CASE REPORT

Community-associated methicillin-resistant Staphylococcus aureus infection in Portugal

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Abstract Methicillin-resistant Staphylococcus aureus (MRSA) has recently emerged as a cause of community-acquired infections among individuals without risk factors. Community-associated MRSA (CA-MRSA) appears to be more virulent, causing superficial mild skin and soft tissue infections to severe necrotizing fasciitis, and in rare cases, pneumonia.

Community-associated MRSA was first reported in Australia in the early 80s, after almost two decades in the USA, and then in several countries in Europe, Asia and South America. No data exists in Portugal.

We report the first case of CA-MRSA infection in Portugal, in a young adult with severe necrotizing pneumonia, complicated with bilateral empyema and respiratory failure.

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comunidade associada;
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Pneumonia da comunidade por Staphylococcus aureus resistente à meticilina em Portugal

Resumo Recentemente assistiu-se à emergência de infeções na comunidade por Staphylococcus aureus meticilina-resistente (MRSA) em indivíduos sem fatores de risco. O MRSA associado à comunidade (CA-MRSA) parece ser mais virulento, causando desde infeções superficiais da pele e tecidos moles até afasseite necrosante e, raramente, pneumonia.

O CA-MRSA foi inicialmente identificado na Austrália no início da década de 80 e, após cerca de duas décadas, surgiu nos EUA e em vários países da Europa, Ásia e América do Sul. Não existe informação disponível acerca da prevalência em Portugal.

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Background

*Staphylococcus aureus* causes different types of infections, mostly minor skin and soft tissue infections (SSTI), but also severe pneumonia and sepsis, associated with high morbidity and mortality.¹

Methicillin-resistant *S. aureus* (MRSA), first reported in the United Kingdom in 1961,² is one of the most important agents of antibiotic-resistant health care-associated infections worldwide.³ In 2008, Portugal was the only European country with a prevalence of MRSA higher than 50%.⁴

During the past decade, community-associated MRSA (CA-MRSA) infections emerged worldwide among healthy individuals who did not have risk factors for hospital-acquired MRSA (HA-MRSA), mostly children and young adults.⁵,⁶ Both agents are epidemiological, genotypical and phenotypically unrelated.⁷ Community-associated MRSA was first reported in Australia in the early 80s,⁸ about a decade later in the USA⁹ and then in Europe, Asia and South America.¹⁰

Its exact prevalence is unknown. Outbreaks have been described in different settings in the community.¹⁰ A high prevalence was found in patients with SSTI,¹¹ namely intravenous drug users in North America,¹²,¹³ as well as in the UK.¹⁴ Initially, most of CA-MRSA isolates were only resistant to β-lactams, associated with the smallest types (IV and V) of the staphylococcal cassette chromosome *mec* (SCCmec).¹⁵ However, in recent years there has been increased resistance to other antibiotic classes.¹³ It frequently carries Panton–Valentine leukocidin (PVL) gene, an exotoxin causing leukocyte destruction and tissue necrosis, increasing severity of infections, especially pneumonia, with higher mortality rate.¹⁶

At present, the predominant CA-MRSA clones in the USA are USA300 (ST8-IVa) and USA400 (ST1-IV),¹⁷ particularly USA300, which is widely disseminated in the community and hospitals,¹⁸ whereas in Europe and Australia, the most relevant are the European clone (ST80-IVc)¹⁹ and the Southwestern Pacific clone (ST30-IV),²⁰ respectively.

Skin and soft tissue infections are the most common manifestations of CA-MRSA, but serious invasive infections, namely pneumonia, are also described.²¹ In a large USA study only 2% of CA-MRSA infections were pneumonia.²²

We describe the first documented case of CA-MRSA infection in Portugal, of a patient with severe necrotizing pneumonia complicated with bilateral empyema.

Case presentation

A 33-year-old homeless Armenian man, who had been living in Portugal for seven years, with a past medical history of chronic B and C hepatitis and active parentral drug abuse came to the emergency department (ED) with a 5-day history of right pleuritic chest pain and, in the previous two weeks, non-quantified fever and purulent sputum.

The chest X-ray showed a lower bilateral pulmonary infiltrate and right-sided pleural effusion. HIV-check (4th generation ELISA method) was positive. A community-acquired pneumonia (CAP) with parapneumonic effusion was diagnosed and the patient was discharged on amoxicillin/clavulanate.

Two days later he returned to the ED with worsening symptoms. He was febrile, tachycardic and tachypneic, with pulse oxygen saturation of 95% on room air and had diminished breath sounds on the right hemithorax. Arterial blood gases revealed arterial partial pressure of oxygen (PaO₂) of 67.3 mmHg. Laboratory tests showed elevated C-reactive protein (35.4 mg/dL, which 2 days earlier had been 15.6 mg/dL) and leucocytosis (14.5 × 10⁹/μL; neutrophils 94%). No acid-fast bacilli were found on sputum smear (three samples). The patient was admitted to the Infectious Diseases ward. Clarithromycin was added and, since he had markedly depressed immunological state (46 CD4 T-cells/μL, 10.3% with viral load > 180,000 copies/mL), prophylactic therapy with trimethoprim–sulfamethoxazole was initiated. In the following 2 days, his clinical condition rapidly deteriorated with acute respiratory failure needing invasive mechanical ventilation. He was transferred to the intensive care unit (ICU).

In the ICU a bilateral thoracocentesis was performed, revealing two large-volume empyemas. The chest CT scan showed right lung consolidation. Methicillin-resistant *S. aureus* was recovered from pleural fluid, bronchoalveolar lavage (BAL) and blood cultures. The microorganism was susceptible to vancomycin, with *in vitro* minimum inhibitory concentration (MIC) of 2 μg/mL (Etest®) and resistant to ciprofloxacin, erythromycin and clindamycin; it was also susceptible to linezolid (MIC = 2 μg/mL), teicoplanin (MIC < 0.5 μg/mL), gentamicin (MIC < 0.5 μg/mL) and trimethoprim–sulfamethoxazole (MIC < 10 μg/mL). Vancomycin was started by continuous infusion adjusted to maintain serum levels of 20–25 mg/L. No improvement was noted after 7 days. A transesophageal echocardiogram excluded endocarditis.
Cultures were repeated revealing persistence of MRSA on BAL and tracheal secretions, with the same pattern of susceptibility. The hypothesis of CA-MRSA was suggested and linezolid IV was started. After a 10-day course there was complete clinical resolution.

The molecular characterization of the isolates was done by pulsed-field gel electrophoresis,23 spa typing,24 multilocus sequence typing22 and SCCmec typing and subtyping.16,27 The presence of PVL was also assessed.16 The etiological agent was identified as CA-MRSA belonging to the USA300 epidemic clone (ST8-IV a, t008, PVL positive).

The patient had a long ventilator course. A tracheostomy was performed on the 21st day. He was discharged from ICU on the 56th day and from hospital on the 179th day.

Conclusions

This is the first published case report of a CA-MRSA identified in Portugal, which led to a rare infection, necrotizing pneumonia with empyema.

The isolated CA-MRSA belongs to the epidemic clone USA300, which is wide spread in the USA, where it is also found in a hospital environment, being reported as the most common agent of SSTI.29 It has also been isolated in Europe,9 but there were no prior cases reported in Portugal.

Most CA-MRSA infected patients reported recent or concomitant influenza-like illness and/or recent antimicrobial exposure,30 which was not the case with our patient. Nor did he have any other recognised risk factors for HA-MRSA, such as recent hospital admission, observation in a health care centre or recent antibiotic therapy. However, he was a homeless man with intravenous drug abuse habits, so in this context he could have had prior MRSA SSTI or exposure to another infected person. Not all cases have an identified risk factor like this one.

Necrotizing pneumonia associated with PVL producing strains has a high mortality rate that can reach 75%.16 In a series of 24 patients with CA-MRSA pneumonia, all patients with PVL producing strains died, compared with 47% of PVL non-producing strains (increased risk of 1.56).31 In another larger study, which included 50 patients with pneumonia caused by PVL producing CA-MRSA, the overall mortality was 56%.32 In our patient, CA-MRSA had elevated in vitro MIC to vancomycin and resistance to several antibiotic classes. Clinical deterioration may be explained by an increase in PVL levels, which can occur with sub-inhibitory concentrations of oxacillin and vancomycin.33 In contrast, even sub-inhibitory concentrations of clindamycin and linezolid were shown to reduce PVL levels,31 probably by inhibition of protein synthesis, which may explain the therapeutic success in our patient. Finally, others have shown that patients not responding to vancomycin frequently got better with the association of linezolid and rifampicin.34 There are few available guidelines and no randomized clinical studies for comparing the different antibiotic therapies.

The recovery of a multidrug-resistant USA300 isolate from a drug user is worrying because of the high rate of transmission in this specific population,33 causing concerns about possible increased rates of this agent in community-acquired infections in Portugal.

This report underlines the importance of CA-MRSA as a potential pathogen of severe CAP and the need to reinforce epidemiological surveillance. CA-MRSA infections do not cause specific signs or symptoms. However, it is crucial that attending clinicians and hospital microbiology laboratories have a high suspicion index to CA-MRSA when MRSA is isolated from patients with no risk factors for HA-MRSA but who have skin and soft tissue infections or pneumonia with a marked toxic and necrotizing component. Control efforts aimed at preventing the spread of the infection are feasible and can ultimately be successful.30

Consent

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of Portuguese Journal of Pulmonology.

Author’s contributions

RN drafted the manuscript. PF made substantial contribution by acquisition of data. JGP, JS, VM, CT and PP participated in the sequence alignment and also revised the manuscript critically for important intellectual content. EG and FM performed the microbiological assays and also revised the manuscript. AT, MM and MHL carried out the molecular genetic studies and also made substantial contribution in the manuscript’s revision. JPG and PP have given final approval of the version to be published. All authors read and approved the final manuscript.

Conflicts of interest

The authors have no conflicts of interest to declare.

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References


