker leads were sent to microbiology for culture and 16s rRNA polymerase chain reaction, both were reported as negative. He continued intravenous ceftriaxone 2 g 24 hourly for a further 4 weeks following device removal, through the hospital's outpatient parenteral antibiotic therapy service. His inflammatory markers including C-reactive protein returned to normal levels. At 1-month follow-up post-cessation of antibiotics, he remained well.

5 | DISCUSSION

Aggregatibacter actinomycetemcomitans is part of the HACEK group of fastidious gram-negative organisms, known to rarely cause infective endocarditis. Its involvement in CIED infections and subsequent management is less documented. A comprehensive review of HACEK endocarditis was recently performed on Swedish registry data; in this study, they analyzed 10 years of endocarditis data and found that *Aggregatibacter* spp. was the most common of the HACEK endocarditis cases at 51% ($N = 49$).[3] When compared to more common causes of endocarditis, the prevalence of HACEK endocarditis as a whole was relatively low at 1.8%, however the rate of CIED involvement was proportionally higher at 16%, with *Staphylococcus aureus* second at 12%; *Aggregatibacter* spp. specifically had CIED involvement in 24% of cases.[3] *Aggregatibacter actinomycetemcomitans* is known to form bacterial biofilms in periodontal disease[4]; however, the role of using biofilm-active antimicrobial agents in CIED infections is less clear, with almost no usage of fluoroquinolones seen in the Swedish registry study.[3] The 2023 European Society of Cardiology guidelines for infective endocarditis management advises that for CIED infections, prompt device removal with prolonged antibiotic therapy for at least 4 to 6 weeks is recommended, although the suggested duration of therapy if device removal is delayed is not stated. Recommended timing of device reinsertion following removal is 2 weeks with negative blood cultures if vegetations seen, however in the setting of pacemaker dependence, transvenous pacing or alternatively an epicardial pacemaker can be implanted prior to device extraction, as was performed in this patients' case.[5] There is one published case report that describes a similar infection with the same organism as our patient; a young male in his twenties who had a pacemaker, and presented with a febrile illness with positive peripheral blood cultures for *A. actinomycetemcomitans*. In this case, there was an attempt at antibiotic treatment only, but the patient subsequently developed a relapsed infection and eventually had his device removed, followed by outpatient cefepime with vancomycin, and achieved complete recovery.[6] A second case report describes an *Aggregatibacter aphrophilus* pacemaker infection, who also similarly required device removal followed by 4 weeks of intravenous ceftriaxone for curative management.[7] A summary of currently published *Aggregatibacter* spp. CIED infections can be seen in Table 2. There has been significant recent interest in the role of nuclear imaging in CIED infections, as was used for this patient; for device lead infections in particular, a recent meta-analysis found a pooled sensitivity and specificity of 76% and 83%, respectively.[8]

6 | CONCLUSION

Our case serves as an example that fastidious organisms like *Aggregatibacter* spp. can be a rare but significant cause for CIED infection and that device removal with adjuvant antibiotics remains to be the mainstay of treatment.

TABLE 2 Summary of current published cases of *Aggregatibacter* spp. cardiac implantable electronic device infections.

Case	Year published	Organism	Age, gender	Device type and number of years inserted prior to infection	Presenting complaint	Initial white cell count ($\times 10^9$/L)	Transesophageal echocardiography findings	Number of days after blood culture collection before *Aggregatibacter* spp. identified	Device removal timing	Device reinsertion timing	Definitive antibiotic management and duration
1	2013 (Li et al.)	*A. actinomycetemcomitans*	25, Male	Pacemaker, inserted 12 years prior	Dizziness, dyspnoea, fever, weight loss	17.3	Several vegetations (0.6–0.9 cm size) on atrial and ventricular leads	10 days	After 21 days of antibiotics	Not reinserted	Cefepime & vancomycin, duration not stated
2	2014 (Patel et al.)	*A. aphrophilus*	62, Male	Pacemaker, originally inserted 21 years prior, revised 10 years prior due to ventricular lead fracture	Fevers, night sweats, fatigue, weight loss	14.2	Tricuspid valve vegetation (1.2 × 0.7 cm size), and smaller vegetation on right ventricular lead (unsized)	7 days	Not stated	Not stated	Ceftriaxone, 42 days total
3 (our case)	2024	*A. actinomycetemcomitans*	83, Male	Pacemaker, inserted 3 years prior	Fatigue, abdominal bloating, nausea	6.6	Singular vegetation (0.9 × 0.4 cm size) on right atrial lead	7 days	After 28 days of antibiotics	Immediately	Ceftriaxone, 56 days total, including 28 days following device removal

AUTHOR CONTRIBUTIONS

Hayden Zhang: Conceptualization; investigation; project administration; writing – original draft. **Varsha Sivalingam:** Investigation; resources; writing – review and editing. **Pierre Qian:** Conceptualization; supervision; writing – review and editing. **Shobini Sivagnanam:** Conceptualization; supervision; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare there is no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical.

ETHICS STATEMENT

Ethical approval was granted by the Western Sydney Local Health District Human Research Ethics Committee.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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