Multiple peripheral pneumococcal mycotic aneurysms without aortic involvement: A unique case confirmed with the novel use of a molecular diagnostic technique

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Mycotic aneurysms confer a high morbidity and mortality. *Streptococcus pneumoniae* aneurysms usually affect the aorta and are rare, although bacterial cultures from aneurysm tissue may be difficult following prior antimicrobial therapy. We report a unique case of mycotic femoral and popliteal artery aneurysms following pneumococcal pneumonia and meningitis, which were managed by resection, revascularization with autologous vein, and intravenous benzylpenicillin. Although blood and aneurysm sac cultures were negative, arterial wall *S pneumoniae* DNA was detected by polymerase chain reaction (PCR). Appropriate molecular diagnostic techniques can facilitate diagnosis and direct antimicrobial therapy; an important consideration with increasing antimicrobial resistance. (J Vasc Surg 2007;45:1253-5.)

Mycotic aneurysms account for 1% to 3% of aneurysms.[1] They are defined as aneurysms resulting from, or secondarily infected by, bacteria seeding from a distant site.[2] Diagnosis depends upon detection of bacteria within aneurysm tissue. However, culture of aneurysm tissue may be difficult,[1-6] particularly following antibiotic therapy. Common pathogens include *Salmonella spp*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Escherichia coli.*[7,8] In the preantibiotic era, >80% of mycotic aneurysms were secondary to bacterial endocarditis,[8] the majority caused by β-*haemolytic streptococci*, *Haemophilus influenzae*, and *Streptococcus pneumoniae.*[7]

S pneumoniae accounted for approximately 10% of endocarditis episodes pre-1945, but it is now responsible for <5% of episodes.[9] Thus, pneumococcal mycotic aneurysms are rare. The majority are aortic[1,10-12] although isolated reports of coexistent peripheral aneurysms have been published.[3,13,14] This report describes a unique case of mycotic femoral and popliteal artery aneurysms without aortic involvement following pneumococcal pneumonia and meningitis. The novel use of a technique to identify the causative organism overcomes difficulties encountered following preoperative antimicrobial therapy.

CASE REPORT

A 72-year-old male was referred with bilateral calf claudication. Duplex ultrasonography revealed left common femoral (CFA) and popliteal artery aneurysms of 2.2 and 2.3 cm diameter, respectively. There was diffuse stenotic disease in the left superficial femoral artery (SFA) and a 2.2 cm right popliteal aneurysm. Magnetic resonance angiography confirmed normal calf vessels bilaterally. The patient was listed for bilateral femoro-popliteal bypass.

Three months later, the patient was admitted to another institution with left groin and popliteal fossa pain. Ultrasound examination excluded DVT and aneurysm size was unchanged. After 24 hours, the patient became less responsive (Glasgow Coma Score of 10/15) developing a fever (39.3°C) with signs of right sided pneumonia. The white cell count (WCC) was 22.44 × 10^9/L with a neutrophilia of 21.08 × 10^9 /L (normal 4-11 × 10^9/L, neutrophils 40% to 75%). Ventilation was required for progressive respiratory failure. Blood cultures grew penicillin-susceptible *S pneumoniae*, and CSF gram stain revealed gram positive cocci. CSF pneumococcal polymerase chain reaction (PCR)[15] was positive. A 2-week course of benzylpenicillin (1.2 g qds) was administered, and the patient discharged after 26 days.

Eleven days later, emergency admission to the vascular surgery department was required for left leg pain and tender left femoral and popliteal aneurysms. An ultrasound scan showed these now measured 4.2 cm and 5.5 cm, respectively. Although serial blood cultures and serum PCR were negative, a diagnosis of pneumococcal mycotic aneurysms was made and intravenous benzylpenicillin 1.2 g 6-hourly recommenced. A Technicium-99 radio-labeled WBC scan (Ceretec, GE Healthcare, Worldwide) revealed increased uptake confined to the left hip and left popliteal fossa. (Fig 1). Transthoracic echocardiogram showed no evidence of bacterial endocarditis.

At operation a 4.5 cm femoral aneurysm (Fig 2, *a*) and a contained popliteal artery aneurysm rupture (Fig 2, *b*) were resected completely, and an anatomical in-situ below knee femoro-popliteal reversed vein graft performed. The excised aneurysms were sent immediately to the microbiology department in a sterile container for urgent gram stain and culture. Tissue was also stored at −4°C until PCR was performed. Posterior compartment fas-

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Competition of interest: none.

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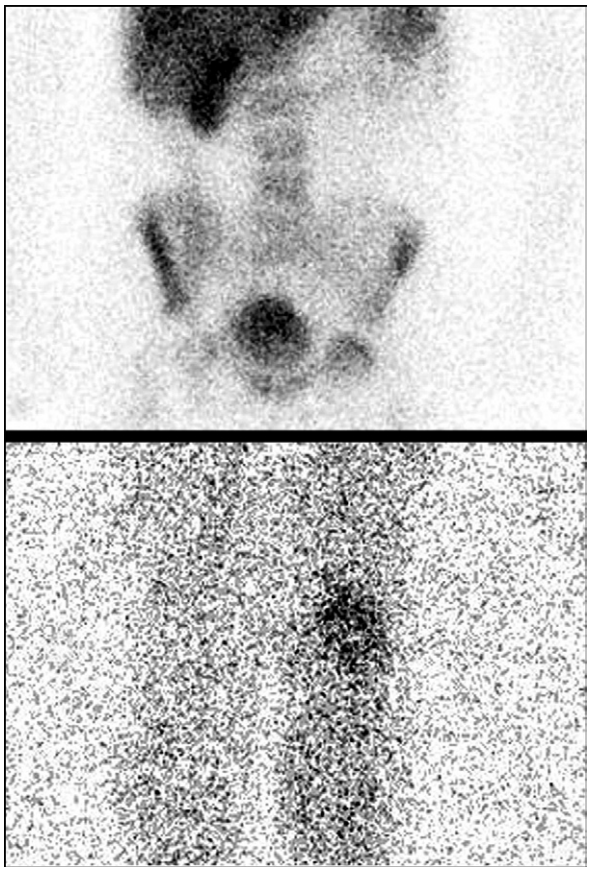

Fig 1. Technicium-99 radiolabelled white cell scan: increased uptake over left hip (above) and left popliteal fossa (below).

ciotomies were undertaken as popliteal aneurysm rupture led to edema and bulging of this compartment.

Aneurysm histology showed atheromatous disease with inflammatory changes but revealed no microorganisms. Aneurysm sac cultures were negative, but pneumococcal PCR[15] was positive for both sites. Intravenous benzylpenicillin was continued for 4 weeks. At the 6-month follow-up, the patient was well and graft patent.

DISCUSSION

In 1885, Sir William Osler described "mycotic aneurysms" secondary to bacterial endocarditis.[16] The postantibiotic era has seen marked decline in their prevalence and pneumococcal aneurysms are now rare. Since 1945, only 57 cases have been documented in the English speaking literature,[5,6,10-12,17] all affecting the abdominal or thoracic aorta. Two cases of peripheral aneurysms are described in association with aortic involvment.[1,3] Peripheral mycotic pneumococcal aneurysms without aortic involvement have not previously been reported in the English literature. It is likely that these occurred following bacterial seeding of thrombus lining the atherosclerotic aneurysms which predated the *S pneumoniae* bacteraemia.

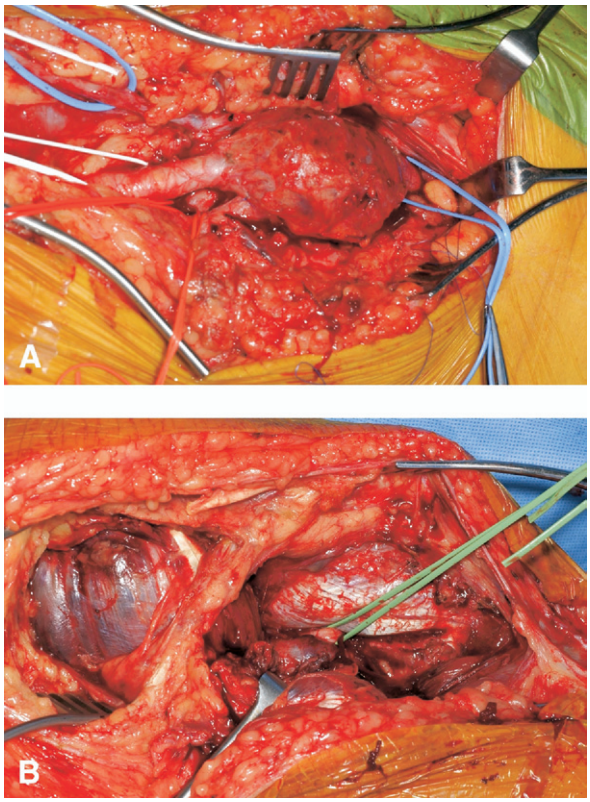

Fig 2. A, Mycotic femoral artery aneurysm. **B**, Ruptured mycotic popliteal artery aneurysm.

Although preoperative serial blood cultures and serum pneumococcal PCR were negative, a low grade pyrexia, elevated C-reactive protein, and a positive radio-labeled WCC scan suggested mycotic aneurysms. Nevertheless, confirmation of the diagnosis is normally dependent upon culture of organisms from aneurysm tissue.[1] This may prove difficult[1,3-6] particularly with prior antibiotic therapy. Indeed, sac cultures were negative in 36/57 (63%) of previously reported cases, as in this patient. For *S pneumoniae*, recovery in culture appears to be influenced by pretreatment with antimicrobials more frequently than for other pathogens, eg, *Staphylococcus aureus*. Further, it is not uncommon for CSF PCR to be positive for *S pneumoniae* but with negative cultures. No evidence exists suggesting correlation with organism virulence and clinical severity of illness. The novel application of pneumococcal-specific PCR in this patient[15] demonstrated presence of pneumococcus in both aneurysm sacs. This is the first time this technique has been employed to confirm the diagnosis of a mycotic aneurysm.

Given that blood and tissue cultures are frequently negative in patients with mycotic aneurysms, use of molecular diagnostic techniques on aneurysm tissue may have an important role in the future. Polymerase chain reaction (PCR) is an in vitro technique for the replication of DNA.[18] Specific regions of DNA can be amplified using this tech-

nique. PCR is commonly used to identify infectious diseases eg, CSF in meningitis. Briefly, it involves denaturing DNA into single strands and attachment of primers to these strands; the enzyme Taq polymerase then catalyses synthesis of new strands on this template. This process continues allowing increased number of fragments which are subject to molecular analysis. This occurs in a thermocycler to alter temperature and allow denaturing and synthesis of DNA.

Pneumococcal PCR was used in this case due to strong clinical suspicion that *S pneumoniae* was the causative organism. In other settings, a "broad range" or 16S ribosomal RNA gene PCR could be employed, although the diagnostic value in patients where there is suspicion of a mycotic aneurysm requires further evaluation. However, positive results have been reported in patients with vascular graft infection,[19] and selective use of PCR in some aneurysms may be justified. Confirmation of microbiological diagnosis, despite not providing information on antibiotic susceptibility, should allow more specific antimicrobial therapy. This confers advantages over broad spectrum regimes in terms of efficacy, lower side effect profile, and cost.

Mycotic aneurysms have a high morbidity and mortality due to enhanced risk of rupture, sepsis, and subsequent prosthetic graft infection.[1,4,17] Early diagnosis is vital enabling appropriate, and timely surgical and antimicrobial therapy. This case highlights the need for vigilance to detect mycotic seeding of pre-existing aneurysms in patients developing bacteraemia or distant septic focus. Important signs of this complication include rapid aneurysm expansion, coexistent sepsis, and peri-aneurysmal inflammatory change on CT. [7,12] Earlier diagnosis in this patient may have prevented popliteal aneurysm rupture and morbidity associated with fasciotomies.

Optimal surgical management of mycotic aneurysms includes debridement of infected tissue and revascularization using an autologous vein graft. The duration of postoperative antibiotic therapy remains contentious due to lack of good data. Although most authors recommend 4 to 8 weeks of therapy, some advocate lifelong administration.[1,3]

In summary, this report describes a unique case of peripheral pneumococcal mycotic aneurysms without aortic involvement. Further, the novel use of a molecular biological technique (PCR) allowed confirmation of the diagnosis and guided antimicrobial therapy, important in an era of increasing antimicrobial resistance.[20]

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