CASE REPORT

Haemophilus parainfluenzae prosthetic valve endocarditis complicated by septic emboli to brainJ J Liang,¹ P L Swiecicki,¹ A M Killu,¹ M R Sohail²

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SUMMARY

A 51-year-old man with a history of injection drug use presented to the emergency room with fevers, chills and headaches. Five months earlier, he had undergone bioprosthetic aortic valve replacement for infective endocarditis owing to *Corynebacterium auricumosum* involving a bicuspid aortic valve. Blood cultures obtained during current hospitalisation grew *Haemophilus parainfluenzae* and patient underwent a transesophageal echocardiogram that revealed a large mitral valve vegetation. Owing to persistent headache and right lower extremity weakness, MRI of the brain was performed which demonstrated multifocal, acute infarctions secondary to septic embolisation. He was initiated on parenteral antibiotics and experienced no further neurological setbacks. After 2 weeks of antibiotic therapy, he underwent bioprosthetic aortic and mitral valve replacement, aortic root debridement and replacement, and reconstruction of the intravalvular fibrosa without complication. He was discharged to a skilled nursing facility to complete six more weeks of intravenous ceftriaxone.

BACKGROUND

With an ageing population, the number of patients being treated with prosthetic heart valves and intracardiac devices continues to increase. As such, there is likely to be a coinciding increase in the incidence of infective endocarditis (IE). Septic embolisation occurs in up to 50% of patients with IE and may lead to various complications including renal infarcts, splenic infarcts and central nervous system (CNS) emboli. Cerebral embolisation accounts for nearly two thirds of systemic embolic events¹ and are particularly worrisome. A majority of CNS emboli lodge in the middle cerebral artery distribution,¹ and this may result in catastrophic consequences. The optimal management of septic embolisation to CNS and strategies for prevention remain unclear. We describe an interesting case of IE owing to *Haemophilus parainfluenzae*, a member of the HACEK (*Haemophilus* species, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominus*, *Eikenella corrodens*, and *Kingella Kingii*) group of fastidious gram negative organisms, complicated by septic embolisation to the brain that was successfully treated with antibiotic therapy and cardiac surgery. This case highlights the workup, risk stratification and management of patients with IE with suspected septic CNS emboli.

CASE PRESENTATION

A 51-year-old Caucasian man presented to his local emergency department owing to a 2-week history

of worsening fevers, chills, malaise, dyspnoea on exertion and daily frontal headaches.

The patient had a history of polysubstance abuse (including injection cocaine and methamphetamine use), untreated hepatitis C infection, type 2 diabetes mellitus and bipolar affective disorder. Five months prior to current presentation, he was diagnosed with infective endocarditis with *Corynebacterium auricumosum* involving his native bicuspid aortic valve. This organism was susceptible to penicillin and vancomycin, but resistant to ceftriaxone. Owing to severe aortic regurgitation and cardiac decompensation, he underwent aortic valve replacement with a 27 mm Hancock porcine bioprosthesis. He received 4 weeks of intravenous antibiotics prior to home discharge with a peripherally inserted central catheter to complete the last 2 weeks of therapy. Unfortunately, he was non-compliant with the final 2 weeks of antibiotic therapy.

On arrival to the local hospital, he appeared fatigued, but was without fever (97.8 °F) with normal heart rate and blood pressure. Physical examination demonstrated right-sided conjunctival petechiae, an apical grade 3/6 holosystolic murmur radiating to the axilla and right lower extremity weakness. Examination of the extremities demonstrated no evidence of Osler's nodes, Janeway lesions or splinter haemorrhages.

INVESTIGATIONS

On initial presentation, his complete blood count was significant for a haemoglobin of 9.3 g/dl (normal 13.5–17.5 g/dL) and leucocyte count $26\,400 \times 10^3/\mu\text{L}$ (normal $3.5\text{--}10.5 \times 10^3/\mu\text{L}$). Serum electrolytes and creatine were within normal limits. C reactive protein was at the upper limit of normal at 8.0 mg/L (normal <8.0 mg/L). One set of blood cultures, drawn prior to the initiation of antibiotics, eventually grew *H parainfluenzae* (β-lactamase negative) after 2 days of incubation, while all other cultures remained negative. Serological testing for HIV was negative and he denied having had frequent prior infections to suggest the presence of an underlying immunosuppressed state.

Chest radiography was normal and ECG demonstrated sinus tachycardia (heart rate 104 bpm) without ST-segment or T-wave changes. A CT scan of the abdomen did not reveal any evidence of intra-abdominal septic emboli. Transthoracic echocardiogram visualised a possible anterior mitral valve leaflet vegetation and a normal-appearing, well-functioning bioprosthetic aortic valve without the evidence of vegetation. Although the mitral

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Figure 1 Transoesophageal echocardiogram image visualising a 1.8 mm mobile vegetation (arrow) extending from the aortic root along the atrial surface of the anterior mitral valve leaflet.

valve itself appeared to be functioning properly, a perivalvular fistula connecting the left atrium and the left ventricle was visualised, resulting in moderate to severe perivalvular mitral regurgitation. Transoesophageal echocardiogram (figure 1) better delineated a 1.8 mm mobile vegetation extending from the aortic root along the atrial surface of the anterior mitral leaflet. Owing to concern for septic emboli causing his right lower extremity weakness, MRI brain was performed which showed numerous multifocal, acute, small-vessel infarcts in the pons as well as the cerebral and cerebellar hemispheres bilaterally (figure 2).

DIFFERENTIAL DIAGNOSIS

- ▶ Septic emboli from IE
- ▶ Ruptured mycotic aneurysms
- ▶ Vasculitis
- ▶ Marantic endocarditis
- ▶ Connective tissue disease
- ▶ Fever of unknown origin
- ▶ Atrial Myxoma.

TREATMENT

The patient was started empirically on intravenous cefepime (for coverage of the Gram-negative rods growing in the blood culture) and daptomycin (to cover the possible relapse of inadequately treated *Corynebacterium* IE) prior to referral to our institution. A brain MRI demonstrated multifocal acute infarcts. He was subsequently transferred to our hospital for cardiovascular surgery evaluation. On arrival here, the bacterial cultures were speciated as *H parainfluenzae*. His antibiotic regimen was

switched to ceftriaxone monotherapy. Frequent neurological examinations revealed stable findings. Dental evaluation revealed two decayed teeth that were extracted. In view of his clinical and haemodynamic stability, and the risk of haemorrhagic transformation of cerebral infarcts with the full anticoagulation that is required with cardiac surgery, it was decided to complete 2 weeks of intravenous ceftriaxone before cardiac surgery. Following that, he underwent redo sternotomy. Intraoperatively, he was noted to have IE involving the prosthetic aortic valve and native mitral valve, as well as anterior mitral leaflet dehiscence, destruction of the intravalvular fibrous body and dehiscence of the aorta from the left ventricular outflow tract. He underwent successful mitral valve replacement with a Hancock porcine bioprosthesis, aortic valve replacement with a Carpentier-Edwards pericardial tissue valve, reconstruction of the intravalvular fibrous body from trigone to trigone with bovine pericardial patch reconstruction, reconstruction of the left ventricular outflow tract with a bovine pericardial patch and bovine pericardial patch closure of his aorta and aortic root enlargement. Following surgery, he was treated with intravenous ceftriaxone and vancomycin (added to cover for the unlikely possibility of persistent low-grade *C auriculosum* infection) to complete a 6-week course of therapy.

OUTCOME AND FOLLOW-UP

The patient was discharged to an inpatient facility for extensive inpatient chemical dependency rehabilitation and to complete a 6-week course of intravenous antibiotics. Thereafter, he was started on lifelong antibiotic suppression with oral amoxicillin 500 mg three times daily on the basis that he is unlikely to be a candidate for repeat cardiac surgery should he have further recurrence of IE.

DISCUSSION

H parainfluenzae is an aerobic, Gram-negative, pleomorphic coccobacilli which is an uncommon cause of IE. A member of the slow-growing group of HACEK organisms, which are normal oral flora in humans, *H parainfluenzae* is fastidious growing organism that only grows on chocolate agar or traditional agar supplemented by nutrients. One study demonstrated a mean time of 5 days to culture *H parainfluenzae* in cases of IE with lengths varying from 1 to 20 days.² This reinforces the importance of holding bacterial cultures for prolonged incubation when there is suspicion of IE. One case series reported 42 cases of *Haemophilus* IE, of which 62% were due to *H parainfluenzae*. As a group, it was noted that the majority of the cases of IE due to *Haemophilus* species had a rather indolent onset, tended to affect the mitral valve and were associated with

Figure 2 MRI brain (diffusion imaging, axial slices at multiple levels) revealing numerous small diffusion-restricted lesions (arrows) involving both cerebral hemispheres, the pons and both cerebellar hemispheres, consistent with multifocal acute small vessel infarcts.

native valve disease. Cerebral emboli were identified in 21% of the cases.²

Septic embolisation to the CNS is a dreaded complication of IE that has been estimated to occur in between 22% and 50% of the cases.³ Cerebral embolisation leads to death in 60% of these cases.⁴ Hence, the management of embolic events in IE has been an area of much interest. Historically, antimicrobial therapy has been the only proven medical treatment to prevent embolic events,⁵ and the risk for embolisation of pre-existing vegetation is highest in the first 2 weeks of therapy.⁶ However, more recently, there has been close examination of agents that may modify this risk for embolisation. Given that platelet activation and fibrin deposition play a vital role in the pathogenesis of vegetation formation, antiplatelet agents (including aspirin and clopidogrel) have been investigated as possible treatments to mitigate this risk. Although originally supported in animal models as an adjunctive therapy,⁷ data from prospective randomised trials have suggested that the use of aspirin in addition to the initiation of antibiotic therapy did not decrease the incidence of embolic events or new intracranial lesions; however, there was a trend towards increased bleeding.⁸ The role of chronic antiplatelet use as a risk modifier for the occurrence of embolic events has been probed in several retrospective studies. In the largest study to date, patients treated with long-term antiplatelet agents had significantly lower rates of embolic events. Of the patients on chronic antiplatelet therapy, the lowest rate of embolic events was observed in the subset of patients who were on antiplatelet therapy without a history of cardiovascular disease.⁹ Long-term statin use was investigated as a possible risk modifier as these agents have been demonstrated to have anti-inflammatory, immune-modulatory and antimicrobial properties.¹⁰ At least one study found that chronic statin therapy was associated with a decreased risk for symptomatic emboli, however, with no significant impact on mortality.⁹

Recently, the role of early surgical intervention was examined in patients with large left-sided vegetations associated with severe valvular dysfunction. Patients in this study underwent surgical intervention within 48 h and it was found that early intervention was associated with decreased risk of both embolic events at 6 weeks as well as at 6 months.¹¹

Contributors All authors contributed significantly in writing the initial manuscript and editing it for the final submission. All contributors also took care of the patient while he was hospitalised.

Competing interests None.

Patient consent Obtained.

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Learning points

- Blood and tissue cultures should be held for prolonged incubation (up to 14 days) in patients with suspected infective endocarditis (IE) to allow detection of slow growing and fastidious organisms such as HACEK group.
- Cerebral embolisation is a dreaded complication of IE and is associated with increased mortality.
- Evidence suggests that early surgery in patients at high risk for embolisation is associated with decreased rates of embolic events.
- Prior antiplatelet and statin use have been associated with a decreased risk for embolic events in IE. However, there have been no prospective trials demonstrating benefit of these agents in reducing rate of septic embolisation when initiated after the diagnosis of IE.

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