CASE REPORT

Rare case of simultaneous enterococcal endocarditis and prosthetic joint infection

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SUMMARY

A 59-year-old man was admitted with a 3-month history of daily fevers as well as bilateral knee pain and swelling. Medical history was significant for bilateral knee arthroplasties 4 years prior to admission. Two sets of peripheral blood cultures as well as bilateral knee synovial fluid grew *Enterococcus faecalis* within 10 hours. Transoesophageal echocardiography revealed aortic and mitral valve vegetations suggestive of infectious endocarditis, with severe regurgitation secondary to large size. The patient's hospitalisation was complicated by acute heart failure, necessitating emergent mitral valve repair and aortic valve replacement, followed shortly thereafter by bilateral total knee arthroplasty resection with placement of antibiotic spacers. He was treated with intravenous penicillin and gentamicin for 4 months and recovered fully. He underwent repeat bilateral knee arthroplasties and was placed on amoxicillin for 6 months postoperatively, with no further evidence of infection.

BACKGROUND

This case is important because it highlights the unusual presentation of a patient with endocarditis presenting with a chief symptom of bilateral knee pain and fevers. Even during active infectious endocarditis (IE), osteoarticular infections (OI), including prosthetic joint infections (PJI), are uncommon and are particularly rare in the setting of enterococcal IE. The clinician should consider endocarditis in the differential diagnosis when evaluating any fever of unknown origin, particularly when accompanied by arthralgias. Treatment should include a prolonged course of antibiotic therapy.

CASE PRESENTATION

A 59-year-old man presented to the emergency department, with intermittent fevers, abdominal pain, bilateral knee pain and migratory polyarthralgias. His medical history was notable for hypertension, depression, morbid obesity and bilateral knee replacement 4 years prior, for osteoarthritis. He had no history of prior cardiovascular disease or immunodeficiency, and was not on any immunosuppressive medications. Three months prior to presentation, he was in his usual state of health, when he developed unprovoked left knee pain and swelling. This persisted for 1 week before spontaneously resolving. Over the subsequent weeks, he experienced episodic migrating polyarthralgias primarily involving both knees, as well as both shoulders and his lower back, along with frequent fevers. These were variably accompanied by headaches and

photosensitivity. As per the recommendation of an orthopaedic surgeon, he had intentionally lost 25 kg in an attempt to minimise his knee pain, although his body mass index following weight loss remained elevated at 38 kg/m². Despite regular use of hydrocodone and over the counter analgesics, his knee pain escalated to the point where he required a walker to ambulate, which ultimately prompted his presentation to the emergency department. Notably, he denied any history of tick bites, travel or new sexual contacts, and his review of systems was otherwise negative. His home medications on admission were ibuprofen, acetaminophen, losartan, hydrocodone and bupropion.

On initial examination, his heart rate was elevated at 114 bpm. His temperature was 36.8°C, blood pressure was 128/75 mm Hg and SpO₂ was 100% while on room air. He had pain and restricted movement at both knees as well as tenderness to palpation at the right upper and lower abdominal quadrants, along with a positive Murphy's sign. Cardiovascular examination was unremarkable, and neither skin rashes nor stigmata of endocarditis were noted.

INVESTIGATIONS

Initial ECG was remarkable for sinus tachycardia and premature atrial complexes, and chest X-ray demonstrated thoracic kyphosis. A complete blood count revealed a white cell count (WCC) of $12.7 \times 10^9/L$ and haemoglobin 9.6 g/dL with a mean corpuscular volume of 73.1 fL. Erythrocyte sedimentation rate (ESR) and C reactive protein were elevated at 51 mm/hour and 227 mg/L, respectively, and creatinine was 1.4 mg/dL. Lyme disease testing was negative. Urinalysis with microscopy revealed dysmorphic casts and 4–10 WCCs/hpf. Urine culture was negative. Two sets of peripheral blood cultures grew *Enterococcus faecalis* at 10 hours. Radiographs of the knees demonstrated an abnormal lucency beneath the tibial component of the left knee, consistent with loosening of the prosthesis and bilateral synovitis. Radiographs of the thoracic and lumbar spine were unrevealing. Transoesophageal echocardiogram (TEE) was consistent with native aortic and mitral valve endocarditis, with a 1.3×0.8 cm globular, bilobed mobile mass observed on the mitral valve (figure 1A). The aortic valve had two complex masses on its ventricular aspect (figure 1B). Perforations of both valves were noted, resulting in severe aortic and mitral valve regurgitation.

In an attempt to identify a source as well as potential additional seeding sites, colonoscopy and

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Figure 1 Transoesophageal echocardiogram: (A) 1.3×0.8 cm mobile mass on the atrial aspect of the A2 leaflet of the mitral valve. Leaflet perforation was associated with this mass, contributing to severe mitral regurgitation; (B) 1.9×0.3 cm mass originating from the non-coronary aortic valve cusp. A second aortic valve mass (not pictured) originated from the right coronary cusp.

limited abdominal ultrasound (US) were performed. The US noted two heterogeneously hypoechoic lesions in the spleen, consistent with abscess, while the colonoscopy was unremarkable. Abdominal CT performed on hospital day 4 suggested splenic infarcts. A follow-up abdominal MRI on hospital day 18 identified a fluid-containing collection in the inferior pole of the right kidney (figure 2A), and suggested the splenic lesions were abscesses rather than infarctions (figure 2B). Subsequent cultures were taken from the synovial fluid of both knees, the right kidney and the mitral valve, all of which grew *E. faecalis*.

DIFFERENTIAL DIAGNOSIS

Based on the patient's initial clinical presentation, area of residency and elevated ESR, initial differential diagnosis focused on a bacterial septic arthritis or possible autoimmune disorder. Tick borne illnesses, gonorrhoeal arthralgia, early rheumatoid arthritis and Whipple disease were all considered possible but less likely. The Orthopaedics and Infectious Disease services were consulted, and when initial blood cultures grew enterococcus, emphasis shifted to concern for potential endocarditis. The source was thought to be gastrointestinal or urinary.

TREATMENT

Given the high rates of antimicrobial resistance among *E. faecalis*, the patient was initiated on intravenous vancomycin (20 mg/kg×1 dose, then 15 mg/kg every 12 hours), penicillin G (20 million

Figure 2 MRI of intra-abdominal abscesses: (A) Axial T2 sequence demonstrating a 3.1×2.0 cm abscess in the lower pole of the right kidney (arrow); (B) Axial Fast Imaging Employing Steady State Acquisition sequence of two irregular splenic lesions (arrows).

units via continuous infusion every 24 hours) and gentamycin (100 mg every 12 hours). Susceptibilities later revealed sensitivity to penicillin (minimal inhibitory concentration of penicillin, 2 µg/mL), and vancomycin was discontinued. Blood cultures became negative 5 days after admission. On hospital day 3, shortly following TEE, the patient's heart rate increased to 132 bpm, his SpO₂ decreased to 85% on room air and his respiratory rate increased to >30 respirations per minute, necessitating transfer to a cardiac intensive care unit. A chest X-ray was consistent with pulmonary oedema presumed secondary to severe mitral and aortic regurgitation. The patient was treated with nitroprusside for afterload reduction and aggressively diuresed. Owing to the acuity of his heart failure as well as persistent hypotension, emergent surgical management was discussed and undertaken on hospital day 4, despite the short duration of antimicrobial therapy, and the known presence of splenic abscesses and infected bilateral knee prosthesis. The patient underwent emergent mitral valve annuloplasty and patch closure of the anterior leaflet perforation, as well as aortic valve replacement with a bioprosthetic valve. This was tolerated well. Owing to the risk for further septic seeding, he underwent bilateral total knee arthroplasty resection and placement of articulating antibiotic cement spacers on hospital day 6. The patient then remained haemodynamically stable and afebrile for several days, with serial negative blood cultures. His creatinine remained elevated, however, postponing further imaging in order to avoid contrast nephropathy. Abdominal MRI was performed on hospital

day 17, revealing two splenic abscesses. The patient therefore underwent laparoscopic splenectomy on hospital day 19.

OUTCOME AND FOLLOW-UP

The patient recovered well from all procedures and was discharged after a 24-day hospital stay, with an expectation to complete 6 weeks of penicillin and at least 4 weeks of gentamicin. Follow-up renal US revealed persistent abscess, so his duration of treatment was extended. He was briefly readmitted several weeks later out of concern for a new renal lucency seen on US, but subsequent abdominal CT demonstrated that this was consistent with focal scarring rather than a new abscess. His antibiotics were stopped at that time, after completing a 4-month course.

Several months after dismissal, he was readmitted for planned removal of knee implant and antibiotic spacers, and reimplant bilateral total knee arthroplasty. Following this, he completed a 6-month course of amoxicillin for chronic suppression. He has since remained off chronic antibiotics and is free from recurrent infection. He received vaccines towards *Streptococcus pneumoniae*, *Neisseria meningitidis* and *Haemophilus influenza* serotype B just prior to splenectomy.

DISCUSSION

Among non-intravenous drug users, *Staphylococcus*, *Streptococcus* and *Enterococcus* species are the most common microbes associated with native valve IE.¹ *Enterococcus* species are Gram positive, catalase-negative, non-spore-forming facultative anaerobes that commonly inhabit the human gastrointestinal and biliary tracts, and, less often, the vagina and male urethra. Clinically significant infections are thought to result from translocation of enterococcus across the epithelial surface with subsequent haematogenous spread.² The majority of enterococcal endocarditis cases occur in elderly males with comorbidities, and typically involve damaged or artificial heart valves, although endocarditis of intact native valves has been previously documented.³ Long-term sequelae can include embolic stroke, perivalvular abscesses, conduction abnormalities and congestive heart failure; 1-year mortality can reach 40%.⁴ Diagnosis of IE involves a combination of clinical, radiographic and laboratory findings, and relies on the widely-cited modified Duke criteria.⁵ While the utility of the modified Duke criteria for suspected IE is well established, enterococcal endocarditis can often present with a non-specific constellation of fever, myalgias and malaise, often in the absence of typical physical stigmata of endocarditis, resulting in delayed echocardiographic evaluation and diagnosis.⁶

In this particular case, it is uncertain whether the initial site of colonisation was the patient's native heart valves or prosthetic knee joints. Given that bilateral knee pain was his chief symptom, it is possible that his knee prosthesis were initially infected, with seeding of his native heart valves occurring secondarily. Similar to IE, PJIs are uncommonly caused by enterococcus. Of all PJIs, 3–7% are attributed to enterococcus, while the vast majority are caused by staphylococcal and streptococcal species.⁷ Bacterial IE in general appears to be only rarely described as a complication of PJIs. A literature search identified two reports. The first describes a patient with *Streptococcus bovis* endocarditis associated with late (more than 2 years after implantation) infection of arthroscopic knee joints. The second report describes *Campylobacter* infection of an arthroscopic hip joint and accompanying pacemaker lead endocarditis in an immunocompromised patient.^{8,9} The rarity of the association of PJIs and IE is impressive given that more than 1 million hip and

knee arthroplasties are performed in the USA annually, with ~0.5% complicated by late PJIs occurring 2–10 years after implantation.^{10,11} More broadly, osteoarticular infections as a whole are only infrequently found to accompany IE. A retrospective study of 693 patients with IE found 30 (4.3%) were complicated by septic arthritis or osteomyelitis, one of which was caused by *Enterococcus* species.¹² A case report and literature review seeking to identify cases of enterococcal IE complicated by OI found 14 cases published between 1966 and 1998.⁴ Similar to the present case, a significant delay in diagnosis was frequently observed, with a median interval of 60 days occurring between the onset of symptoms and the establishment of diagnosis (range 7 days–9 months).

Regardless of accompanying complications, once a patient has been diagnosed with definite or probable IE, treatment should be initiated immediately. Current guidelines recommend combining a cell wall-active agent, such as penicillin or vancomycin, with an aminoglycoside such as gentamicin.¹³ Treatment guidelines for enterococcal PJIs are similar, and additionally suggest long-term or indefinite suppressive therapy with amoxicillin or penicillin.¹⁴ A 2-stage prosthesis exchange strategy, including temporary placement of an antibiotic cement spacer, is generally preferred.

To the best of the authors' knowledge, this case represents the first report of simultaneous enterococcal endocarditis and prosthetic joint infection. Diagnosis of enterococcal endocarditis is frequently delayed due to its subacute, non-specific presentation and lack of typical physical stigmata. Successful management requires early recognition and well-coordinated treatment efforts.

Learning points

- ▶ Enterococcus endocarditis should be considered in patients presenting with unexplained fevers and migratory arthralgias.
- ▶ Indolent endocarditis can seed abscesses in multiple organs, requiring an extensive investigation to identify all involved sites.
- ▶ Prosthetic joint infection is a rare but serious potential complication of endocarditis.
- ▶ A short blood culture time to positivity (ie, 10 hours) is pathognomonic for endocarditis if the organism is known to commonly cause endocarditis and is supported by the clinical picture.
- ▶ Treatment of simultaneous endocarditis and prosthetic joint infection requires extended duration antibiotics and a multidisciplinary approach.

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