Correspondence

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Does every *Staphylococcus aureus* infection require anti-MRSA drugs? Three case reports of a *Staphylococcus aureus* infection

Guangbin Chen[1], Hong-Zhou Lu[2,*]

[1] Department of Pharmacy, The Third People's Hospital of Shenzhen, Shenzhen, China;
[2] National Center for Infectious Diseases Research, The Third People's Hospital of Shenzhen, Shenzhen, China.

SUMMARY *Staphylococcus aureus* is a common clinical pathogen. Does every *S. aureus* infection require anti-MRSA drugs? Reported here are three cases of a community-acquired infection with S. aureus. The first case involveds a 45-year-old male who was admitted due to right ankle pain for 1 month; he was diagnosed with chronic suppurative osteomyelitis and an acute soft tissue infection of the ankle. S. aureus was cultured from the pus and was resistant to penicillin and sensitive to oxacillin and vancomycin. After receiving oxacillin, he was cured and discharged 45 days after admission. The second case involved a 44-year-old male who was admitted due to lumbar pain with right lower limb numbness for more than 1 month and fever for 1 day. *S. aureus* was cultured from blood specimens and was resistant to penicillin and sensitive to oxacillin and vancomycin. After receiving oxacillin, he as cured. The third case involved a 7-day-old newborn who was admitted due to skin jaundice for 6 days. *S. aureus* was cultured from skin secretions specimens and was resistant to penicillin and sensitive to oxacillin, erythromycin, and vancomycin. The newborn was treated with oxacillin for 4 days, and she was cured and discharged. Not all cases a suspected *S. aureus* infection require anti-MRSA drugs; instead, previous *S. aureus* susceptibility results in the area and hospital, as well as the patient's clinical profile, need to be taken into account.

Keywords *Staphylococcus aureus*, MRSA, antimicrobials, culture, adverse reactions

The abuse of antimicrobials is one of the reasons for increasingly serious antimicrobial resistance. *Staphylococcus aureus* is a common clinical pathogen. There are 3 forms of *S. aureus* that are sensitive to antibiotics. One is sensitive to penicillin, oxacillin, the first, second, third, and fourth generation of cephalosporins, and vancomycin, and this form does not produce B lactamases. The second form produces B lactamases and is commonly known as methicillin-sensitive *Staphylococcus aureus* (MSSA), which is resistant to penicillin but sensitive to oxacillin, all four generations of cephalosporins, and vancomycin. The third form is commonly known as methicillin-resistant *Staphylococcus aureus* (MRSA), which is resistant to penicillin, oxacillin, and many antibiotics including all four generations of cephalosporins. There are few antimicrobial agents available; only vancomycin, teicoplanin, linezolid and other drugs can be selected, and moxifloxacin and rifampin can be selected in some cases. Clinically, when some clinicians encounter suspected cases of an *S. aureus* infection, such as skin and soft tissue infections (SSTIs), they often choose anti-MRSA drugs such as vancomycin, linezolid, and teicoplanin for treatment empirically due to the concern that the case involves an MRSA infection before the bacterial culture results are received. Nevertheless, does every *S. aureus* infection require anti-MRSA drugs?

On one hand, the incidence of adverse reactions to drugs such as vancomycin, linezolid, and teicoplanin is relatively high and the symptoms of those adverse reactions are relatively serious. On the other hand, these drugs are expensive, causing a waste of medical resources, which does not conform to the principles of pharmacoeconomics. Therefore, understanding the drug resistance spectrum of pathogenic bacteria in this area, including the characteristics of the pathogen resistance spectrum in various hospital departments, is of great help to empirically selecting appropriate antibacterials before the results of a specimen bacterial culture are available. Below are three cases of a community-acquired infection with *S. aureus*, and the results of a culture of *S. aureus* in our hospital are analyzed.

The first case involved a 45-year-old male who was admitted to our hospital on September 7, 2021 due to right ankle pain for 1 month that had intensified over 4 days. The right ankle was swollen and painful after

acupuncture 4 days prior, and the skin temperature was high. He denied having a fever, cough, nausea, or vomiting. He also denied a history of chronic diseases such as hypertension and diabetes. A physical examination on admission revealed a normal body temperature of 36.6℃, a blood pressure of 123/80 mmHg, a normal sinus rhythm of 78 beats per minute, and a respiratory rate of 20 breaths per minute. The patient was conscious, cooperative during the physical examination, and coherent. A physical examination of the heart and lungs was normal. Swelling, tenderness, and an increased skin temperature were noted in the right ankle. Laboratory results revealed a C-reactive protein (CRP) level of 85.1 mg/L (normal range: 0 mg/L to 6 mg/L). The procalcitonin level of 0.12 ng/mL was within the normal range. The white cell count was 16.27 × 10^9/L and the neutrophil count was 13.15 × 10^9/L. Computed tomography (CT) on admission revealed osteomyelitis and a local abscess in the lower segment of the right tibia. The patient was diagnosed with chronic suppurative osteomyelitis and an acute soft tissue infection of the ankle.

Given that the most common pathogen causing chronic osteomyelitis and SSTIs is *S. aureus* and based on the drug resistance of *S. aureus* cultured from various specimens at our hospital, a consultation recommended oxacillin for empirical anti-infection therapy before obtaining the results of a bacterial culture and drug sensitivity test. The consultation was heeded and an oxacillin sodium injection was initiated starting on the day of admission. On the third day of hospitalization, vacuum sealing drainage (VSD) and tibial drainage were performed to treat osteomyelitis of the right tibia and a peripheral abscess. Four days later, *S. aureus* was cultured from the pus and was resistant to penicillin and sensitive to oxacillin and vancomycin. Oxacillin was continued (2.0 g, *i.v.*, q8h) for 6 weeks. Fourteen days after admission, secondary osteomyelitis of the right tibia was removed, and debridement and suturing were performed. Forty-five days after admission, the patient was cured and discharged.

The second case involved a 44-year-old male who was admitted to our hospital on February 9, 2019 due to lumbar pain with right lower limb numbness for more than 1 month and a fever for 1 day. He had a history of chronic hepatitis B with cirrhosis and diabetes. A physical examination on admission revealed a body temperature of 40.1℃, blood pressure of 122/71 mmHg, sinus tachycardia of 140 beats per minute, and a respiratory rate of 21 breaths per minute. Laboratory results revealed a CRP level of 92.25 mg/L. The procalcitonin level of 0.899 ng/mL was high (normal range: 0 to 0.5 ng/mL). The white cell count was 7.86 × 10^9/L, and the neutrophil count was 6.43 × 10^9/L. CT revealed bone destruction of the fourth lumbar vertebra with a soft tissue mass, and the possibility of tuberculosis with a paraspinal cold abscess was considered. After admission, the patient's condition was as follows: 1) The lumbar lesion was investigated for a potential tuberculous infection, 2) Type 2 diabetes mellitus, and 3) Chronic hepatitis B with cirrhosis. Since the pathogen was unknown, a tuberculous infection and brucellosis could not be ruled out, and levofloxacin and amikacin were empirically initiated starting on the day of admission. Ten days after admission, *S. aureus* was cultured from blood specimens and was resistant to penicillin and sensitive to oxacillin, levofloxacin, amikacin, and vancomycin. Levofloxacin was stopped and oxacillin was substituted. Lumbar debridement was performed. Fifty days after admission, the patient was cured and discharged.

The third case involved a 7-day-old newborn who was admitted to this hospital on September 22, 2020 due to skin jaundice for 6 days and a rash for 1 day. After admission, the patient's condition was as follows: 1) Neonatal impetigo and 2) Neonatal hyperbilirubinemia. The child's general condition was good. Given that the most common pathogen causing cutaneous impetigo is *S. aureus*, oxacillin was used empirically. Symptomatic treatment was also administered. *S. aureus* was cultured from skin secretions and was resistant to penicillin and sensitive to oxacillin, cefazolin, erythromycin, and vancomycin. The newborn was treated with oxacillin for 4 days, and she was cured and discharged.

All three of these cases have the following common characteristics: 1) *S. aureus* cultured from various specimens was resistant to penicillin but sensitive to oxacillin, various generations of cephalosporins, and vancomycin, 2) The patient's general condition was satisfactory and the clinical symptoms were not very serious, and 3) Oxacillin was efficacious.

A large-scale study of the HealthCore Integrated Research Database found that the incidence of SSTIs was approximately 48.46 cases/1,000 people per year (*1*). Another study found that the main pathogenic bacteria causing SSTIs were Gram-positive and Gram-negative bacteria, and *S. aureus* was the most common pathogenic bacterium detected in SSTIs (*2*).

S. aureus is a common opportunistic pathogen. It mainly colonizes the groin, perineum, nasal vestibular mucosa, and neonatal umbilical cord stump and can occasionally colonize the skin and oropharynx. It can produce a variety of hemolytic toxins, leukocidin, enterotoxin, and plasma coagulase. It mainly causes a variety of diseases, including suppurative infections and inflammation of the skin, mucosa, and deep tissue, postoperative infections at various sites, deep abscesses in various organs, bacteremia, toxic-shock syndrome, and a microflora disorder involving the whole body (*3*). Some cases of an *S. aureus* infection have been serious and even fatal. *S. aureus* is one of the common pathogens infecting communities and hospitals. The skin and mucosa are generally believed to be the main sites of *S. aureus* colonization (*4*). In patients with

skin diseases, *S. aureus* colonization is likely to cause a local or systemic infection due to the damaged skin protective barrier.

The drug resistance of community-acquired *S. aureus* infections differs from that of nosocomial *S. aureus* infections. MRSA is considered to be the most common pathogen causing nosocomial infections. MRSA is reported to account for 25.5% of community-associated *S. aureus* infections and 67.4% of nosocomial infections in China, South Korea, and Japan (*5*). The rate of MRSA detection in the community is relatively low. The average rate of MRSA detection in some hospitals in China from 2014-2018 was 31.7%, and the rate of MRSA detection decreased from 69.0% in 2005 to 35.3% in 2017 (*6*).

From January 1, 2017 to October 31, 2022, 1,004 specimens of *S. aureus* infections were cultured in our hospital, and 540 of those specimens (53.8%) did not produce B lactamases. Three hundred and two specimens were MSSA (including 92 cases of the MLSB phenotype), accounting for 30.1%; 162 were MRSA, accounting for 16.1%. Regrettably, distinguishing between community-acquired and nosocomial infections was not possible for those 1,004 specimens of *S. aureus*.

In recent years, there has been an increase in vancomycin-intermediate *S. aureus* (VISA) and heterogeneous VISA (hVISA), particularly in Asia (*7*). Nonetheless, the incidence of VISA and hVISA is low, i.e., less than 10%. MRSA resistant to vancomycin has not been reported in China. Therefore, vancomycin is still considered to be the preferred drug for an MRSA infection (*8*). Therefore, when clinicians encounter suspected cases of an *S. aureus* infection, vancomycin, linezolid, teicoplanin, and other anti-MRSA drugs are often used empirically before the results of a bacterial culture are available out of fear of MRSA and to ensure efficacy.

Compared to oxacillin or penicillin, vancomycin causes relatively more adverse reactions (*9*). The most serious adverse reactions can lead to death (*10*). Antimicrobial agents are the most common cause of drug reactions in the form of eosinophilia and systemic symptoms (DRESS), and vancomycin is responsible for about two-thirds of DRESS cases induced by antimicrobial agents (*11*). Vancomycin can cause renal impairment (*12,13*), as well as red man syndrome (*14*), thrombocytopenia (*15*), and severe exfoliative dermatitis (*16*). Other drugs commonly used to treat MRSA infection, such as teicoplanin and linezolid, cause relatively more adverse reactions and serious symptoms of adverse reactions.

Based on the information presented thus far, appropriate antibiotics can be selected empirically based on a comprehensive assessment of previous *S. aureus* drug sensitivity results in the region and the hospital, as well as the patient's clinical condition, in patients with suspected *S. aureus* infections before the culture results are received. This can avoid the waste of resources and avoid adverse reactions to drugs to the extent possible. If the incidence of MRSA in previous cultures of *S. aureus* in the local area and the hospital is low, *e.g.*, the rate of MRSA detection in our hospital is only 16.1%, and the patient's condition is not very serious, then initiation of oxacillin and other drugs such as cephalosporins can be considered. Antibiotics are then adjusted in accordance with the *S. aureus* drug sensitivity results and the patient's condition. Unless these patients have severe disease and are likely to have MRSA, then empirically selecting anti-MRSA drugs such as vancomycin, linezolid, and teicoplanin for all suspected cases of *S. aureus* infection is not necessary.

In conclusion, not all suspected cases of *S. aureus* infection require anti-MRSA drugs. Instead, previous *S. aureus* susceptibility results in the area and hospital, as well as the patient's clinical profile, need to be taken into account.

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**Address correspondence to:*
Hongzhou Lu, Department of Infectious Diseases, National Clinical Research Center for Infectious Diseases, the Third People's Hospital of Shenzhen, 29 Buji Bulan Road, Shenzhen, Guangdong Province 518112, China.
E-mail: luhongzhou@fudan.edu.cn

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