Clinical Image

Infective endocarditis as a rare cause for acute limb ischemia

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INTRODUCTION

Infective endocarditis (IE) occurs at a rate of approximately 1–7/100 000 people per year, and has a high morbidity and mortality despite advances in antibiotic and surgical treatments.^[1,2] Prosthetic valve endocarditis (PVE), in particular, remains an infrequent but serious complication of cardiac valvular replacement.^[3] Systemic embolism occurs in 22%–50% of IE patients; emboli may involve major arteries, mostly affecting the central nervous system as well as other organs.^[4] However, peripheral arterial emboli that result from bacterial endocarditis may be silent or catastrophic.^[5]

The present report presents an unusual case of PVE due to *Staphylococcus epidermidis* causing peripheral arterial embolism and acute lower limb ischemia. Proper emergency management is discussed and conclusions are made regarding indications of conservative and invasive treatment.

CASE

An 80-year-old male patient was brought to the emergency department because of acute pain in the left lower extremity during the last three hours as well as fever during the last week. Paresis, paleness and pulseless of the left lower extremity indicated acute limb ischemia. The extremity of the patient showed a decreased temperature, although the patient's core temperature was 37.5 °C and no other symptoms were present. Patient's medical history revealed arterial hypertension and a mitral valve replacement with a non-metallic prosthetic valve. The patient was under per os warfarin therapy and anti-hypertensive treatment.

Clinically, auscultation and palpation of the abdomen

were unremarkable. Thorax imaging revealed no typical picture of a lower respiratory tract infection. Laboratory investigations showed significant leucocytosis (white blood cells 31 200/ μ L; neutrophils 91.8%, hematocrits 37.4%, hemoglobin level 12.5 g/dL, platelets 80 000/ μ L) and deteriorated renal function (glucose 206 mg/dL, urea 134 mg/dL, creatinin 2.09 mg/dL, K⁺ 3.8 mmol/L, Na⁺ 139 mmol/L, SGOT 52 IU/L, SGPT 68 IU/L, LDH 447 IU/L, amylase 63 IU/L, and cardiac Troponin-I 0.48 ng/mL). Finally, international normalized ratio (INR) levels were sub-therapeutic (INR=1.5).

Due to ischemia of the left lower extremity, the patient underwent an emergency thrombembolectomy. During surgery, emboli were removed to be examined histologically. Postoperatively, there were palpable pulses and renal function was improved. However, inflammatory markers (WBC count, CRP) remained high during the first postoperative days. Blood cultures were collected as well. After surgery, the patient continued to receive empirical antibiotic therapy (ciprofloxacin 400 mg $\times$ 2, teicoplanin 400 mg $\times$ 2) and anti-coagulant treatment (enoxaparin 80 $\times$ 2).

Ultrasound examination of the abdomen was unremarkable. Urine collection did not show any signs of infection. However, cultures of blood and emboli were positive for *Staphylococcus epidermidis*, indicating possibly endocarditis as a source of peripheral emboli. Transthoracic echocardiography (TTE) indicated arrhythmia, atrial dilatation, and a non-metallic artificial mitral valve without signs of endocarditis. This examination showed severe tricuspid valve regurgitation. Transesophageal echocardiography (TEE) showed subtle stenosis of the prosthetic valve and suspicious tissues for

Figure 1. Transesophageal echocardiography (TEE) showing the needle-sized vegetations on the prosthetic mitral valve (arrow).

vegetations (Figure 1).

Based on anti-biographic and ultrasound findings, intravenous antibiotic treatment was modified (oxacillin 2 g×6, rifampin 300 mg×2, and gentamicin 80 mg×1). Inflammatory markers were normalized in the following days, and the patient remained afebrile. The triple antibiotic regimen was continued for 4 weeks although both oxacillin and rifampin were given for two more weeks until discharge. The patient was asymptomatic at discharge. After a 6-month follow-up, he did not present fever or other symptoms.

DISCUSSION

In our patient, PVE was caused by an uncommon pathogen leading to ischemia of the left lower extremity. The patient was treated surgically for peripheral arterial thrombo-embolism and conservatively for cardiac valve endocarditis with satisfactory results.

There were no typical symptoms in the patient but acute ischemia of the left lower extremity. In general, such patients present with fever, often associated with systemic symptoms of chills, poor appetite and weight loss. Heart murmurs are found in 85% of the patients and new murmurs in 48%.^[6] Laboratory signs of infection, such as elevated C-reactive protein or erythrocyte sedimentation rate, leucocytosis, anemia and microscopic hematuria, may be present in patients with IE but they are not specific.^[6] In addition, vascular complications of IE are frequently seen.^[7] Patients with endocarditis associated with peripheral embolism including those with cerebral infarctions,^[8,9] myocardial infarction,^[10] and pulmonary embolization^[11] have been reported. However, patients with thrombo-embolism of the arteries of the extremities are unusual, with most studies reporting an incidence of

4%–5% in patients with native valve endocarditis.^[12,13]

The pathogen in the present patient was *Staphylococcus epidermidis*. Coagulase-negative staphylococci are a frequent cause of PVE, although native valve endocarditis caused by such pathogens is not common.^[14] However, *Staphylococcus aureus* causes endocarditis in patients with prosthetic valves more frequently than other staphylococcal species.^[15] Valve replacement is considered to be a risk factor for infective endocarditis.^[6]

As far as the diagnostic modalities are concerned, TTE was not diagnostic in our patient, although TEE confirmed the final diagnosis. According to the recent guidelines, TTE should be the initial investigation in patients with IE (level of evidence C). However, the sensitivity of TTE ranges from 70% to 80% and that of TEE from 90% to 100%.^[16–18] Echocardiographic findings are major criteria in the diagnosis of IE, and may include the presence of a vegetation, abscess, new dehiscence of a prosthetic valve and newly noted valvular regurgitation. Our case showed small, needle head-like vegetations on the prosthetic valve that caused peripheral thrombo-embolism. However, the main risk factors for peripheral embolism are large floppy vegetations in the left heart on echocardiography; and 2 to 3 weeks from onset of endocarditis are the peak time for embolic risk.^[5] The risk of embolism seems to increase with increased size of vegetation, and this is particularly significant both in mitral and aortic endocarditis and staphylococcal endocarditis.^[19,20]

The general approach to the treatment of IE is initial clinical stabilization, early acquisition of blood cultures, and definitive medical and/or surgical treatment.^[3] Antibiotic treatment of IE depends on whether the involved valve is native or prosthetic, as well as on the causative microorganism and its antibiotic susceptibilities. After definite diagnosis of endocarditis in our patient, the empirical antibiotic treatment was substituted by oxacillin, rifampin and gentamicin, based on blood cultures. The guidelines recommend anti-staphylococcal penicillin for methicillin-susceptible staphylococci (2 g every 6 hours, increasing to 2 g every 4 hours in patients weighing over 85 kg; level of evidence A).^[1] However, the initiation of gentamicin is not supported as a first-line treatment for patients with native valve staphylococcal IE (level of evidence A).^[1]

Finally, surgery is indicated for most patients with PVE, *Staphylococcus aureus* endocarditis, fungal endocarditis, and endocarditis associated with large vegetations (≥ 10 mm).^[1] An accepted approach is to intervene only if two episodes of peripheral embolism

occur.^[5] Therefore, the small-size vegetations in our patient, the first episode of IE, and the immediate response to antibiotic treatment were the main motivations to follow a conservative management. Another study^[13] suggested valve replacement in patients with multiple or recurrent embolic events. Early operation may be recommended for patients with >15 mm vegetations and high mobility, irrespective of the degree of valve destruction, heart failure and response to antibiotic therapy.^[20] Accurate assessment of outcomes in PVE patients requires a long-term follow-up at least 6 months after diagnosis.^[21]

In conclusion, PVE could cause peripheral thromboembolism in patients under subtherapeutic anticoagulative treatment. After primary surgical management of acute peripheral ischemia, conservative treatment of endocarditis could lead to satisfactory results in selected patients. Transesophageal echocardiography should verify the diagnosis in suspicious patients.

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Conflicts of interest: The authors declare there is no competing interest related to the study, authors, other individuals or organizations.

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