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A rare case of acute osteomyelitis due to Panton-Valentine leukocidin-positive community-acquired methicillin-resistant *Staphylococcus aureus* in a young healthy adult

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ABSTRACT

INTRODUCTION: Most community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infections affect skin or soft tissues, while invasive and life-threatening illnesses including osteomyelitis are less common. CA-MRSA infections occur especially in the pediatric age group, while the occurrence of CA-MRSA osteomyelitis in adults is uncommonly reported.
PRESENTATION OF CASES: A rare case of acute osteomyelitis of the femur caused by Panton-Valentine leukocidin (PVL)-positive CA-MRSA in a 37-year-old man in good health is presented. A pure bone biopsy revealed extensive inflammation, suggestive of acute osteomyelitis, with no evidence of neoplasm, and PVL-positive MRSA was isolated from the culture. Antibiotic treatment, with 6 weeks of intravenous vancomycin and 4 weeks of clindamycin, followed by 2 weeks of oral linezolid, was given, and 2 years after treatment completion, there has been no relapse of infection.
CONCLUSION: This case strongly suggests that we need to be aware of CA-MRSA osteomyelitis, which requires a high level of suspicion, prompt diagnosis, and appropriate antibiotic treatment.

1. Introduction

Community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is defined as MRSA isolated from outpatients with no history of hospitalization within the past 1 year, and who present no other established risk factors for MRSA infection, such as surgery, residence in a long-term care facility, dialysis, or indwelling percutaneous medical devices or catheters. CA-MRSA strains often produce Panton-Valentine leucocidin (PVL), a cytotoxin that causes leukocyte destruction. PVL is an emerging infectious pathogen associated with skin and soft tissue infections, as well as life-threatening invasive diseases including osteomyelitis.

The number of CA-MRSA infections is increasing rapidly. Skin and soft tissue infections represent the majority of CA-MRSA clinical presentations, while invasive and life-threatening illnesses including osteomyelitis are less common. Osteomyelitis alone accounts for only 1% of all CA-MRSA infections [1,2], and it has been widely described in the pediatric age group [3]. CA-MRSA osteomyelitis is uncommonly reported in adults, and, to the best of our knowledge, there have been only nine reported cases of osteomyelitis caused by CA-MRSA in adults [4–10]. The radiographic features of CA-MRSA osteomyelitis in healthy individuals often suggest primary bone tumors [6], and a high level of suspicion with prompt diagnosis is needed for adequate treatment to achieve a better prognosis. In this article, a rare case of acute osteomyelitis of the femur in a young healthy adult caused by CA-MRSA is presented, along with a review of the relevant current literature. This manuscript was written in accordance with the Surgical CAse REport (SCARE) guidelines [11].

2. Presentation of case

A 37-year-old man in good health was admitted to our hospital for left thigh pain that had worsened progressively over 2 months. He had severe pain in his left thigh even at rest, but he had no fever, chills, or night sweats. Physical examination on admission showed no swelling of the thigh and limitation of the range of motion of the hip joint. The peripheral white blood cell count on admission was 4680/μL (3000/μL–9000/μL) with a normal differential, and C-reactive protein (CRP) was 1.82 mg/L

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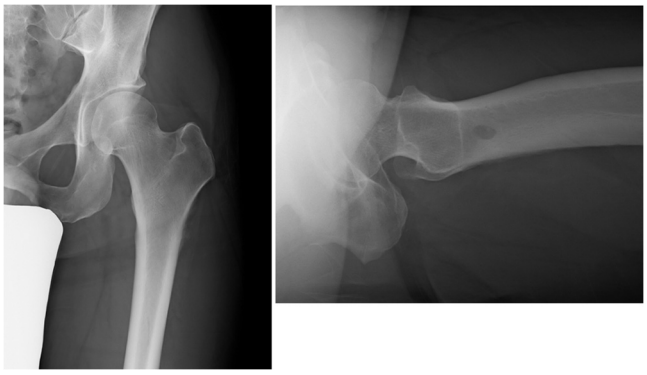

Fig. 1. Plain radiographs of the left femur on admission.

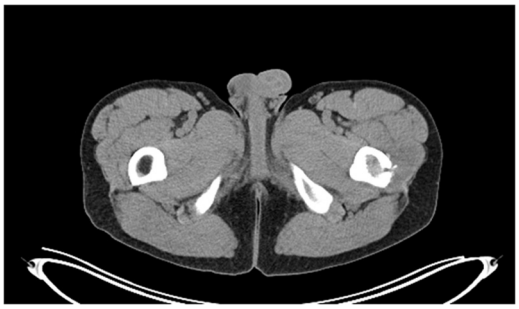

Fig. 2. Computed tomography of the left femur.

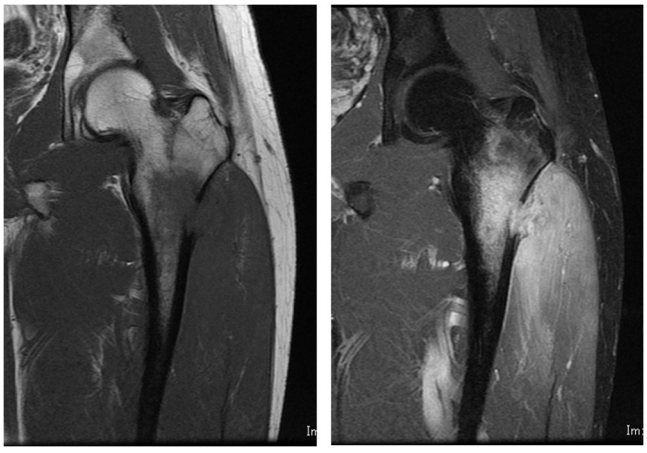

Fig. 3. Magnetic resonance imaging of the left femur. T1-weighted (a) and T2-weighted (b) coronal images.

(0.0–0.3 mg/L). Other laboratory values including alkaline phosphatase and lactate dehydrogenase were within normal limits. Plain radiographs (Fig. 1) and computed tomography (Fig. 2) of the left lower extremity demonstrated a destructive osteolytic lesion in the lateral cortex of the greater trochanter of the left femur with cortical erosion and an irregular periosteal reaction. Subsequent magnetic resonance imaging showed a diffuse abnormal marrow signal throughout the greater trochanter of the left femur extending to the extramedullary area, demonstrating a destructive osteolytic lesion in the lateral cortex of the mid-shaft of the left femur (Fig. 3). Whole body ^{18}F-fluorodeoxyglucose-positron emission tomography (FDG-PET) scanning showed FDG uptake in the left femur, with a standardized uptake value (SUV) of 13.37 (Fig. 4). Clinical differential diagnoses were osteomyelitis and benign or malignant bone tumors, and the patient underwent a pure bone biopsy for histopathological diagnosis. There were granulation tissues with

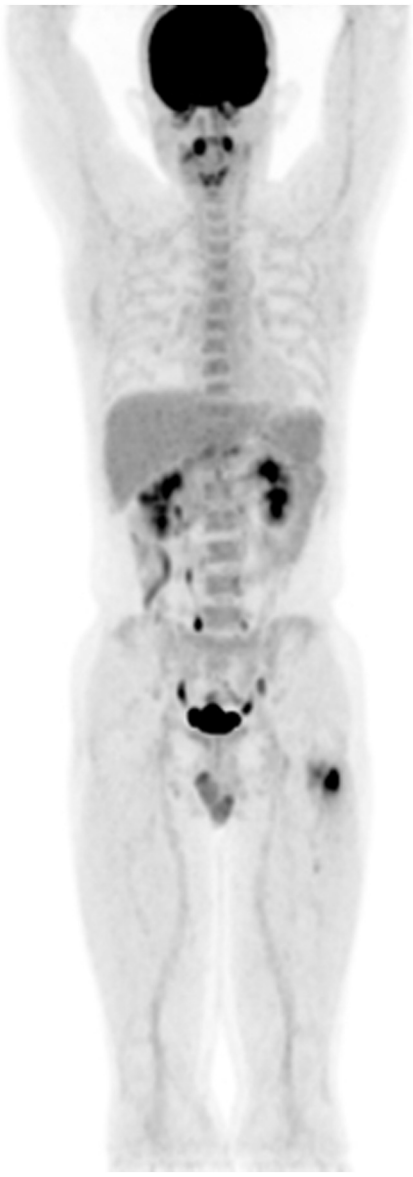

Fig. 4. Whole body FDG-PET imaging. SUV in the left femur is 13.37.

purulent material coming out of the femur, and no obvious tumor lesion was observed. Microscopically, the specimens of the granulation tissues from both extra- and intra-osseous lesions showed extensive inflammation, suggestive of acute osteomyelitis with no evidence of neoplasm, and PVL-positive MRSA was isolated from the surgical specimens. The patient was then diagnosed with acute osteomyelitis of the femur due to PVL-positive CA-MRSA. Based on the antibiotic sensitivity tests, the patient was given 6 weeks of intravenous vancomycin with 4 weeks of clindamycin, followed by 2 weeks of oral linezolid. At 25 days after the start of treatment, his CRP value decreased to within the normal range. At final follow-up, 2 years after surgery, the function of his left lower limb had recovered perfectly, and he felt no pain at all. He had been able to perform his usual activities of daily living without any problems. On final plain radiographic examination, the osteolytic lesion had disappeared (Fig. 5). Blood examinations also reverted to normal.

3. Discussion

CA-MRSA is defined as MRSA isolated from outpatients with no history of hospitalization within the past year and who

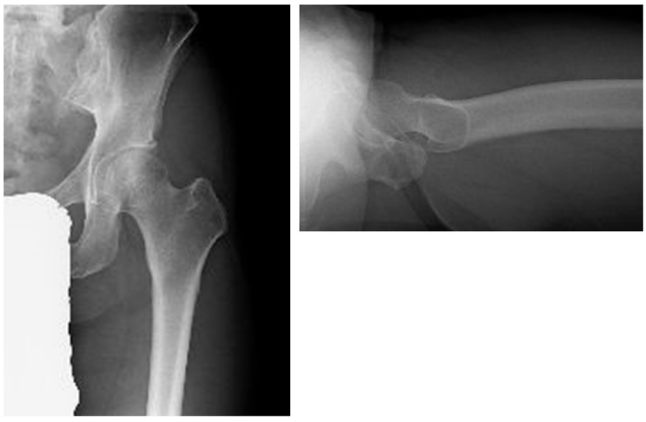

Fig. 5. Final plain radiographs of the left femur 2-years after surgery.

have no other established risk factors for MRSA infection, such as surgery, residence in a long-term care facility, dialysis, or indwelling percutaneous medical devices or catheters [12]. The characteristic bacteriological feature of CA-MRSA is that it often produces PVL, a cytotoxin that causes leukocyte destruction, and the PVL positivity rate is 77–100% in CA-MRSA patients, while it is less than 4% in HA-MRSA patients [12,13]. Clinically, the majority of CA-MRSA infections are in skin or soft tissues, while invasive and life-threatening illnesses, such as necrotizing pneumonia, osteomyelitis, and sepsis, have been described in children; osteomyelitis is an extremely rare CA-MRSA presentation among healthy adults [3].

To the best of our knowledge, there have been only nine cases of osteomyelitis caused by CA-MRSA in adults [4–10], but none in Japan. Among the nine cases, the PVL gene was positive in all five tested patients [6]. PVL plays an important role in the pathogenesis of severe invasive infections. PVL-positive isolates had significantly higher erythrocyte sedimentation rates and CRP levels at presentation and were more likely to be blood culture-positive. For these reasons, PVL gene detection appears strongly associated with the severity of acute osteomyelitis [3,6].

People at high risk for CA-MRSA infection who have been previously identified include neonates, school or university students, athletes, military personnel, cystic fibrosis patients, jail inmates, men who have sex with men, household contacts, urban underserved communities, indigenous populations, HIV-positive patients, people with tattoos, and those in contact with animals [12,14]. However, in the present case, the source of the infection was unknown, because the present patient had no such risk factors and no history of trauma.

One noteworthy finding is that CA-MRSA osteomyelitis involving the long bones has a propensity to mimic malignant bone tumors [6]. Four of nine reported cases with acute osteomyelitis caused by CA-MRSA in adults presented with radiographic findings initially suggestive of primary bone malignancy [4–6]. Most symptoms in CA-MRSA osteomyelitis, such as fever, bone pain, weight loss, and loss of appetite, are non-specific and may not help differentiate between osteomyelitis and malignant bone tumors. In the present case, osteomyelitis and benign or malignant bone tumors were possible clinical diagnoses, and a bone biopsy was therefore performed for histopathological diagnosis. Biopsy could also identify the causative pathogen so that appropriate antibiotic treatment could be administered if osteomyelitis were present.

For invasive CA-MRSA infections, vancomycin is the first-line intravenous antibiotic drug [1]. There is no evidence showing that any one drug or combination of drugs is better than vancomycin alone to treat severe MRSA infections [1]. Oral antibiotic agents are used for long-term treatment after the initial therapy with parenteral agents. After intensive intravenous vancomycin treatment for 2–4 weeks, switching to oral agents such as clindamycin, doxycycline, co-trimoxazole, rifampicin, or fusidic acid [3] is recommended, but the optimal route of administration of antibiotic therapy for CA-MRSA infections has yet to be established. In addition, the optimal duration of therapy for MRSA osteomyelitis is also unknown. A minimum 8-week course is recommended, but some experts suggest an additional 1–3 months of oral rifampin-based combination therapy [15].

4. Conclusion

PVL-positive CA-MRSA can lead to invasive life-threatening disease. Heightened vigilance is needed for CA-MRSA osteomyelitis of long bones in adults, especially those in good health, because the disease is an uncommonly reported entity and often radiographically mimics bone malignancies, which can be ruled out based on a bone biopsy supported by microbiological evidence. In addition, appropriate identification of the organism and detection of the presence of PVL will help to more rapidly provide adequate treatment and improve the prognosis.

Conflicts of interest

The authors have no conflict of interest.

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Ethical approval

In our case report there was no experimentation, we just described our clinical practice.

Consent

In our case report there was no experimentation, we just described our clinical practice, written informed consent for procedures was obtained from the patient.

Author contribution

All contributors who do not meet the criteria for authorship should be listed in an acknowledgements section. Examples of those who might be acknowledged include a person who provided purely technical help, writing assistance or a department chair who provided only general support.

Guarantor

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