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NO FEVER, NO MURMUR, NO PROBLEM? A CONCEALED CASE OF INFECTIVE ENDOCARDITIS

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☐ **Abstract—Background: Infective endocarditis is associated with significant morbidity and mortality, despite advances in diagnosis and treatment strategies. Injecting drug users are particularly at risk of endovascular infections, especially with multi-resistant and virulent microorganisms. Typically, patients with endocarditis present with constitutional symptoms, such as high fever and malaise combined with cardiorespiratory symptoms of valvular failure or emboli, such as septic pulmonary embolism. Case Report: A 33-year-old female with a history of peptic ulcer disease presented to the emergency department with 3 days of increasing unilateral calf pain and swelling. There was no history of trauma or immobilization, no fever or clinical signs of sepsis or cardiopulmonary symptoms. A history of recent i.v. amphetamine injection in the forearm was elicited and empiric treatment for endovascular infection was commenced. Workup revealed methicillin-resistant *Staphylococcus aureus* mitral papillary endocarditis with gastrocnemius pyomyositis, multi-joint septic arthritis, and brain abscesses. After a 60-day inpatient stay, including intensive care admission for septic shock, the patient made a good recovery. Why Should an Emergency Physician Be Aware of This?: The incidence of injecting drug use is increasing, and these patients are at risk of severe invasive infections with multi-resistant organisms. The emergency physician is most often responsible for the initial workup and treatment of patients with suspected infective endocarditis, with timely collection of blood cultures and appropriate antibiotics being essential interventions. This case highlights that even without fever, murmurs, or constitutional symptoms, severe multisystem infections from endocarditis can occur.**

☐ **Keywords—infective endocarditis; sepsis; injection drug use; papillary muscle**

INTRODUCTION

Since Osler's work in the late 19th century, infective endocarditis (IE) has remained a continuously evolving and heterogeneous disease. Previously affecting those with congenital and rheumatic heart disease, IE is now strongly associated with health care procedures, prosthetic heart valves, the elderly, and virulent multi-resistant organisms (1,2). Recent data from Europe suggest that between 15% and 25% of cases were associated with health care procedures and 7% linked to i.v. drug use (IDU) (3,4). The proportion of IE associated with IDU has increased markedly in the United States, rising from 7% to 12.1% between 2000 and 2013, which closely mirrors the epidemic of opioid abuse across the country (5,6). Endocarditis secondary to IDU is more frequently due to *Staphylococcus aureus*, including methicillin-resistant strains, and often

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involves the tricuspid valve resulting in septic pulmonary emboli (7). IE is associated with an in-hospital mortality rate of approximately 20%, with right-sided disease conferring a more favorable outcome compared to left-sided infections and those due to *S. aureus*, which are associated with a poor prognosis (2,4).

CASE REPORT

A 33-year-old female presented to the emergency department (ED) with 3 days of increasing unilateral calf pain and swelling. There was no history of trauma; recent immobilization or surgery; or symptoms of dyspnea, chest pain, or fever. She had been seen in the ED the day prior with the same symptoms and was discharged with a diagnosis of a muscular strain and given a single prescription of acetaminophen/codeine (500 mg/30 mg). Her medical history was significant for peptic ulcer disease due to *Helicobacter pylori* and she took no regular medications. She admitted to intermittent use of i.v. amphetamines and had no personal or family history of venous thromboembolism. She denied drug injection into the lower limbs, but revealed a small venepuncture site on the forearm corresponding to amphetamine use 1 week prior, which had not been elucidated in the previous admission. Her last dose of analgesia was more than 4 h prior to admission.

She was alert and orientated, with normal vital signs and a temperature of 36.8°C (98.2°F, tympanic measurement). There were no cardiac murmurs, breath sounds were normal, no cellulitis at the right forearm injection site or Janeway lesions or Osler's nodes. The right calf was markedly swollen and was tender to touch with pitting edema to the knee. There were no wounds or ulcers on the limb and peripheral pulses were palpable with good capillary perfusion.

A provisional diagnosis of deep vein thrombosis (DVT) was made and enoxaparin 1 mg/kg was administered with a Doppler ultrasound booked 5 h later when the radiology department opened at 7:30 AM. Blood tests revealed a hemoglobin of 142 g/L (reference: 120–160 g/L), white cell count of 19.5 $\times$ 10^9/L (reference: 4–11 $\times$ 10^9/L), 90% neutrophils, and normal electrolytes and renal function. Despite escalating doses of analgesia, including oxycodone and i.v. fentanyl, the patient became progressively distressed with increasing pain and swelling in the affected limb. She remained afebrile and hemodynamically stable; however, the patient's pain and progression of swelling was believed to be disproportionate to that of a DVT, thus concerns for deep soft-tissue infection were considered. A C-reactive protein added to the blood chemistry was 350 mg/L (reference: <3 mg/L) and due to the patient's history of IDU, endovascular infection was postulated, given the absence of wounds or trauma to the limb. Blood cultures were drawn and i.v. flucloxacillin 2 g q.i.d, vancomycin 20 mg/kg b.i.d, and gentamicin 6 mg/kg daily were administered as empiric therapy. The pain soon settled, so urgent imaging for compartment syndrome or necrotizing fasciitis was not sought and she was admitted to the ward.

Six of six blood culture bottles were positive for methicillin-resistant *S. aureus* (MRSA). Echocardiography

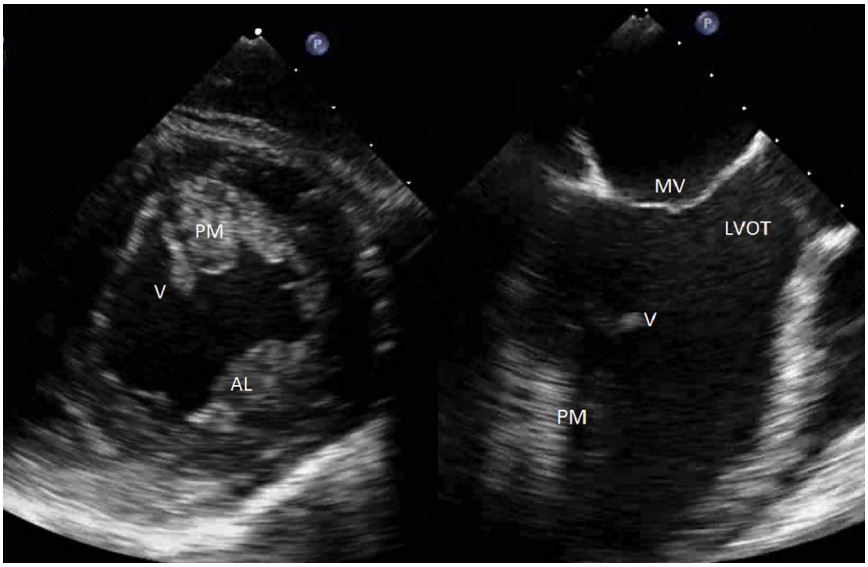

Figure 1. Transesophageal echocardiogram illustrating the 1.5 $\times$ 0.8 cm mitral posteromedial papillary vegetation (V) in transgastric short axis (left) and esophageal two-chamber views (right). Posteromedial papillary muscle (PM), anterolateral papillary muscle (AL), mitral valve (MV), and left ventricular outflow tract (LVOT).

revealed a 15 × 8 mm posteromedial mitral papillary muscle vegetation (Figure 1) with mild mitral regurgitation and normal biventricular function. Ultrasound of the limb was consistent with gastrocnemius pyomyositis with no evidence of DVT. The patient soon developed bilateral wrist and ankle pain with swelling and erythema and was taken to the operating room for surgical exploration. Bilateral septic arthritis of the wrists and ankles was confirmed and a large gastrocnemius abscess was found, all culturing MRSA. Intraoperatively, the patient became profoundly hypotensive, requiring vasopressor support and admission to intensive care for septic shock. Seven days after debridement of her wrists and lower limbs, the patient complained of increasing right arm paresthesia without significant disruption to motor function. A magnetic resonance imaging scan of the brain revealed multiple left-sided mycotic aneurysms with vasogenic edema and associated cerebritis consistent with watershed emboli (Figure 2). Eight weeks of i.v. vancomycin 15 mg/kg b.i.d was completed, followed by 4 weeks of oral sulfamethoxazole/trimethoprim 800/160 mg b.i.d, with resolution of the intracranial and endocardial lesions and no recurrence of the septic joints. The patient was discharged after a 60-day hospital admission and she remained well at 18-month follow-up.

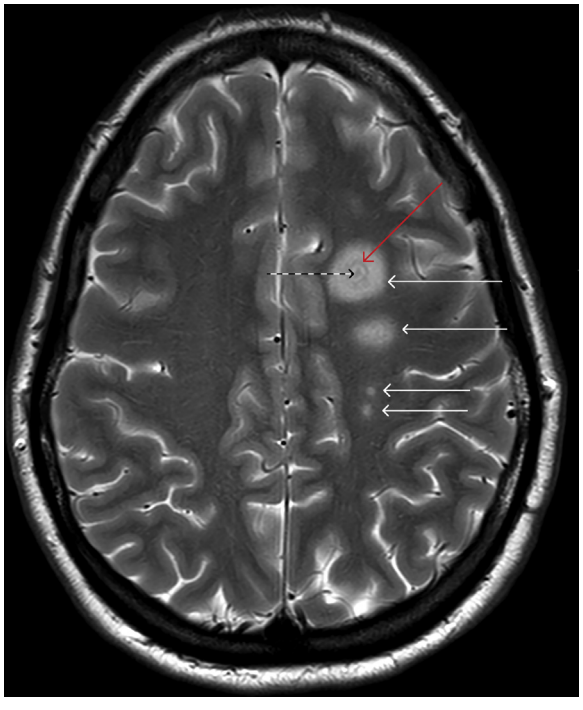

Figure 2. Magnetic resonance imaging with gadolinium enhancement revealing multiple left-sided septic emboli with associated vasogenic edema (white arrows). The largest lesion (dashed arrow) has surrounding cerebritis (red arrow).

DISCUSSION

Emergency physicians often care for people who inject drugs, as they often present to the ED with complex medical and psychosocial sequelae of IDU, such as infection, blood-borne viruses, psychosis, and overdose. Most patients who present with suspected IE have systemic signs of infection or sepsis, evidence of cardiorespiratory failure, or signs of metastatic infection or emboli (4). Fever is common (approximately 90%) and a murmur is present in a majority of patients (85%), with the pathognomonic features of Osler's nodes and Janeway lesions being specific but rare findings (4). Interestingly, our patient was completely afebrile for the duration of her ED admission, potentially due to prior antipyretics and without any cardiorespiratory signs or symptoms to suggest IE. Her presenting symptom was suggestive of DVT, rather than an embolic complication of sustained bacteremia from an endovascular source. Isolated mitral posteromedial papillary IE is rare, with seven cases reported in the literature, six of which were associated with acute papillary muscle rupture, severe mitral regurgitation, and combined septic/cardiogenic shock syndromes (8). Mitral papillary muscle endocarditis has been suggested to be highly associated with embolic phenomena, which correlates with the extensive multisite involvement of her infection, including intracranial lesions. Given that most reported cases of posteromedial papillary IE are associated with surgical repair, our case also suggests that with early, effective antimicrobial therapy, a potentially destructive endocardial lesion can be managed with medical therapy alone.

WHY SHOULD AN EMERGENCY PHYSICIAN BE AWARE OF THIS?

The incidence of IDU is increasing and these patients are at risk of invasive infections with multi-resistant organisms. The emergency physician is most often responsible for the initial workup and treatment of patients with suspected infective endocarditis, with timely collection of blood cultures, resuscitation for severe sepsis, and appropriate antibiotics being essential interventions. Isolated mitral posteromedial papillary endocarditis is a rare entity and highlights that even without fever, murmurs, or constitutional symptoms, severe multisystem infections from endocarditis can occur. It is essential that risk factors for endovascular infection, such as IDU, be elicited so that early diagnostic and therapeutic interventions can be commenced prior to the onset of severe septic or cardiogenic complications.

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