J Infect Chemother 25 (2019) 212–214

Contents lists available at ScienceDirect

Journal of Infection and Chemotherapy

journal homepage: http://www.elsevier.com/locate/jic

Case Report

A case of acute septic arthritis of the hip joint caused by Panton-Valentine leukocidin-positive ST772 community-acquired methicillin-resistant *Staphylococcus aureus*☆

Shunsuke Takadama [a, 1], Yuka Yamagishi [b, 1], Hidemasa Nakaminami [a, *], Takkan Morishima [c], Masataka Deie [c], Hiroshige Mikamo [b], Norihisa Noguchi [a]

[a] Department of Microbiology, School of Pharmacy, Tokyo University of Pharmacy and Life Sciences, 1432-1 Horinouchi, Hachioji, Tokyo, 192-0392, Japan
[b] Department of Clinical Infectious Diseases, Aichi Medical University, Japan
[c] Department of Orthopedic Surgery, Aichi Medical University, Japan

ARTICLE INFO

Article history:
Received 31 July 2018
Received in revised form
7 August 2018
Accepted 21 August 2018
Available online 11 September 2018

Keywords:
Acute septic arthritis
Community-acquired methicillin-resistant *Staphylococcus aureus*
Panton-Valentine leucocidin
Bengal-Bay clone

ABSTRACT

Acute septic arthritis (ASA) caused by *Staphylococcus aureus* can lead to fulminant arthritis and cause permanent joint destruction. In particular, infection caused by methicillin-resistant *Staphylococcus aureus* (MRSA) becomes intractable and severe owing to limitation of therapeutic drugs. Here, we report the case of a young patient with ASA without any record of overseas travel, who was infected by the Panton-Valentine leukocidin-positive Bengal-Bay clone, which is a predominant community-acquired MRSA in India.

1. Introduction

Acute septic arthritis (ASA) develops as a result of bacterial growth and colonization at the synovia or synovial surface in patients with bacteremia [1–3]. Additionally, ASA occurs as a secondary disease associated with trauma. Bacteria that cause ASA are classified as gonococci and non-gonococci. In particular, non-gonococcal bacteria have the potential to destroy the joint cartilage and may cause permanent tissue damage. *Staphylococcus aureus* is one of the most common pathogens causing non-gonococcal ASA [4]. The infection caused by methicillin-resistant *Staphylococcus aureus* (MRSA) may become intractable and severe because of limitation of therapeutic drugs. Various adhesion factors and toxins produced by *S. aureus*, including MRSA, contribute to incidence of ASA [4].

Here, we report that the case of a young patient with ASA without any record of overseas travel, who was infected by the Panton-Valentine leukocidin (PVL)-positive Bengal-Bay clone, which is a predominant community-acquired MRSA (CA-MRSA) in India.

2. Case report

An 11-year-old Japanese boy presented with ASA in right hip joint caused by MRSA. In mid-June in 2017 (day -5), he acquired mosquito bites on the right arm and left chest and applied a commercially available chlorhexidine ointment. Five days later (day 0), he developed fever and felt uncomfortable on the right hip joint. He visited clinic A and was prescribed cefcapene pivoxil. On the following day (day 1), the patient underwent incision and drainage of left chest subcutaneous abscess at the dermatology department of hospital B and received cefazolin intravenously for 2 days. On day 9, the patient complained of difficulty in walking due to right hip joint pain. He was evaluated to have ASA at the orthopedic surgery department of hospital B and was admitted to the hospital. On day 17, incision, drainage, and catheterization for drainage were performed. MRSA was detected in the pus at this stage. Based on the results of the antimicrobial susceptibility test (Table 1), the MRSA

☆ All authors meet the ICMJE authorship criteria.
* Corresponding author.
E-mail address: nakami@toyaku.ac.jp (H. Nakaminami).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.jiac.2018.08.015
1341-321X/

Table 1
Antimicrobial susceptibility of methicillin-resistant *Staphylococcus aureus* isolated in this case.

Antimicrobial agent	MIC (μg/mL)	R/S	Antimicrobial agent	MIC (μg/mL)	R/S
PCG	≥0.5	R	LVFX	4	R
SBT/ABPC	8	R	EM	1	I
MPIPC	≥4	R	CLDM	≤0.25	S
CEZ	≥4	R	VCM	1	S
CXM	4	S	TEIC	≤0.5	S
IPM	≤1	S	MINO	≤0.5	S
AMK	4	S	FOM	≤8	S
GM	≥16	R	ST	≥320	R
ABK	≤1	S			

PCG, benzylpenicillin; SBT/ABPC, sulbactam/ampicillin; MPIPC, oxacillin; CEZ, cefazolin; CXM, cefuroxime; IPM, imipenem; AMK, amikacin; GM, gentamicin; ABK, arbekacin; LVFX, levofloxacin; EM, erythromycin; CLDM, clindamycin; VCM, vancomycin; TEIC, teicoplanin; MINO, minocycline; FOM, fosfomycin; ST, sulfamethoxazole-trimethoprim.
R, resistant; S, susceptible.

isolate was determined to be CA-MRSA, and 50 mg minocycline (twice daily) during days 20 and 36 and 1.5 g vancomycin (twice daily) during days 22 and 35 were administered to the patient. From day 31, the dose of vancomycin was elevated to thrice daily, as no improvement in condition was observed. On day 36, magnetic resonance imaging (MRI) revealed dissemination of inflammation to the bone marrow (Fig. 1). Furthermore, the C-reactive protein (CRP) level did not improve. Hence, the patient was transferred to the University Hospital.

On day 37, the patient had a body temperature of 37.9 °C, CRP of 6.49 mg/dL, erythrocyte sedimentation rate (ESR) of 76 mm, and osteomyelitis. Hence, the synovial tissue was washed and removed maximally with laminectomy punch, and two drainage catheters were placed at the surgical site. MRSA was detected from the yellowish-white opacified synovial fluid obtained during the surgery. Linezolid (10 mg/kg) was administered via intravenous drip injection thrice daily from the day of transfer (day 36) to day 49, and it was switched to oral administration on day 50. On day 53, epiphysiolysis and osteolysis of acetabulum were observed and indirect traction was started. On day 57, a brownish viscous liquid was observed in the drain waste liquid, in which MRSA and *Klebsiella pneumoniae* were detected. Meropenem (1 g) and ciprofloxacin (400 mg) were administered via intravenous drip injection thrice daily from days 57 and 67, respectively, when the symptoms did not improve. On day 77, reoperation was performed for washing, debridement, and removal of distant epiphysis. Following reduction in CRP level, meropenem was discontinued, and ciprofloxacin administration was switched to the oral route. In addition, linezolid was changed to oral clindamycin, as the MRSA isolate in this case was susceptible to this drug (Table 1). Following normalization of ESR, the patient wore the right lower limb orthosis from day 109. The patient was discharged from the University Hospital on day 115 and was followed up by his previous doctor.

3. Discussion

Among infectious arthritis, non-gonococcal acute arthritis tends to be severe, and the mortality rate associated with this disease ranges from 10 to 25% [1,5–7]. Furthermore, previous studies reported that 25–50% of survivors incur permanent joint disorders [1,5–7]. *S. aureus* accounts for 50% of the causative bacteria of non-gonococcal arthritis [4]. In our case, CA-MRSA was the predominant pathogen. We predicted that skin or nasal CA-MRSA invaded into the scratched site of mosquito bites. In addition, *K. pneumoniae* detected on day 57 was also presumed to be one of the factors responsible for deterioration of symptoms in this case. Further analysis revealed that the CA-MRSA strain isolated in this case was positive for the gene encoding PVL. PVL induces apoptosis or necrosis of neutrophils and is possibly involved in evasion from immune cells and enhancement of inflammatory response [7]. In addition, the high virulence of PVL is attracting extensive attention.

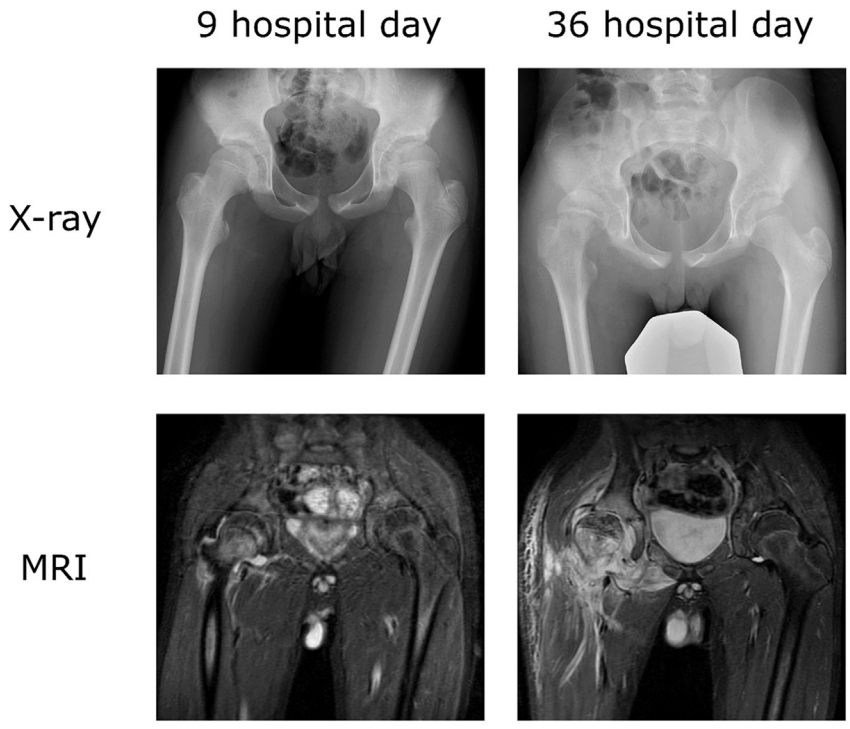

Fig. 1. X-ray and magnetic resonance imaging (MRI) images of hip joints on days 9 and 36.

Recently, the population of the sequence type (ST) 8-staphylococcal cassette chromosome (SCC) *mec* type IV (ST8-IV) USA300 clone, which is the PVL-positive CA-MRSA responsible for most epidemics worldwide, has been on the rise in Japan [8–11]. However, the CA-MRSA of this case was of the ST772-V genotype, called the Bengal-Bay clone, which is predominant in India [12]. The Bengal-Bay clone is a multidrug-resistant CA-MRSA clone carrying PVL gene and associated with skin and soft tissue infections (SSTIs) [12]. To our knowledge, this is the first report of ASA caused by the Bengal-Bay clone. The MRSA isolate exhibited resistance to gentamicin, levofloxacin, and sulfamethoxazole-trimethoprim. Previous study also reported that the Bengal-Bay clone showed resistance to aminoglycosides and quinolones despite CA-MRSA, whereas sulfamethoxazole-trimethoprim maintained susceptibility to them [13]. Further study is necessary to evaluate the sulfamethoxazole-trimethoprim resistance of our case. Although the Bengal-Bay clone is rare in Japan, two previous reports mention its existence [9,14]. Yamaguchi et al. reported that a patient infected by the Bengal-Bay clone had a travel history to India [14]. However, the patient in the present case had no record of travel to India. This suggests that the PVL-positive ST772-V Bengal-Bay clone had disseminated in the Japanese community and was capable of causing community-acquired infections similar to this case. Furthermore, *fnbB* (fibronectin-binding proteins B), *clfA/B* (clumping factors A and B), *eno* (enolase), and *cna* (collagen adhesin) were detected in this strain. These genes encode for Microbial Surface Components Recognizing Adhesive Matrix Molecules (MSCRMMs) that are present in Gram-positive bacteria, including MRSA. MSCRAMMs are known to be involved in adhesion to cells and biofilm formation, and they play key roles in initiation of endovascular, bone and joint, and prosthetic-device infections [15]. This patient was an 11-year-old Japanese boy who had atopic dermatitis as a basic disease in addition to the mosquito bites several days before onset of ASA. Therefore, these risk factors may have constituted the infection route of MRSA in this case. In addition, hip arthritis is frequently caused by secondary bacteremia in children, and the symptoms progress rapidly. This is one of the reasons underlying the intractable nature of the infection in this case. Furthermore, MSCRAMMs and PVL, which are involved in colonization and exacerbation of inflammation, might have resulted in persistent detection of MRSA despite repeated surgical treatments and long-term antimicrobial administration.

The patient's mother had also acquired some mosquito bites and developed a subcutaneous abscess at the same time. Although the abscess samples were not available, we presumed that the parent and child were infected by the same CA-MRSA. Therefore, it is necessary to pay more attention to the trend of PVL-positive CA-MRSA, including the ST772-V Bengal-Bay clone.

Conflicts of interest

None to declare.

Acknowledgements

We would like to thank Editage (www.editage.jp) for English language editing. This work was supported by the Nagai Memorial Research Scholarship from the Pharmaceutical Society of Japan.

References

[1] Klein RS. Joint infection, with consideration of underlying disease and sources of bacteremia in hematogenous infection. Clin Geriatr Med 1988;4:375–94.
[2] Morgan DS, Fisher D, Merianos A, Currie BJ. An 18 year clinical review of septic arthritis from tropical Australia. Epidemiol Infect 1996;117:423–8.
[3] Ross JJ. Septic arthritis. Infect Dis Clin North Am 2005;19:799–817.
[4] Ross JJ. Septic arthritis of native joints. Infect Dis Clin North Am 2017;31:203–18.
[5] Gardner GC, Weisman MH. Pyarthrosis in patients with rheumatoid arthritis: a report of 13 cases and a review of the literature from the past 40 years. Am J Med 1990;88:503–11.
[6] Goldenberg DL. Infectious arthritis complicating rheumatoid arthritis and other chronic rheumatic disorders. Arthritis Rheum 1989;32:496–502.
[7] Kaandorp CJ, Krijnen P, Moens HJ, Habbema JD, van Schaardenburg D. The outcome of bacterial arthritis: a prospective community-based study. Arthritis Rheum 1997;40:884–92.
[8] Nimmo GR. USA300 abroad: global spread of a virulent strain of community-associated methicillin-resistant *Staphylococcus aureus*. Clin Microbiol Infect 2012;18:725–34.
[9] Takadama S, Nakaminami H, Sato A, Shoshi M, Fujii T, Noguchi N. Dissemination of Panton-Valentine leukocidin-positive methicillin-resistant *Staphylococcus aureus* USA300 clone in multiple hospitals in Tokyo, Japan. Clin Microbiol Infect 2018. https://doi.org/10.1016/j.cmi.2018.02.012.
[10] Nakaminami H, Ito A, Sakanashi D, Suematsu H, Yamagishi Y, Mikamo H, et al. Genetic diversity of *pvl*-positive community-onset methicillin-resistant *Staphylococcus aureus* isolated at a university hospital in Japan. J Infect Chemother 2017;23:856–8.
[11] Takadama S, Nakaminami H, Aoki S, Akashi M, Wajima T, Ikeda M, et al. Prevalence of skin infections caused by Panton-Valentine leukocidin-positive methicillin-resistant *Staphylococcus aureus* in Japan, particularly in Ishigaki, Okinawa. J Infect Chemother 2017;23:800–3.
[12] Blomfeldt A, Larssen KW, Moghen A, Haugum K, Steen TW, Jorgensen SB, et al. Bengal Bay clone ST772-MRSA-V outbreak: conserved clone causes investigation challenges. J Hosp Infect 2017;95:253–8.
[13] Blomfeldt A, Larssen KW, Moghen A, Gabrielsen C, Elstrom P, Aamot HV, et al. Emerging multidrug-resistant Bengal Bay clone ST772-MRSA-V in Norway: molecular epidemiology 2004-2014. Eur J Clin Microbiol Infect Dis 2017;36:1911–21.
[14] Yamaguchi T, Nakamura I, Chiba K, Matsumoto T. Epidemiological and microbiological analysis of community-associated methicillin-resistant *Staphylococcus aureus* strains isolated from a Japanese hospital. Jpn J Infect Dis 2012;65:175–8.
[15] Archer NK, Mazaitis MJ, Costerton JW, Leid JG, Powers ME, Shirtliff ME. *Staphylococcus aureus* biofilms: properties, regulation, and roles in human disease. Virulence 2011;2:445–59.