Available online at www.medicinescience.org

ORIGINAL ARTICLE

Medicine Science International Medical Journal

Medicine Science 2018;7(1):162-5

Clinical features and follow-up results of the patients with methicillin-resistant Staphylococcus aureus (MRSA) in orthopedic practice

Resit Sevimli[1], Aydin Arslan[2], Yucel Duman[3], Mehmet Fatih Korkmaz[1], Mehmet Nuri Erdem[4]

[1] Inonu University School of Medicine Department of Orthopaedics and Traumatology, Malatya, Turkey
[2] Medicalpark Anadolu Hospital, Orthopaedics and Traumatology, Istanbul, Turkey
[3] Inonu University School of Medicine Department of Microbiology, Malatya, Turkey
[4] Kolan Hospital Orthopaedics and Traumatology, Istanbul, Turkey

Received 08 November 2017; Accepted 17 December 2017
Available online 08.02.2018.with doi: 10.5455/medscience. 2017.06.8744

Abstract

Treatment of the infections caused by methicillin-resistant Staphylococcus aureus (MRSA) strains in orthopedic patients is a difficult and laborious process for both the patient and physician. Staphylococcus aureus(S. aureus) is one of the leading causes of community-acquired and nosocomial infections. In this study, we aimed to investigate the susceptibilityof the MRSA strainsisolated in orthopedic patients cultured for different reasons in our clinic to various antibiotics, and to evaluate clinical characteristics of the patients and factors affecting the prognosis.

A total of 40 patients with MRSAisolated in our orthopedics clinic between December 2012 and November 2016 were retrospectively analyzed. Data including age, sex, comorbidities, previous surgeries, and previous antibiotic treatments were obtained from patients' files and electronic information system.

Of 40 patients, 60% were male, and 56% were over 60 years old. While 80% of the patients underwent an orthopedic surgery, 20% of them received no surgical intervention before the diagnosis. A total of 90% were in-patients, and the mean length of hospital stay was 22 days. The mean time from the date of hospitalization to the isolation of MRSA was 12 days. According to the consultation findings, in the clinical recovery process of the patients and in the treatment algorithm given to those patients, vancomycin and teicoplanin were found to be among the most important treatment options, in addition to significant debridement to be done, for MRSA strains. Our study results suggestthat, in addition to the surgical debridement, timely antibiotherapy is of utmost importance to reduce mortality and morbidity in MRSA-positive orthopedic patients.

Keywords: Orthopedic Infections, Methicillin-Resistant Staphylococcus Aureus, MRSA, Debridement

Introduction

Staphylococcus aureus (S. aureus) is one of the Gram-positive pyogenic bacteria which has aggregation features and can be found in the human skin and mucous membranes [1]. This microorganism may cause serious systemic infections such as bacteremia, endocarditis, toxic shock syndrome, and skin infections such as cellulitis, impetigo, and wound infections [2]. The major problem in the treatment of staphylococcal infections, which are one of the leading causes of community-acquired and nosocomial infections, is methicillin resistance. Methicillin-resistant S. aureus (MRSA) strains were previously isolated from nosocomial infections. However, they are seen in the community-acquired infections in recent years [3]. In several studies, S. aureus bacteremia was reported to have a mortality rate ranging from 13 to 34% [4,5].

In this study, we aimed to investigate the susceptibility of the MRSA strains of the MRSA strains isolated in orthopedic patients cultured for different reasons in our clinical microbiology laboratories to various antibiotics, and to evaluate clinical characteristics of the patients and factors affecting the prognosis.

***Coresponding Author:** Mehmet Fatih Korkmaz, Inonu University School of Medicine Department of Orthopaedics and Traumatology, Malatya, Turkey,
E-mail: fatih.korkmaz@inonu.edu.tr

Materials and Methods

This retrospective study included a total of 40 patients who were diagnosed with MRSA in our orthopedics clinic and underwent serial debridement in combination with antibiotherapy between December 2012 and November 2016. Data including age, sex, comorbidities, previous surgeries, and previous antibiotic treatments were obtained from patients' files and electronic information system. A written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis

Statistical analysis was performed using the SPSS for Windows version 15.0 software (SPSS Inc., Chicago, IL, USA). Descriptive data were expressed median. The chi-square test was used to analyze the risk factors of mortality. Ap value of <0.05 was considered statistically significant.

Results

Of the patients, 18 ere males and 22 were females with a mean age of 48.2 (range: 8 to 84) years. Demographic and clinical characteristics of the patients are shown in Table 1.

Table 1. Treatment stages in MRSA-positive patients

Treatment stages	Resistance	Drugs	Number of patients	Total
First Stage	Penicillin resistance 1950	1. Penicillin, SAM or first, second, third, fourth and fifth generation cephalosporins (cefazolin, cefamandole, ceftri-axone, ceftazidime, ceftaroline)	16	20
		2. Quinolones (ciprofloxacin, levofloxacin, trovafloxacin)	2	
		3. Cefalosporin + Aminoglycoside (gentamicin, amikacin)	2	
Second Stage	Penicillin 1950, Methicillin 1980, Glycopeptide 1997	1. Rifampicin (+quinolone, +SAM, +TMP_SMX, +teicoplanin)	4	17
		2. Vancomycin or teicoplanin (+gentamicin, +ciprofloxacin, + tazo-bactam)	9	
		3. Meropenem (+SAM)	2	
		4. Tazobactam	1	
		5. Ertapenem (+nidazole)	1	
		6. Ticlopidine	-	
Third Stage	Penicillin 1950, Methicillin 1980, Glycopeptide 1997, Linezolid 2001 Daptomycin 2005	1. Linezolid	1	3
		2. Daptomycin (+ciprofloxacin)	1	
		3. Tigecycline (+teicoplanin, + ticlopidine)	1	
		4. Quinupristin/dalfopristin	-	

All patients were followed in the in-patient setting, and the mean length of hospital stay was 22 (range: 7 to 83) days. The mean time from hospitalization to the MRSA recurrence was 12 days. Treatment algorithms consisting of three steps were performed, according to the antibiotic resistance of the patient (Table 2).

The patients in the orthopedics clinic underwent surgery within the last two months. The risk gradually increased in the patients with arthroplasty and open fractures, in elderly, and in those with prolonged hospitalization. All MRSA cases were considered as nosocomial infections or infectious agent associated with the health care by the relevant department. During follow-up, five patients (12.5%) died before cure was achieved. Non-survivors were elderly patients with joint arthroplasty.

Age, sex, comorbidities, previous surgeries, hospitalization within the last month, infection-related hospitalization, duration of hospitalization, and the presence of accompanying infections were found to be among the main factors affecting mortality. Of 35 patients who underwent orthopedic interventions and serial debridement, adequate response was achieved in 22 (62.8%) in their clinical follow-up ($p<0.05$).

Discussion

The prevalence of MRSA varies between countries and between hospitals [6]. This ratio was found to be changed between 0.1% and 34.4% in a multi-center study including European countries [7]. In Turkey, it ranges between about 9 and 40% [8]. Therefore, infections caused by multidrug-resistant bacteria, such as MRSA, complicate the treatment.

The treatment of MRSA is expensive and difficult, and it is considered a serious problem, as it can spread rapidly [9]. It may be present in hospitals endemically, which means it can be present without leading to an epidemic outbreak. However, it may result in outbreaks in some cases. To date, a great number of epidemic MRSA strains, which lead to epidemics, have been identified [10]. Expensive antibiotic treatments, intensive isolation measures, and prolonged hospitalization lead to a great financial burden on the health care settings.

In several studies, all isolated strains are recommended to be typed, when an epidemic or endemic increase is detected in the infection rates related to MRSA, and it is recommended to investigate the common source if a large clonal relationship is found between the strains in the results of typing [11]. Typing methods are important, since they are the indicators of the Infection Control Committee to prevent the nosocomial outbreaks and in the discovery of the causative agent and mode of transmission.

In previous studies, the mortality rate associated with MRSA has been reported between 10 and 40% [12,13]. Similarly, the mortality rate in our study was 12.5%. Monitoring and treatment of MRSA infections have become to be more dwelled on, since the mortality rates in orthopedic patients are high and the incidence of the nosocomial infections increases.

The main goal of the treatment is to provide eradication of the infection, and is to make the joint painless and functional. The treatment has two components which are surgical approach and antibiotherapy. Early diagnosis increases the success of antibiotherapy as well as it reduces the invasive procedures. Recognition of the risk factors also provides rational antibiotic use in a timely manner. The surgical choice, virulence, and susceptibility of the pathogen, duration of the symptoms, implant stability, status of peripheral tissues (bone stock), and epidemiological data (place where the surgery is performed, procedure and surgical team or relapse rates of the center, factors and mortality) are determined by the experience of the surgeon [14,15].

In studies examining the risk factors on the mortality, rational empirical antibiotic choice and timely treatment as well as the serial debridement in orthopedic patients have been found to be significant factors in the eradication of the infection [16]. In our study, serial debridement and the removal of infected bone and tissue structures from the medium played a critical role in for the treatment. In previous studies, mortality was reported to be high in the MRSA infections of the elderly with organ failure [17,18]. In our study, mortality was similarly found to be high in elderly.

Usual hygienic measures and prevention of transmission are the main factors in the prevention and control of MRSA. The small number of patients and the lack of control group as a limitation of this study. However, there is a nSeed for further multi-center studies which would explain the role of surgical debridement in the infected patients as well as the role of antimicrobial drug administration.

Conclusions

In conclusion, our study results suggest that, in addition to the surgical debridement, timely antibiotherapy is of utmost importance to reduce mortality and morbidity in MRSA-positive orthopedic patients.

Table 2. Treatments in MRSA-positive orthopedic patients

Active ingredient	Trade Name	Number of Patients Included	Reason of being preferred	Reason of not being preferred
Penicillin group (SAM) and first, second, third, fourth and fifth generation cephalosporins 1. Cefazolin sodium 2. Cefamandole 3. Ceftriaxone 5. Ceftaroline	Duocid Augmentin Alfacid	16 patientsa İ.Y. 77 (Ankle) A.Ş. 68 (Cruris abscess) A.S. 52 (Cruris) M.Ş. 63 (Cruris abscess) Ş.B. 38 (Thigh osteomyelitis) N.A. 87 (Cruris compound fracture) K.K. 48 (Tibial fracture) C.Y. 80 (Finger abscess) E.K. 13 (Humerus fracture) G.E. 22 (Operated scoliosis) M.A.A. 8 (Humerus fracture) A.Y. 62 (Olecranon bursitis) E.A. 27 (Cruris abscess) S.S. 61 (Finger fracture) Ş.S. 55 (Ankle fracture) A.T. 64 (Thigh abscess)	First Stage of the Treatment	Penicillin resistance - Since 1950
Quinolons Ciprofloxacin Levofloxacin Trovafloxacin		2 patients A.S. 48(TDP) G.G. 61 (TDP)	First Stage of the Treatment	Rapid resistance to staphylococcus
Rifampin Rifampin+Quinolon Rifampin+TMP-SMX Rifampin+Teicoplanin Rifampin+SAM	Rifcap,Rif Rif+Cipro Rif+Bactrim Rif+Targocid Rif+Augmentin	4 patients M.A.U. 43 (Cruris abscess) K.İ. 67 (Cruris fracture) Z.S. 84 (Thigh abscess) S.G. 51 (Cruris osteomyelitis)	Second Stage of the Treatment -In the cases with an implant	
Glycopeptide group Vancomycin Teicoplanin Teicoplanin+Tazobactam Teicoplanin+Vancomycin+Gentamicin Teicoplanin+ciprofloxacin	Vanko Targocid Targocid+Tazocin Targocid+Vanko+-Genta Targocid+Cipro	9 patients Y.B. 28 (Pelvical fracture) A.A. 15 (Operated scoliosis) M.S.Y. 55 (Cruris abscess) A.A. 38 (Cruris fracture) H.A.O. 46 (Cruris fracture) E.D. 43 (Cruris fracture) E.A. 13 (Hip replacement) K.D. 43 (Thigh abscess) S.Ö. 80 (Knee abscess)	Second Stage of the Treatment -It is used in patients who are refractory to penicillin or cephalosporin and in patients who have penicillin allergy.	1.Glycopeptide resistance - Since 1997 2.Formation of vancomycin resistance enterococcus 3.Nephrotoxicity
Linezolid	Zyvoxid	1 patient G.K. 47 (Knee-Cruris abscess)	Third Stage of the Treatment -If there is vancomycin resistance, 2.Transition to oral therapy is easy. 3.Diabetic foot 4.In Chronic kidney disease (CKD)	1.Linezolid resistance - Since 2001
Daptomycin Daptomycin+Ciprofloxacin	Cubicin Cubicin+Cipro	1 patient E.K. 23 (Cruris fracture)	Third Stage in the Treatment -In the staphylococcus bacteria	1.Daptomycin resistance - Since 2005 2.Bacteriostatic 3.Do not use in children
Tigecycline Tigecycline+Teicoplanin+Ticlopidine	Tygacil Tygacil+Targocid+Tienam	1 patient G.A. 81 (77.1%) (TKP)	Third Stage in the Treatment -It can be used in CKD and KCY.	1.Bacteriostatic 2.Do not use in children
Cephalosporin + aminoglycoside Cefazolin + Gentamicin Cefazolin + Amikacin Ceftazidime + Amikacin	Cefazole+Genta Cefazole + Amikacin Ceftazidime + Amikacin	2 patients Ö.B. 15 (Toe fracture) U.T. 17 (Foot abscess)	First Stage of the Treatment	
Meropenem Meropenem-SAM	Meronem Meronem-Duocid	2 patients M.K. 45 (Knee prosthesis) R.M. 43 (Hip replacement)	Second Stage of the Treatment -It is used in empiric treatment	Neutropenia
Tazobactam sodium	Tazocin	1 patient H.G. 28 (Ankle fracture)	Second Stage of the Treatment -Methicillin-sensitiveStaphylococcus and Pseudomonas mixed infections	Penicillin allergy
Ertapenem Ertapenem+Nidazolin	Invanz Invanz+Nidazol	1 patient Ü.V. 40 (Thigh abscess)	Second Stage of the Treatment -It is safe to use in children.	Penicillin allergy

References

1. Jensen AG, Wachmann CH, Poulsen KB, Espersen F, Scheibel J, Skinhøj P, Frimodt-Møller N. Risk factors for hospital-acquired Staphylococcus aureus bacteremia. Arch Intern Med. 1999;159(3):1437-44.
2. Zafar AB, Butler RC, Reese DJ, Gaydos LA, Mennonna PA. Use of 0.3% triclosan (Bacti-Stat) to eradicate an outbreak of methicillin-resistant Staphylococcus aureus in a neonatal nursery. Am J Infect Control. 1995;23(3):200-8.
3. Cameron DR, Howden BP, Peleg AY. The interface between antibiotic resistance and virulence in Staphylococcus aureus and its impact upon clinical outcomes, Clin Infect Dis. 2011;53(6):576-82.
4. Centers for Disease Control and Prevention. Staphylococcus aureus resistant to vancomycinUnited States 2002, MMWR. 2002;51(26):565-7.
5. Ayliffe GAJ. The progressive intercontinental spread of methicillin-resistant Staphylococcus aureus. Clin Infect Dis. 1997;24(Suppl 1):574-9.
6. Hudson IRB. The efficacy of intranasal mupirocin in the prevention of Staphylococcal infections: A review of recent experience. J Hosp Infect. 1994; 27(2):81-98.
7. Crowcroft NS, Ronveaux O, Monnet DL, Mertens R. Methicillin-resistant Staphylococcus aureus and antimicrobial use in Belgian Hospitals. Infect Control Hosp Epidemiol. 1999;20:316.
8. Jernigan JA, Clemence MA, Stott GA, Titus MG, Alexander CH, Palumbo CM, Farr BM. Control of methicillin-resistant Staphylococcus aureus at a university hospital: One decade later. Infect Control Hospital Epidemiol. 1995;16(12):686-96.
9. Boyce JM, Potter-Bynoe G, Chenevert C, King T. Environmental contamination due to methicillin-resistant Staphylococcus aureus. Infect Control Hosp Epidemiol. 1997;18:622-7
10. Holmes NE, Turnidge JD, Munckhof WJ, Robinson JO, Korman TM, O'Sullivan MV, Anderson TL, Roberts SA, Gao W, Christiansen KJ, Coombs GW, Johnson PD, Howden BP. Antibiotic choice may not explain poorer outcomes in patients with Staphylococcus aureus bacteremia and high vancomycin minimum inhibitory concentrations, J Infect Dis. 2011;204(3):340-7.
11. Kluytman J, Belkum A, Verbrugh H. Nasal carriage of Staphylococcus aureus: Epidemiology, underlying mechanisms and associated risks. Clin Microbiol Rev. 1997;10(3):505-20.
12. Bannerman TL, Hancock GA, Tenover FC, Miller JM. Pulsed-field gel electrophoresis as a replacement for bacteriophage typing of Staphylococcus aureus. J Clin Microbiol. 1995;33(3):551-5.
13. Lowy F. Staphylococcus aureus infections. N Engl J Med. 1998;339:520-32.
14. Doebbeling BN. Nasal and hand carriage of Staphylococcus aureus in healthcare workers. J Chemotherapy. 1994;6(Suppl 2):11-7.
15. Nicolle LE, Dyck B, Thompson G, Roman S, Kabani A, Plourde P, Fast M, Embil J. Regional dissemination and control of epidemic methicillin-resistant Staphylococcus aureus. Infect Control Hosp Epidemiol. 1999;20(3):202-5.
16. Onorato M, Borucki MJ, Baillargeon G, Paar DP, Freeman DH, Cole CP, Mayhall CG. Risk factors for colonization or infection due to methicillin-resistant Staphylococcus aureus in HIV-positive patients: A retrospective case control study. Infect Control Hosp Epidemiol. 1999;20(1):26-30.
17. Miller MA, Dascal A, Portnoy J, Mendelson J. Development of mupirocin resistance among of methicillin-resistant Staphylococcus aureus after widespread use of nasal mupirocin ointment. Infect Control Hosp Epidemiol. 1996;17(12):811-3.
18. Tenover FC, Arbeit K, Archer G, Biddle J, Byrne S, Goering R, Hancock G, Hébert GA, Hill B, Hollis R, Comparison of traditional and molecular methods of typing isolates of Staphylococcus aureus. J Clin Microbiol. 1994;32(2):407-15.