CASE REPORT

Diagnostic approach in persistent *Staphylococcus aureus* bacteraemia

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SUMMARY

Staphylococcus aureus is the leading cause of bacteraemia and can lead to complicated infections that may be difficult to diagnose and hence lead to higher morbidity. Failure to identify such could lead to severe complications or relapsing bacteraemia due to inadequate treatment. The authors report a patient presenting with methicillin-resistant *S. aureus* (MRSA) bacteraemia and septic arthritis, who developed a complicated infection with multiple metastasis and persistent bacteraemia despite adequate treatment. A fluorodeoxyglucose (FDG)-positron emission tomography scan 2 weeks after the initial presentation identified a linear area of intense FDG uptake within the right upper extremity which raised suspicion for an infected thrombus within the right cephalic vein. Adequate treatment of the infected thrombus helped resolve the patient's persistent MRSA bacteraemia and complicated infection. This case highlights the importance of considering suppurative thrombophlebitis in the setting of persistent bacteraemia and metastatic infections due to MRSA.

BACKGROUND

Staphylococcus aureus is the leading organism detected in patients presenting with bacteraemia. *S. aureus* bacteraemia can lead to complicated infections that may be difficult to diagnose and hence lead to higher morbidity. Treatment failure defined as death within 30 days following treatment, persistent bacteraemia lasting for >10 days after initiation of appropriate therapy or recurrence of bacteraemia within 60 days of discontinuing therapy is fairly common, particularly in infections due to methicillin-resistant *S. aureus* (MRSA).¹ Metastatic seeding could occur within the first few days of hospitalisation although it could take few weeks before it gets diagnosed. Failure to identify such complications could lead to severe morbidity (paralysis) and mortality,² or relapsing bacteraemia due to inadequate treatment.³

CASE PRESENTATION

A 68-year-old man presented to the hospital with fever and swelling of the right knee for 2 days prior to presentation. The right knee was swollen, erythematous, with restricted and painful movements. The patient denied any trauma to his knee and described this as the first occurrence of these symptoms. The patient had a history of uncontrolled diabetes mellitus and had a recent hospitalisation a

month ago for a respiratory infection requiring 7 days of hospitalisation and intravenous antibiotics in a different city, details of which were not known.

The patient was a retired married man living in an urban inner city apartment. He denied illicit drug use ever in his life and denied recent alcohol intake and smoking.

On examination the patient was febrile (T=102.3 °F) and tachycardic (pulse=108 bpm) with stable blood pressure. On physical examination, the right knee was swollen, erythematous and range of movement was severely restricted due to pain. Remainder of the physical examination was well within normal limits.

INVESTIGATIONS

The patient had blood cultures positive for MRSA and arthrocentesis demonstrated purulent synovial fluid with gram stain and culture revealing infection with MRSA. The vancomycin minimum inhibitory concentration (MIC) testing performed using agar-gradient diffusion (E test) demonstrated a vancomycin MIC of 1 mcg/mL.

TREATMENT

The patient was started on intravenous vancomycin and underwent surgical debridement of the right knee. Blood cultures remained positive for MRSA, 72 hours after initiation of antibiotics and the patient remained febrile despite adequate vancomycin trough levels (15–20 mcg/mL). A transthoracic and transoesophageal echocardiogram did not demonstrate any valvular vegetation or dysfunction.

A few days later, the patient developed left shoulder monoarticular arthritis and investigations confirmed septic arthritis caused by MRSA. A day later, the patient had mild neck pain and MRI spine demonstrated an epidural abscess in the lower cervical spine. The patient underwent arthroscopic debridement of the left shoulder and decompression and debridement of the cervical epidural abscess. The patient became afebrile at this time, however continued to have positive blood cultures for MRSA with vancomycin MIC of 1 mcg/mL despite adequate vancomycin trough levels. Ten days after his initial presentation, the patient developed MRSA septic arthritis of his left knee, which was arthroscopically drained and debrided. The CT scan of the chest and abdomen demonstrated multiple peripheral subcentimetre lesions in bilateral lungs suggestive of septic emboli (figure 1); however, no focus of infection

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Figure 1 CT scan of the chest demonstrating multiple peripheral subcentimetre lesions in bilateral lungs suggestive of septic emboli.

was identified. There was no intravascular catheter or prosthesis which could explain his persistent bacteraemia. The patient at this stage had been hospitalised and on appropriate antibiotics for 14 days and been persistently bacteraemic with MRSA. A fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET) scan (figure 2) was performed at this stage to identify a source of infection.

OUTCOME AND FOLLOW-UP

The FDG-PET scan (figure 2) identified a linear area of intense FDG uptake (max standardised uptake value 20) within the right upper extremity which raised suspicion for an infected thrombus within the right cephalic vein. An echogram Doppler of the right upper extremity confirmed the presence of an acute occlusive thrombosis of the cephalic vein. Further questioning revealed that the patient was hospitalised a month prior to this admission at another hospital for a respiratory infection. During that hospitalisation, the patient had a peripherally inserted central catheter which had malfunctioned and removed 6 days after insertion. The patient never had any external signs which could have been picked up on examination at that site.

Antibiotics were continued and the patient was started on anticoagulation with low-molecular-weight heparin (enoxaparin subcutaneous injection 1 mg/kg/dose every 12 hours). Vascular surgery was involved and the plan was to consider thrombectomy or phlebectomy if the bacteraemia persisted. Over the next few days, the patient had negative blood cultures and no episodes of further septic emboli. The patient was treated with intravenous vancomycin for 6 weeks after his first negative blood culture and a 3-month course of anticoagulation with oral warfarin therapy (therapeutic international normalised ratio between 2 and 3) for his first documented thrombus.

DISCUSSION

Suppurative thrombophlebitis refers to the presence of an infected thrombus identified on radiographic methods in the presence of high-grade bacteraemia. Suppurative thrombophlebitis may

Figure 2 FDG-PET scan demonstrating a linear area of intense FDG uptake (max SUV 20) within the right upper extremity. FDG-PET, fluorodeoxyglucose positron emission tomography; SUV, standardised uptake value.

involve central or peripheral veins or arteries and should be suspected in patients with persistent bacteraemia after 72 hours of appropriate antimicrobial therapy, particularly in the setting of an intravascular catheter.⁴ Peripheral vein suppurative thrombophlebitis is mostly observed in the setting of peripherally inserted venous catheter or illicit intravenous drug use.⁴ *S. aureus* is the most common causative organism in cases of suppurative thrombophlebitis, as demonstrated in various case series.^{4,5}

Suppurative thrombophlebitis involves the formation of microabscess within the affected veins.⁶ Involved venous segments may serve as a source of persistent bacteraemia which may result in septic pulmonary emboli and other metastatic infections may complicate this condition.^{7,8} Because the infected

intravascular thrombus and intraluminal abscess may remain intact after catheter removal, the infection may manifest after catheter removal and the patient may remain febrile and bacteraemic for prolonged periods of time despite initiation of appropriate antimicrobial therapy. Few patients have physical examination signs suggestive of suppurative thrombophlebitis,⁹ hence use of radiographic methods should be considered early in these cases. Use of Doppler ultrasonography or venography could be employed looking for thrombus at suspected sites. Use of FDG-PET scan has been proposed in identifying cases of suppurative thrombophlebitis and has been shown to differentiate suppurative thrombophlebitis from cases of non-infected thrombus.¹⁰

The current clinical practice guidelines recommend a minimum of 3–4 weeks of antimicrobial therapy. Surgical resection of the vein is recommended for patients with purulent superficial veins, when the infection extends beyond the vessel wall, and in patients who experience failure on appropriate medical therapy. The role of anticoagulation in this setting is still unresolved.¹¹ Results of a systematic review suggest that the use of anticoagulants in combination with antibiotics is associated with

the relatively shorter time to defervescence and low mortality in patients with suppurative thrombophlebitis, and suggests early administration of anticoagulants in such cases.¹²

This case highlights the importance of considering suppurative thrombophlebitis in the setting of persistent bacteraemia, septic pulmonary emboli and metastatic infections, even when the physical examination fails to elicit signs of suppurative thrombophlebitis.

Contributors LS is solely responsible for this manuscript.

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Learning points

- ▶ Failure to identify such complications secondary to methicillin-resistant *Staphylococcus aureus* bacteraemia may lead to catastrophic complications or relapsing bacteraemia due to inadequate treatment.
- ▶ Suppurative thrombophlebitis refers to the presence of an infected thrombus identified on radiographic methods in the presence of high-grade bacteraemia.
- ▶ Suppurative thrombophlebitis may involve central or peripheral veins or arteries and should be suspected in patients with persistent bacteraemia after 72 hours of appropriate antimicrobial therapy, particularly in the setting of an intravascular catheter.
- ▶ Use of fluorodeoxyglucose positron emission tomography scan has been proposed in identifying cases of suppurative thrombophlebitis and has been shown to differentiate suppurative thrombophlebitis from cases of non-infected thrombus.

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