Ceftaroline in the treatment of concomitant methicillin-resistant and daptomycin-non-susceptible Staphylococcus aureus infective endocarditis and osteomyelitis: case report

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Sir,

A middle-aged male presented to the emergency department with fever and 1 week of sharp right hip pain worsening over the past 2 days. His past medical history included uncontrolled diabetes and chronic active hepatitis C. The patient also had a history of multiple methicillin-resistant Staphylococcus aureus (MRSA) infections, including bacteraemia 1 month prior, for which he was treated with vancomycin (MIC ≤ 0.5–1 mg/L).

Three sets of blood cultures were collected before the patient received a single dose of vancomycin and piperacillin/tazobactam. The blood Gram stain showed Gram-positive cocci. The infectious diseases team was consulted, and given recent vancomycin treatment and recurrent bacteraemia, we recommended high-dose daptomycin (8 mg/kg intravenously every 24 h). Dual therapy with rifampicin was considered, but due to limited in vivo data as well as concomitant hepatic dysfunction, we decided against it.1 Initial blood cultures grew MRSA (3/3 bottles) on hospital day 3, with susceptibility tests showing a daptomycin MIC of 0.38 mg/L (Etest; AB Biodisk, Solna, Sweden) and a vancomycin MIC of 1 mg/L by broth microdilution. Repeat blood cultures on day 4 (2/2 bottles) showed no growth.

On hospital day 2, a transoesophageal echocardiogram (TEE) demonstrated no evidence of vegetations. On day 3, a contrast CT of the hip showed bone and retroperitoneal abscesses along with evidence highly suggestive of osteomyelitis. An MRI was less conclusive about the presence of early osteomyelitis. The surgical team was consulted and recommended that the patient to undergo CT-guided drainage of the retroperitoneal abscess as opposed to any surgical treatment, citing difficult surgical access, a high-risk patient with comorbidities and likelihood of the abnormal synovium in radiographic studies being reactive synovitis as opposed to osteomyelitis and septic arthritis. Drainage proceeded on day 7, though there was continued debate about the diagnosis and need for surgical intervention.

References

The patient continued to have episodes of fever, which had been occurring since admission. On day 14, the patient developed leucocytosis and blood cultures were drawn, which grew MRSA. The MIC of vancomycin increased to 2 mg/L, with that of daptomycin remaining at 0.38 mg/L.

Since the patient continued to be symptomatic, irrigation and debridement was scheduled, but due to surgeon availability issues this was not performed until hospital day 19. A sample was obtained during the procedure and cultured, and on day 22, after >2 weeks of treatment with daptomycin, MRSA grew with a daptomycin MIC of 3 mg/L [daptomycin-non-susceptible S. aureus (DNSSA)]. The primary cause of the daptomycin failure was most likely a delay in incision and drainage of the abscesses. Experimental osteomyelitis models have shown selective resistance with daptomycin monotherapy,\(^5\) which possibly contributed to the resistance in this case. Daptomycin was discontinued and, unfortunately, vancomycin was restarted over the weekend.

After the patient became bacteraemic on day 14, we recommended a TEE, which was ordered but not performed until day 23. Lesions were found on the left coronary cusp (LCC) and the tricuspid valve, consistent with endocarditis. Vancomycin was discontinued, since current expert opinion states alternative antimicrobials should be considered when the vancomycin MIC is ≥2 mg/L, due to treatment failures.\(^3\)\(^,\)\(^4\) Considering this and the severity of infection in this patient, we turned to salvage therapy options and ceftaroline (600 mg intravenously every 12 h), which had an Etest MIC of 0.5 mg/L, was chosen.

Ceftaroline is a fifth-generation cephalosporin with activity against MRSA. Ceftaroline was chosen for a number of reasons. First, it is rapidly bactericidal. Ho et al.\(^5\) reported sterilization in 13 days in a case of endocarditis. Also, the incidence of thrombocytopenia with long-term use is low, which was particularly important since our patient had a history of thrombocytopenia secondary to hepatitis. Finally, a literature search revealed a series of case reports showing successful use of ceftaroline in the treatment of MRSA endocarditis\(^5\) and an experimental model demonstrating potential use in osteomyelitis.\(^6\)

Subsequent blood cultures drawn on days 29 and 32 were negative. On day 32, a repeat irrigation and debridement was performed. After 37 consecutive days of ceftaroline treatment, a TEE showed resolution of echodensities at the base of the tricuspid valve and a stable, fibronodular lesion on the LCC. Ceftaroline was continued for a total of 44 days, with no further episodes of bacteraemia, leucocytosis or fever, which completed his treatment. The patient was discharged home but was lost to follow-up.

This case report demonstrates the importance of surgery for the primary treatment of abscesses and osteomyelitis. A delay in surgical intervention was likely the cause of endocarditis and the development of daptomycin resistance in this patient. Elevated vancomycin MICs have been associated with increased daptomycin MICs, suggesting the possibility of cross-resistance.\(^7\)\(^,\)\(^8\) which might also have been seen in this case. Combined with proper surgical treatment, the efficacy and tolerability of ceftaroline for the treatment of concomitant methicillin-resistant and DNSSA endocarditis and osteomyelitis was demonstrated in this case.

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References

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Failure of 500 mg of ceftriaxone to eradicate pharyngeal gonorrhoea, Australia

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