CASE REPORT

High-dose daptomycin monotherapy cures *Staphylococcus epidermidis* 'endotipsitis' after failure of conventional therapy

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SUMMARY

A 67-year-old gentleman developed persistent *Staphylococcus epidermidis* bacteraemia following transjugular intrahepatic portal shunting. 'Endotipsitis' was diagnosed. Conventional therapy with a vancomycin infusion, amikacin and rifampicin failed after 17 days. He was cured with a 6-week course of high-dose (8 mg/kg) daptomycin monotherapy.

BACKGROUND

- ▶ Endotipsitis is an emerging prosthetic device-related infection in a particularly comorbid patient group where treatment toxicity is a major risk.
- ▶ This is the first reported case of endotipsitis due to a coagulase-negative *Staphylococcus* (CoNS), which is particularly difficult to treat in the setting, owing to its ability to form biofilm and to develop resistance to antibiotics.
- ▶ Cure with high-dose daptomycin monotherapy after failure of conventional therapy and the emergence of rifampicin resistance.

CASE PRESENTATION

A 67-year-old gentleman presented to his local hospital with a 2-day history of haematemesis and melaena. There was a history of significant alcohol consumption, but no previously recorded liver disease. After admission, his hepatic and renal function deteriorated and significant bleeding continued, resulting in his transfer to our hospital for insertion of a transjugular intrahepatic portal shunt (TIPS). At the time of the procedure he was receiving ceftriaxone, in accordance with our hospital's variceal bleeding prophylaxis policy. His clinical condition initially remained stable postprocedure on the adult intensive care unit. Central intravascular lines were removed, and intravenous access was maintained with a peripheral line. One week post-TIPS, he developed fever and *Staphylococcus epidermidis* grew in multiple blood cultures over 3 days. The organism was resistant to methicillin and gentamicin, but susceptible to amikacin and rifampicin, with a vancomycin minimum inhibitory concentration (MIC) of 3 mg/l. The isolate was indistinguishable by antibiogram and pulsed field gel electrophoresis (PFGE) to a *S epidermidis* cultured from a central venous catheter tip removed the day before the bacteraemia was first detected. Treatment with a vancomycin infusion, amikacin 7.5 mg/kg once daily (reduced dosing for

synergy) and rifampicin 300 mg orally twice daily was started. Vancomycin levels were monitored daily and kept in the range 15–25 mg/l. Transthoracic echocardiogram showed normal heart structure, with no evidence of endocarditis (on two occasions). An MRI angiography of his thoracic vasculature did not identify any thrombus. Imaging of the abdomen by CT did not identify any focus of infection, and specifically the liver parenchyma around the TIPS looked normal. No source for the on-going bacteraemia could be identified apart from the TIPS, and 'endotipsitis' was diagnosed.

Initially, the patient had a favourable clinical response to therapy with improvement in both hepatic and renal function. However, 17 days into treatment, fever returned and the patient became haemodynamically unstable. Blood cultures again grew *S epidermidis*. A peripherally inserted central venous catheter (PICC) inserted 2 days previously to facilitate a prolonged course of intravenous therapy was removed. A culture of the tip was sterile. Over the following 8 days *S epidermidis* grew from multiple sets of blood cultures. The isolates were indistinguishable by PFGE and antibiogram to the isolates cultured prior to vancomycin-based therapy, other than the development of rifampicin resistance. Daptomycin MIC was 0.5 mg/l. The therapy was switched to daptomycin, 8 mg/kg via a new peripheral line. He tolerated this very well, and his hepatic and renal functions normalised within 10 days. To assess muscle toxicity, creatine phosphokinase was monitored weekly but remained normal throughout. He was discharged home and completed 6 weeks of Daptomycin therapy via the outpatient antibiotic therapy service.

OUTCOME AND FOLLOW-UP

At follow-up 3 and 6 months after finishing the treatment, he remained well, with negative blood cultures on both occasions.

DISCUSSION

Infection of TIPS is being increasingly recognised, occurring in 1–7% of those undergoing the procedure.^{1–4} Endotipsitis carries a high mortality because the device cannot be removed once sited, and biofilm formation can lead to blockage of the TIPS. Portal hypertension in such patients can then only be managed by transplantation. Most TIPS infections are caused by Gram-positive organisms, with *Staphylococcus aureus* and *Enterococcus* spp predominating.³ Ours is the first case reported due to a CoNS, a particularly virulent organism in this

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setting owing to its ability to produce biofilm.⁵ Biofilm prevents killing by antibiotics and allows any resistance arising by mutation to spread efficiently at the site of infection.⁶ Placement of TIPS without antibiotic prophylaxis and duration of procedure are associated with endotipsitis.⁴ Our case was further complicated by breakthrough bacteraemia and failure of the conventional therapy. The patient was cured with high-dose daptomycin monotherapy. Daptomycin has some attractive in vitro properties in this setting. It has bactericidal activity against staphylococci, and is particularly active against organisms in biofilms.^{7 8} In vivo it is well tolerated by comorbid patients, and is non-inferior to vancomycin for the treatment of *S aureus* bacteraemia and right-sided endocarditis.⁹ It has proven useful for the treatment of prosthetic device-related endocarditis due to CoNS.^{5 10} Resistance to daptomycin can occur during therapy and lead to treatment failure.⁸ Strategies to reduce this risk include using daptomycin in high dose (8–10 mg/kg daily) or in combination with cotrimoxazole, rifampicin or linezolid.^{7 8 10–13}

Several important learning points emerge from our report. Endotipsitis is an emerging prosthetic device-related infection in a particularly comorbid patient group where treatment toxicity is a major risk. Ours is the first reported case due to a CoNS, which is particularly difficult to treat in the setting, owing to its ability to form biofilm and to develop resistance to antibiotics. The conventional therapy failed, yet despite this unpromising setting, high-dose daptomycin was well tolerated and led to cure. We believe the use of daptomycin in our patient was life saving.

Learning points

- ▶ Endotipsitis is an emerging prosthetic device-related infection in a particularly comorbid patient group where treatment toxicity is a major risk.
- ▶ This is the first reported case of endotipsitis due to a coagulase-negative *Staphylococcus*, which is particularly difficult to treat in the setting, owing to its ability to form biofilm and to develop resistance to antibiotics.
- ▶ Cure was achieved with high-dose daptomycin monotherapy without toxicity after failure of the conventional therapy and the emergence of rifampicin resistance.

Contributors All four authors were involved in the care of the patient, and this report was written up by JMC and reviewed by all authors. ICJWB was the lead Microbiology Consultant in this case during inpatient care and MS after patient's discharge from hospital.

Competing interests None.

Patient consent Obtained.

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