CASE REPORT

Mycotic pseudoaneurysm by vancomycin-intermediate *Staphylococcus aureus*: a rare cause of persistent bacteraemia

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SUMMARY

Pseudoaneurysms are vessel wall ruptures, that are often mistaken for deep vein thrombosis (DVT). A middle-aged man presented with right leg pain, swelling and erythema. His history was significant for persistent *Staphylococcus aureus* bacteraemia. Ultrasound revealed subacute DVT and laboratory parameters were suggestive of sepsis. He was started on intravenous heparin and antimicrobials. Owing to persistent anaemia despite blood transfusion, MRI of the right thigh was obtained. It revealed a 13×17 cm superficial femoral artery infected mycotic pseudoaneurysm (MPA) with a fresh haematoma. The patient underwent arterial ligation and extensive debridement. Intraoperative cultures revealed daptomycin-resistant vancomycin-intermediate *S. aureus* (VISA) and he was managed with 6 weeks of intravenous ceftaroline. MPAs are most common in the femoral artery and form <1% of aneurysms. Therapy involves surgical debridement and prolonged antimicrobials. VISA causing MPA is associated with worse outcomes. We report the first time use of ceftaroline in the management of a VISA MPA.

BACKGROUND

False aneurysm or pseudoaneurysm is a localised dilation of an artery with contained rupture through the layers of the vessel wall, characterised by persistent flow outside the vessel, unlike a haematoma which represents clotted blood.^{1 2} Multiple reports document a popliteal artery pseudoaneurysm being mistaken for an acute deep vein thrombosis (DVT).¹ We report a case of a superficial femoral artery (SFA) pseudoaneurysm superinfected with vancomycin-intermediate *Staphylococcus aureus* (VISA) mistakenly managed with anticoagulation, leading to potentially avoidable consequences.

CASE PRESENTATION

A 52-year-old African-American man presented with a 10/10 constant right lower extremity throbbing pain of 2 days duration. This was associated with a swelling in the medial aspect of the thigh, fever, night sweats and weight loss >20 pounds over the past 4 months. His medical history was significant for diabetes mellitus type II, hyperlipidaemia, coronary artery disease with prior surgical revascularisation and ischaemic cardiomyopathy requiring an implantable cardioverter-defibrillator (ICD). He had a history of recurrent DVT of his lower extremities that

was managed with an inferior vena caval (IVC) filter. Owing to poorly controlled diabetes, the patient experienced recurrent diabetic foot infections, necessitating multiple hospital admissions and prolonged antimicrobial therapy. Four months prior to this hospital visit, he received a right leg below-knee amputation due to refractory methicillin-resistant *S. aureus* (MRSA) osteomyelitis with subsequent bacteraemia. Two months prior to this presentation, he was evaluated for recurrent MRSA bacteraemia despite removal of osteomyelitic focus. Owing to complicated *S. aureus* infection, his ICD leads were removed without reimplantation. Lead tip cultures were negative for any bacterial growth. His blood cultures showed MRSA with daptomycin resistance (minimum inhibitory concentration (MIC) 2.0 µg/mL) and vancomycin sensitivity (MIC 2.0 µg/mL). Additionally, the MRSA was sensitive to clindamycin, minocycline and trimethoprim-sulfamethoxazole. He was treated subsequently with vancomycin for a period of 6 weeks. His vancomycin trough levels were aimed for 15–20 µg/mL to help with better penetrance due to moderate elevation in vancomycin MIC. Personal-social history was unrevealing and family history was not significant for any immune deficiency or vascular diseases.

Physical examination revealed a moderately-nourished man, afebrile with stable haemodynamics. Cardiorespiratory examination was unremarkable and abdominal examination revealed stable bowel sounds with no palpable organomegaly. The right lower stump was tender to palpation on the medial aspect with erythema and warmth. The right thigh was 5 cm greater in diameter than the left.

INVESTIGATIONS

Significant laboratory parameters included neutrophilic-predominant leucocytosis of 21 100/mm³, anaemia with haemoglobin 5.7 g/dL (baseline 9.0–10.5 g/dL), thrombocytosis 530 000/mm³, elevated erythrocyte sedimentation rate >120 mm/h and elevated C reactive protein 265 mg/L. Lower extremity venous Doppler studies revealed subacute to chronic DVT of the right SFA with vein dilation and flow at the mid-thigh level.

TREATMENT

The patient was admitted for management of DVT and sepsis with the suspected source being the IVC filter. After obtaining peripheral blood cultures, the

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patient was started on broad-spectrum antimicrobial coverage with vancomycin and piperacillin/tazobactam. He was transfused with packed red blood cells for his acute anaemia and started on intravenous heparin for his DVT. The patient continued to be persistently anaemic despite adequate fluid and blood product resuscitation. MRI of the right lower extremity (obtained to evaluate for osteomyelitis) revealed a large multi-lobular collection within the hamstring musculature likely representing an abscess formation with large mycotic pseudoaneurysm (MPA). In addition to the MPA, a fresh contained hematoma with clearly distinct borders was noted. The lesion was 13×17 cm with the pseudoaneurysmal portion measuring 7 cm (figure 1). The patient's intravenous heparin was stopped and he underwent a right femoral artery cut down, right lower extremity intraoperative angiogram with exploration and resection of the infected haematoma. The aneurysmal sac contained an old consolidated haematoma with calcification clearly demarcated from the infected haematoma and necrotic tissue. His right SFA pseudoaneurysm was ligated and the surrounding skin, subcutaneous tissue, muscle and fascia were extensively debrided. He underwent two repeat debridement procedures, SFA and femoral artery ligation procedures and wound-vac placement with stump preservation. Owing to extensive blood loss during the surgery, the patient had to receive multiple blood transfusions. Histopathological examination of the surgical specimen showed arterial segments with destruction of the normal arterial wall and replacement with fibrous tissue, organised thrombus (figure 2D) and necrosis (figure 2C). Remnants of tunica media intermixed with a variable degree of myxoid degeneration and disorganised

elastic fibres were noted (figure 2A). The tunica adventitia was thickened (figure 2B), and focal separation in the necrotic tissue was noted (Arrow in figure 2F). Transmural acute and chronic inflammation was present as an appropriate response to the bacterial infection. The inflammation was located predominantly in the tunica adventitia and characterised by neutrophilic infiltration and intramural abscess formation (figure 2E). These histological findings were consistent with MPA. Cultures from the surgical specimen showed *S. aureus* with the following MIC—vancomycin 4.0 µg/mL, daptomycin 4.0 µg/mL and ceftaroline 0.38 µg/mL—suggestive of *S. aureus* with resistance to daptomycin (increase in MIC from 2.0 to 4.0 µg/mL) and intermediate resistance to vancomycin (VISA). Additionally, the organism was sensitive to clindamycin and trimethoprim/sulfamethoxazole with continued resistance to rifampicin. Daptomycin is the approved agent for management of VISA, but we were unable to use it due to exceptionally high daptomycin resistance on both the prior and current visit. Despite being approved for use only in pneumonia and skin and soft tissue infection, ceftaroline was used in our patient with good results.

OUTCOME AND FOLLOW-UP

During the 6 weeks of intravenous ceftaroline therapy, the patient showed steady improvement in his clinical course. He was seen in the outpatient centre after completion of his ceftaroline therapy with complete clearance of bacteraemia with normal inflammatory markers and leucocyte counts. At the conclusion of the case, we hypothesise that this infected pseudoaneurysm could have potentially served as a nidus for the persistent VISA bacteraemia. Lack of drainage of the abscess cavity resulted in inadequate penetrance of the antimicrobials with subsequent emergence of the virulent and resistant *S. aureus*.

DISCUSSION

Pseudoaneurysms are aetiologically classified as iatrogenic, traumatic, anastomotic or infected, with arterial catheterisation contributing to the largest incidence.^{2 3} The term mycotic aneurysm was first used by Sir William Osler in 1885 to describe a 'fresh fungal vegetation' and has since been used to describe infected non-syphilitic arterial aneurysms and pseudoaneurysms, not necessarily fungal.^{4 5} MPAs constitute <1% of all aneurysms, and are characterised anatomically by a sac or cavity and a neck communicating with the arterial lumen.^{2 6} MPAs have been reported from various vascular territories, but the femoral artery is the most common followed by the abdominal aorta.⁴⁻⁶ Historically, infective endocarditis served as the most common aetiological basis; however, arterial catheterisation forms the largest share in modern practice.²⁻⁴ In addition to groin access for catheterisation, frequent use of femoral veins for intravenous drug abuse with erroneous arterial puncture increased the changes of femoral artery involvement.² Peripheral MPAs are being more commonly reported due to the use of peripheral catheters for drug administration and haemodynamic monitoring.⁴ They frequently present as swelling, pain and erythema and require a high index of suspicion for diagnosis. Most cases of MPA are associated with a pulsatile swelling, and can be accompanied by signs of distal ischaemia.⁷ Delayed diagnosis is associated with higher mortality and morbidity with complications such as distal ischaemia, acute haemorrhage, nerve palsy and rarely super-infection.^{3 8} They present a significant diagnostic challenge, especially if present in a setting not associated with recent arterial manipulation. They are frequently

Figure 1 MRI of the right thigh showing superficial femoral artery dilatation with two distinct layers of mycotic pseudoaneurysm (outer) and fresh hematoma (inner).

Figure 2 Histopathological examination of the pseudoaneurysmal specimen demonstrating necrosis, fibrosis and abscess formation (details in text).

misdiagnosed as DVTs, thereby placing the patient at a high risk of rupture and haemorrhage.^{3 6}

Laboratory diagnosis involves assessing blood cultures in all suspected cases of MPA. They are positive in 50–85% of the cases and up to 76% of the aneurysmal tissue. *S. aureus* is the most commonly reported pathogen, forming nearly 28% of all MPAs.^{4 9} Imaging modalities employed frequently involve ultrasound with venous and/or arterial Doppler, CT scan, MRI and arteriogram.^{3 7 10 11} Ultrasound with/without Doppler might not accurately define pathology and vessel compromise. Ultrasound requires visualisation of a neck or a hole feeding the false aneurysm, which requires operator expertise.^{2 3} Improper use can result in a misdiagnosis and catastrophic haemorrhage from subsequent anticoagulation for suspected DVT.¹ CT angiography is increasingly being advocated to evaluate these lesions.^{7 10–12} Arteriography is the gold standard and helps assess the flow, extent, variants and planned surgical approach.⁷

Therapy invariably involves surgical debridement of the arterial wall with/without the use of endovascular grafts for revision.^{2 5 7} Graft placement is often complicated by graft infection and endovascular coiling increases the likelihood for necrosis and abscess formation.⁶ There is no role for conservative therapy without removal of the infective focus.^{7 10} Additionally, 4–8 weeks of antimicrobial therapy is advocated with de-escalation of therapy as per sensitivity patterns.⁵

Vancomycin resistance in the *S. aureus* population has led to the evolution of varying degrees of vancomycin resistance categorised as heterogeneous VISA (hVISA) and VISA.¹³ VISA is defined as *S. aureus* with vancomycin MIC of 4–8 µg/mL. These strains typically have a slower growth rate, thickened cell wall and reduced levels of penicillin-binding protein 4 (PBP4). The recent literature has detailed the role of hVISA as a cause

for bacteraemia with very limited literature on the role of VISA. hVISA bacteraemia is associated with prolonged bacteraemia duration, greater rates of complications, rifampin resistance and increased treatment failure with increasing MIC, but without any mortality difference as compared to MRSA. First reported in 2008, hVISA is a rare cause for MPAs.^{14–16} The Infectious Diseases Society of America (IDSA) 2011 guidelines advocate high-dose daptomycin in combination with a second agent for hVISA bacteraemia if the organism is daptomycin-susceptible; however, there is paucity of data on the effective management of VISA infections. Alternately, other agents such as quinupristin-dalfopristin, linezolid or telavancin can be used if it is daptomycin-resistant.¹⁷ Ceftaroline is a fifth-generation cephalosporin with unique action against MRSA and VISA by virtue

Learning points

- ▶ Mycotic pseudoaneurysms (MPAs) frequently mimic deep vein thrombosis on ultrasonography making differentiation a challenging entity.
- ▶ Vancomycin-intermediate *Staphylococcus aureus* (VISA) is increasingly being reported as a causative organism in MPA, creating a therapeutic challenge due to antimicrobial resistance.
- ▶ Ceftaroline can be used to manage patients with methicillin-resistant *S. aureus* or VISA vascular infections, especially in cases of daptomycin-resistance.
- ▶ This is the first reported case of ceftaroline use for VISA MPA and can help generate a discussion on the use of ceftaroline for this indication.

of its ability to inhibit the biochemical activity of PBP2a more robustly than currently existing β -lactam antimicrobials.¹⁸ Ceftaroline is approved by IDSA for use in MRSA/VISA pneumonia and complicated skin infections.¹⁹ Despite an extensive search of the literature, we were unable to record any cases of MPA treated with ceftaroline, making this the first reported case. We believe this experience is potentially hypothesis generating and will need further evaluation in randomised controlled trials.

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Competing interests None.

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