

MRSA bacteremia and new-onset aortic and mitral regurgitation: a pernicious and tricky association

Maria Cinquegrani, Francesco Cei, Matteo Pistoia, Nicola Mumoli

Department of Internal Medicine, ASST Ovest Milanese, Magenta (MI), Italy

ABSTRACT

Methicillin-resistant *Staphylococcus Aureus* (MRSA) bacteremia is a complex and lethal condition. We reported the clinical case of a 58-year-old woman who developed MRSA bacteremia after a 3-month hospitalization for trauma and sepsis. Delay in diagnosis of aortic and mitral endocarditis in the setting of new-onset regurgitations, as the application of suboptimal therapy with linezolid and vancomycin, led to widespread disease with embolic dissemination and development of septic infarctions. Clinicians must be aware of the necessity to consider as high risk of endocarditis new onset valvular regurgitations and of the evidence about the need for daptomycin in treating high-risk MRSA bacteremia.

Correspondence: Nicola Mumoli, MD, Department of Internal Medicine, Ospedale Fornaroli, Via Donatori Sangue, 50, 20013 Magenta (MI), Italy.
Tel.: +39.02979631. Fax: +39.02979611.
E-mail: nicola.mumoli@asst-ovestmi.it

Key words: methicillin-resistant *Staphylococcus Aureus* bacteremia; infective endocarditis; acute cardiac valve regurgitation.

Conflict of interest: the authors declare no potential conflict of interest.

Funding: none.

Ethics approval and consent to participate: no ethical committee approval was required for this case report because this article does not contain any studies with human participants or animals.

Consent for publication: the patient gave her written consent to use his personal data for the publication of this case report and any accompanying images.

Received: 24 June 2023.
Accepted: 27 June 2023.

Publisher's note: all claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claim that may be made by its manufacturer is not guaranteed or endorsed by the publisher.

©Copyright: the Author(s), 2023
Licensee PAGEPress, Italy
Italian Journal of Medicine 2023; 17:1618
doi:10.4081/ijm.2023.1618

This work is licensed under a Creative Commons Attribution NonCommercial 4.0 License (CC BY-NC 4.0).

Case Report

Methicillin-resistant *Staphylococcus Aureus* (MRSA) bacteremia is a complex, and often lethal (20-30% of cases), condition, with sneaky presentations that occult catastrophic clinical scenarios, often hard to treat.¹ It's also a frequent condition, as it represents 25% to 50% of total *Staphylococcus Aureus* (SA) bacteremia in both Southern Europe and the United States, which has an overall incidence of 50 cases per 100,000 people.² Acute valve regurgitation is also a challenging condition, which encompasses a complex diagnostic workup to rule out potentially life-threatening conditions such as infective endocarditis (IE), aortic dissection, and myocardial infarction.³ IE diagnosis is also a challenge, especially in the first days, as transthoracic echocardiography (TTE) and sometimes also transesophageal echocardiography (TEE) had low sensibility, decreasing the accuracy of the modified Duke's criteria.⁴

We describe a complex case of IE due to MRSA characterized by new-onset aortic and mitral regurgitations to elucidate pitfalls, risks, and dramatic consequences of delay in correct diagnosis and correct treatment of these conditions.

A 58-year-old woman was admitted from the rehabilitation department for persistent fever, severe asthenia, and hypotension despite treatment with piperacillin/tazobactam 4mg grams (g) for 3 days. In the past three months, she was hospitalized for septic shock complicating acute infectious colitis and for an accidental fall with a left femur fracture treated conservatively. She was exposed to piperacillin/tazobac-

tam, parental nutrition, and a long immobilization. In her history, she underwent gastric bypass with subsequent sarcopenia and partial thyroidectomy following hypothyroidism, had alcohol abuse, and had bipolar disorder; her cardiac history was unremarkable.

After the first hours, she developed pulmonary edema requiring noninvasive mechanical ventilation and high-dose intravenous furosemide. Bedside echocardiography showed presumed new-onset aortic and mitral regurgitations of moderate severity, no vegetations and left ventricular structural alterations were found (estimated ejection fraction 55-60%). MRSA was found on three blood samples, so, considering a mild degree of renal insufficiency (creatinine 1.8 milligrams/milliliters), linezolid 600 milligrams (mg) two times a day was added with an initial resolution of fever and stabilization of the respiratory failure [minimal inhibitory concentration (MIC) for linezolid was 2 micrograms/milliliter ($\mu\text{g/mL}$)].

After 5 days, right flank pain, fever, and a new episode of pulmonary edema occurred. The blood samples were persistently positive for MRSA, and vancomycin 500 mg three times a day was begun, as MIC was 2 $\mu\text{g/mL}$ and met EUCAST sensibility criteria. Abdominal computed tomography (CT) showed renal and splenic embolic lesions (Figure 1A, arrows). For concomitant respiratory distress, cardiac CT was performed, with confirmation of endocarditis on both non-coronary aortic cusp and a second lesion of 4 mm at the coronary sinus (Figure 1B, arrow). An isoechoic

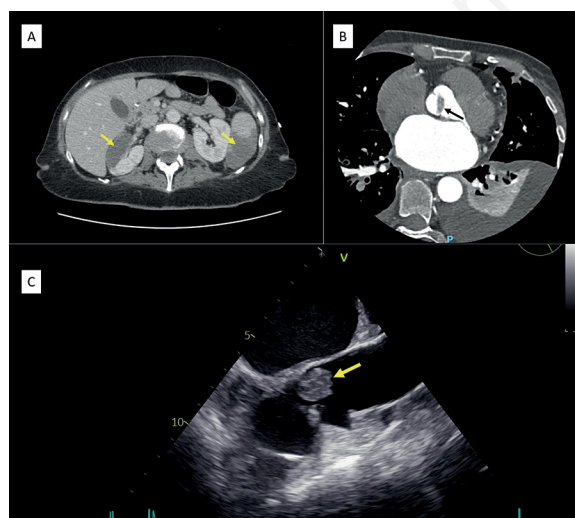


Figure 1. A) Abdominal computed tomography showing renal and splenic embolic lesions (arrows); B) Cardiac computed tomography showing endocarditis on both non-coronary aortic cusp and a second lesion of 4 mm at the coronary sinus (arrow); C) Transthoracic echocardiography showing an isoechoic lesion [15.5 millimeters (mm)] at the non-coronary aortic cusp (arrow).

lesion (15 x 5 mm) was found at the non-coronary aortic cusp at TTE (Figure 1C, arrow); also, both mitral and aortic regurgitations were restaged as severe; systolic function was still normal. For persistent MRSA blood samples, vancomycin was substituted with daptomycin 8 mg/kilogram with the resolution of the bacteremia.

After 20 days of medical therapy, cardiac surgery with implantation of the prosthetic mitral and aortic valve was performed. Finally, the patient was discharged to the rehabilitation department.

Discussion

Approaching MRSA bacteremia is tricky. A large debate about complicated and not-complicated SA bacteremia is reported in the literature, and it's important to choose the correct antimicrobial treatment and its duration. Koujzer *et al.* tried to describe an algorithm, detailed in Table 1, which includes host factors, characteristics of the bacteremia, and clinical course, to identify patients with a low or high risk of metastatic infection.⁵ In our case, previous intravenous treatments (both antimicrobials and parenteral nutrition), persistent fever despite piperacillin/tazobactam, and persistent bacteremia classified it since admission as a high-risk MRSA bacteremia.

Even if in antibiogram MRSA is often sensible to linezolid, its use in MRSA is controversial, and a mild transient sepsis-related elevation of creatinine doesn't appear a good reason to delay vancomycin or dapto-

Table 1. Risk stratification for metastatic Methicillin-resistant Staphylococcus Aureus bacteremia; adapted from Koujzer *et al.*⁵

Predisposing host factors

Implanted prosthesis
Intravenous drug use
History of endocarditis

Features of bacteremia

Duration
Community acquisition
Short time to positivity (at least 24h)
Treatment delay

Clinical course

Persistent fever
Unknown source of infection
Signs of metastatic infection

Low risk

None of the risk factors

High risk

A combination of at least two risk factors in two domains

Intermediate risk

Both criteria of High and Low risk not met

mycin. Linezolid is only bacteriostatic, and appeared unreasonable in high-risk bacteremia; also, there are few randomized trials for this treatment, with an overall success rate of about 50%.⁶ Furthermore, also vancomycin treatment is actually controversial in MRSA bacteremia. It's only low bactericidal, often is underdosed (the suggested dose is 30-60mg/kg), and efficacy, when MIC is >1 µg/mL is discussed, as these values could mask the presence of hetero-Vancomycin intermediate SA (hetero-VISA).⁷ In patients with MRSA bacteremia and a MIC for Vancomycin >1 µg/mL, daptomycin is associated with reduced mortality [odds ratio (OR) 0,53 confidence interval (CI) 0,29-0,98] and higher treatment success rate (OR 2,2, IC 1,63-2,96),⁸ so it's reasonable time to consider it as first-line treatment.

2015 modified Duke's criteria included four echographic criteria for IE: vegetation, abscess, valvular perforation or aneurysm, and dehiscence of a prosthetic valve.⁹ However, especially in the early phases, direct vegetation could not be seen especially in bedside TTE, and perforation it's difficult to demonstrate, so these criteria could lead to delay in diagnosis and treatment. In particular, new-onset aortic and mitral regurgitation, without concomitant left ventricular dysfunction, should be watched with particular attention. Perforation isn't the only mechanism for regurgitation in the course of IE, as leaflet prolapse, annular destruction, and failure of coaptation could concur;³ so, we cannot rely only on modified Duke's criteria, especially in the setting of a High-risk MRSA bacteremia. So, a rapid second-level test should be provided over the course of hours. Even if TEE is the preferred diagnostic modality, multislice CT had shown excellent sensibility (96%) and specificity (88%), with a high degree of association in measuring dimensions of vegetations with TEE ($r=0,95$, $P<0,001$).¹⁰ Our case demonstrates the utility of CT in confirming the diagnosis in the course of clinical instability and plays a role in programming the surgical treatment.

In conclusion, our case showed many pitfalls in approaching risk stratification, diagnostic workup, and treatment of MRSA bacteremia. We emphasized the

role of daptomycin in the treatment in the face of linezolid and vancomycin and the role of CT in the face of TTE and TEE.

References

1. Tabah A, Laupland KB. Update on Staphylococcus aureus bacteremia. *Curr Opin Crit Care* 2022;28:495-504.
2. Lam JC, Stokes W. The Golden Grapes of Wrath - Staphylococcus aureus Bacteremia: A Clinical Review. *Am J Med* 2023;136:19-26.
3. Mokadam NA, Stout KK, Verrier ED. Management of acute regurgitation in left-sided cardiac valves. *Tex Heart Inst J* 2011;38:9-19.
4. Vieira ML, Grinberg M, Pomerantzeff PM, et al. Repeated echocardiographic examinations of patients with suspected infective endocarditis. *Heart* 2004;90:1020-4.
5. Kouijzer IJE, Fowler VG Jr, Ten Oever J. Redefining Staphylococcus aureus bacteremia: A structured approach guiding diagnostic and therapeutic management. *J Infect* 2023;86:9-13.
6. Stevens DL, Herr D, Lampiris H, et al. Linezolid versus vancomycin for the treatment of methicillin-resistant Staphylococcus aureus infections. *Clin Infect Dis* 2002;34:1481-90.
7. Conly JM, Johnston BL. VISA, hetero-VISA and VRSA: the end of the vancomycin era? *Can J Infect Dis* 2002;13:282-4.
8. Samura M, Kitahiro Y, Tashiro S, et al. Efficacy and Safety of Daptomycin versus Vancomycin for Bacteremia Caused by Methicillin-Resistant Staphylococcus aureus with Vancomycin Minimum Inhibitory Concentration >1 µg/mL: A Systematic Review and Meta-Analysis. *Pharmaceutics* 2022;14:714.
9. Habib G, Lancellotti P, Antunes MJ, et al. 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *Eur Heart J* 2015;36: 3075-128.
10. Feuchtner GM, Stolzmann P, Dichtl W, et al. Multislice computed tomography in infective endocarditis: comparison with transesophageal echocardiography and intraoperative findings. *J Am Coll Cardiol* 2009;53: 436-44.