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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.

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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 leukocidin (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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(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 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
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 pneu-
omonia, 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 presen-
tation 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 stu-
dents, 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 involv-
ing 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 symp-
toms in CA-MRSA osteomyelitis, such as fever, bone pain, weight
loss, and loss of appetite, are non-specific and may not help differ-
etiate 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 iden-
tify the causative pathogen so that appropriate antibiotic treat-
ment 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 treat-
ment for 2–4 weeks, switching to oral agents such as clindamycin,
doxycycline, co-trimoxazole, rifampicin, or fusidic acid [3] is rec-
commended, but the optimal route of administration of antibiotic
therapy for CA-MRSA infections has yet to be established. In addi-
tion, 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 dis-
ease. 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 radiograph-
ically mimics bone malignancies, which can be ruled out based
on a bone biopsy supported by microbiological evidence. In addi-
tion, 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 pro-
cedures was obtained from the patient.

Author contribution

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Guarantor

Dr. Osamu Nakamura.

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