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Case Report

Recurrent Septic Arthritis and Osteomyelitis with *Enterococcus gallinarum* in a Child with Acute Lymphoblastic Leukaemia

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Abstract

Vancomycin-resistant enterococci (VRE) are important nosocomial pathogens with a unique pattern of antimicrobial susceptibility. VRE includes *Enterococcus gallinarum* has been implicated in different infections such as bacteremia and endocarditis. Bone and joint infections with enterococcal species are very rare and typically associated with prosthetic joints. We report a case of multifocal recurrent septic arthritis and native bone osteomyelitis due to *E. gallinarum* in a pediatric patient with acute lymphoblastic leukaemia (ALL).

Keywords: VRE; *E. gallinarum*; Osteomyelitis; Acute lymphoblastic leukaemia

Abbreviation:

Vancomycin-resistant enterococci - VRE

Enterococcus gallinarum - *E. gallinarum*

Enterococcus faecalis - *E. faecalis*

Enterococcus faecium - *E. faecium*

Acute Lymphoblastic Leukaemia - ALL

Magnetic Resonance Imaging - MRI

Osteomyelitis - OM

Septic arthritis - SA

Introduction

Vancomycin-resistant enterococci (VRE) are important nosocomial pathogens [1]. They demonstrate a unique pattern of antimicrobial susceptibility that poses a challenge in the treatment of invasive infections. VRE includes *Enterococcus gallinarum* which has been implicated in infections such as bacteremia, endocarditis, meningitis and endophthalmitis [2]. Reports of bone and joint infections with enterococcal species however are very rare, and typically associated with prosthetic joints [3,4]. We report a case of multifocal recurrent septic arthritis and native bone osteomyelitis due to *E. gallinarum* in a pediatric patient with acute lymphoblastic leukaemia (ALL).

Case presentation

The patient was diagnosed with ALL at the age of 13 years and was commenced on the UK ALL 2011 treatment regimen including intrathecal methotrexate, daunorubicin, PEG asparaginase and vincristine. She presented eight months after her initial diagnosis with a one-week history of fever, limp, and pain localizing to the right hip. The patient reported pain on passive and active flexion of the hip and was unable to fully extend the hip joint. Right hip examination showed neither swelling nor erythema.

The patient had a prodrome of bloody diarrhoea in the weeks prior to her complaint and underwent a colonoscopy that revealed ulcerated polyps in the rectosigmoid region. Histopathology however did not demonstrate evidence of either infection or inflammation. Her gastrointestinal symptoms improved, and no therapeutic intervention was needed.

Investigations at the time of her hip pain revealed a white cell count of 2.0 x 10^9/L, a neutrophil count of 1.76 x 10^9/L, elevated inflammatory markers with a CRP of 266 mg/L and an ESR of 125 mm/hr. Ultrasound examination of the hip joint confirmed the presence of an effusion. *E. gallinarum* was identified in the hip aspirate by culture and 16S PCR testing. The isolate was sensitive to amoxicillin, gentamicin, linezolid and teicoplanin while resistant to vancomycin (Table 1).

		Isolate (1)		Isolate (2)	
Antibiotic name	**Method**	**Result**	**Susceptibility**	**Result**	**Susceptibility**
Ampicillin	MIC	< = 2	S	< = 2	S
Quinupristin/Dalfopristin	MIC	1	R	1	R
Linezolid	MIC	2	S	2	S
Teicoplanin	MIC	< = 0.5	S	< = 0.5	S
Tigecycline	MIC	< = 0.12	S	< = 0.12	S
Vancomycin	MIC	4	R	4	R
Daptomycin	MIC	4		1.5	
Gentamicin-High level	MIC		S		S

Table 1: Susceptibility pattern of *E. gallinarum* isolates cultured from patient.

Pelvic MRI confirmed the presence of osteomyelitis of the right femoral neck (Figure 1).

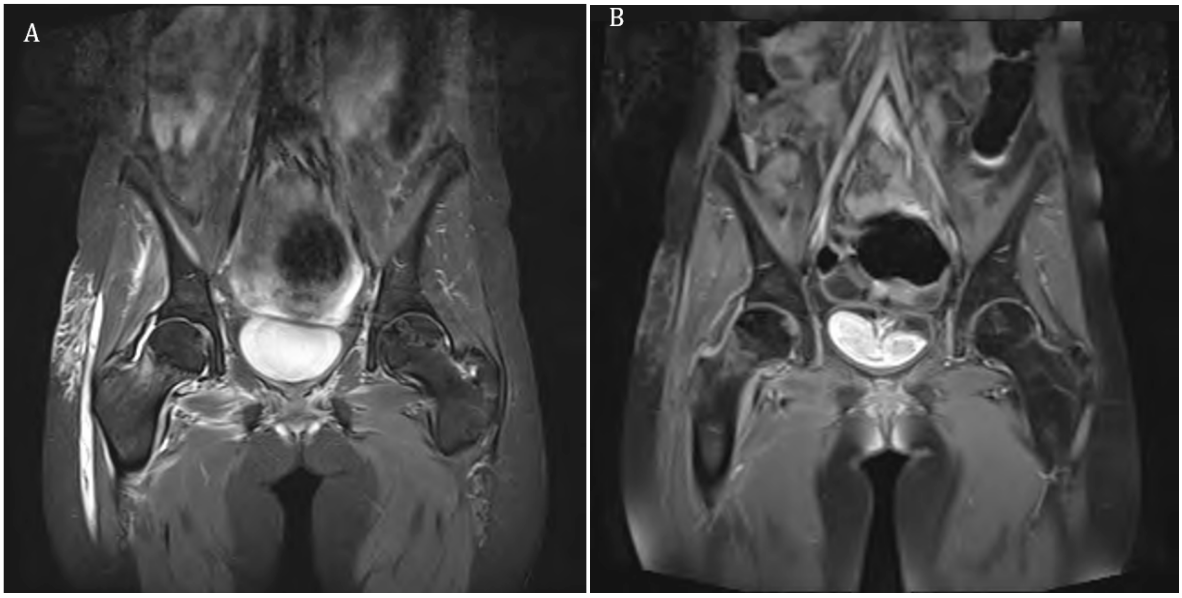

Figure 1: MRI imaging obtained during the first episode of infection; **A)** coronal STIR image demonstrating high signal in the right femoral neck with a small joint effusion, A high T2 signal in the soft is related to prior hip aspiration; **B)** Coronal post-contrast T1 image demonstrating contrast enhancement in the right femoral neck.

The patient was empirically commended on piperacillin-tazobactam and subsequently switched to intravenous (IV) amoxicillin and gentamicin combined with oral linezolid when the organism was identified. The patient required two further joint washouts during her in-patient stay before being discharged, clinically well, on 300mg IV daptomycin daily for 3 further weeks. Thereafter she completed 6 additional weeks with oral amoxicillin 1gm three times daily (Table 2).

	Right femoral neck OM and SA	**Right humerus head OM and SA**
Amoxicillin IV *plus* Gentamicin IV	2g q6h *plus* 1 mg/kg tds	2 grams q6h Plus 7mg/kg daily
Linezolid PO	600 mg BD	600mg BD
Daptomycin IV	300mg Daily for 21 days	
Amoxicillin PO	1 grams tds for 6 weeks	
Rifampicin PO	-	10mg/kg bd for 7 days

Table 2: antibiotic regimen used in patient's management.

Five months later, the patient was re-presented with right shoulder pain and fever. An MRI of the right shoulder confirmed septic arthritis of the joint and osteomyelitis of the right humeral head (Figure 2).

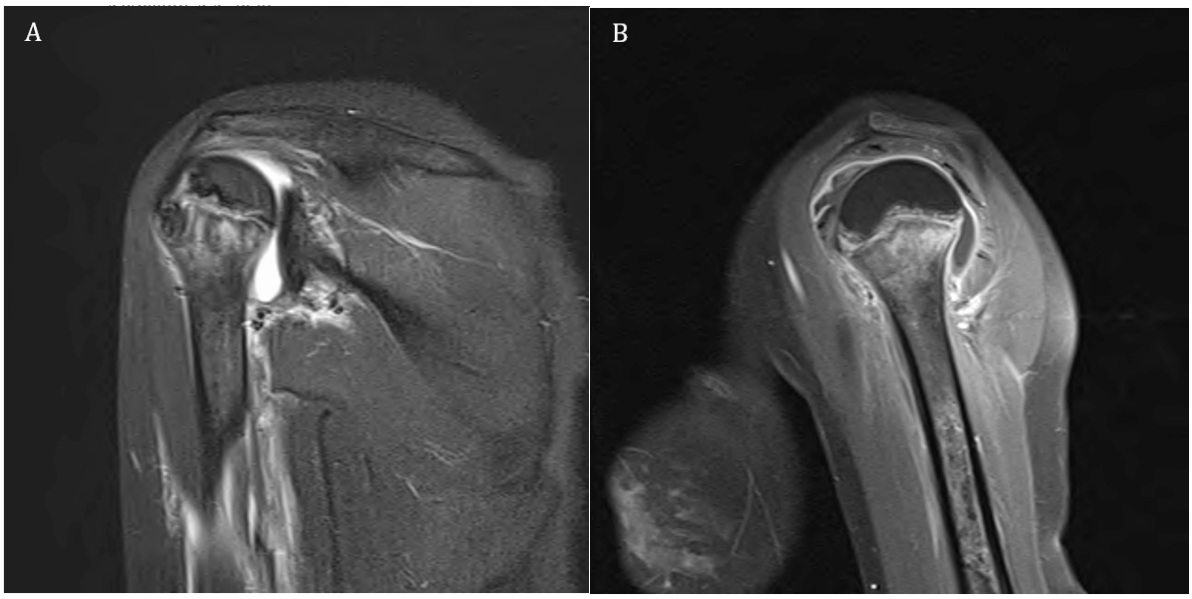

Figure 2: MRI imaging obtained during the first episode of infection; **A)** coronal STIR of the right shoulder demonstrating high T2 signal in the humeral metaphysis with an associated joint effusion; **B)** sagittal post-contrast T1 fat-saturated image demonstrating enhancement in the humeral metaphysis and synovial enhancement. Patchy enhancement and signal dropout in the humeral diaphysis is caused by treatment-related bone infarction.

Culture of shoulder joint aspirate confirmed infection with *E. gallinarum* with a similar pattern of antimicrobial susceptibility as the original isolate (Table 1). Intravenous amoxicillin, gentamicin and oral rifampicin were commenced (Table 2). In this episode, our patient required three washouts until her symptoms settled. The patient transitioned briefly to oral linezolid. However, therapy with intravenous amoxicillin was re-instituted because of increasing CRP, and the patient received 6 weeks of intravenous treatment in total. Because of the recurrent infection and the patient's ongoing immunosuppressed status, long-term suppressive therapy with oral amoxicillin was continued. After 1 year of regular outpatient follow-up, following completion of her chemotherapy and in the absence of

any further recurrence, suppressive therapy was discontinued. Six months later, the patient remains clinically well and in remission.

Discussion

Enterococcal species, including VRE like *E. gallinarum,* are part of gut normal flora and are important nosocomial pathogens [5]. The majority (> 95%) of enterococcal infections are due to *E. faecalis* or *E. faecium* [6]. Patients who are undergoing treatment for haematological malignancy and/or haematopoietic stem cell transplantation are susceptible to invasive infections with enterococci due to the combination of neutropenia and gastrointestinal mucositis, leading to translocation of the bowel flora and bacteremia [7]. Other risk factors include repeated hospital admissions and exposure to broad-spectrum antimicrobials. While enterococcal bacteremia in immunocompromised patients is well described, septic arthritis and osteomyelitis, particularly in the absence of prosthetic material, appear to be very uncommon. To our knowledge, there are no published cases in the medical literature.

Vancomycin resistance in *E. gallinarum* is conferred by the *Van-C* gene which is constitutively expressed and which reduces the affinity of vancomycin for the cell wall [6]. It remains susceptible, however to other glycopeptides such as teicoplanin, as well as other antimicrobials such as amoxicillin, linezolid, and daptomycin. At least one report documents that treatment of invasive infections with daptomycin/linezolid is associated with increased microbiological clearance and decreased treatment failure [8]. Our patient received a prolonged treatment course including both agents, yet disappointingly suffered a recurrence of infection sometime later. Since recurrence was at a different site, this recurrence may represent a separate infective episode rather than a recrudescence of the original infection, with no radiological features of either septic arthritis or osteomyelitis being evident in the shoulder at the time of the original infection. The infection proved difficult to treat on both occasions, with multiple surgical interventions and prolonged parenteral treatment before clinical improvement. A Follow-up MRI of the pelvis was obtained and showed avascular necrosis of bilateral hip joints and that in retrospect could've affected antibiotics delivery to the affected area. It was in this context that we elected to keep the patient on suppressive therapy with amoxicillin to prevent further recurrences.

Conclusion

To conclude, this case demonstrates that *E. gallinarum* can lead to bone and joint infection in immunocompromised patients, and can prove difficult to treat, even with prolonged and rational antimicrobial therapy.

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