



Pneumonia caused by coagulase-positive methicillin-resistant *Staphylococcus aureus*

Pneumonija izazvana koagulaza-pozitivnim meticilin rezistentnim *Staphylococcus aureus*-om

Biljana Lazović*, Radmila Dmitrović*, Isidora Simonović*, Nevena Jovičić†, Sanja Šarac‡, Rade Milić‡, Vuk Aleksić*

*Clinical Hospital Center Zemun, Department of Pulmonology, Belgrade, Serbia;

†University Children's Hospital, Belgrade, Serbia; ‡Military Medical Academy, Pulmonology Clinic, Belgrade, Serbia

Abstract

Introduction. *Staphylococcus (S.) aureus* is one of the most omnipresent and dangerous human pathogens, whose main characteristic is the production of the enzyme coagulase. This characteristic serves to identify and assess the pathogenicity of the bacteria. In addition to skin infections, endocarditis, osteomyelitis, and infectious arthritis, it is a common cause of pneumonia both in children and adults. **Case report.** We described a case of a 65-year-old woman with a dry cough and malaise with patchy areas of consolidation on the chest X-ray and “ground-glass” opacity with bronchial wall thickening and unilateral mediastinal lymphadenopathy on chest computed tomography imaging. Methicillin-resistant *S. aureus* was isolated from the bronchoalveolar aspirate taken during bronchoscopy. The woman was empirically treated with azithromycin, and later, based on the antibiogram findings, azithromycin was replaced with meropenem, after which her health improved. **Conclusion.** We presented a rare case of pneumonia with unconvincing symptomatology and laboratory and radiological findings. Paying more attention to such cases in the future is crucial, especially to the use of antibiotics to which staphylococci are increasingly developing resistance.

Key words:

antibiotics; bronchoscopy; coagulase; methicillin resistance; pneumonia; staphylococcus aureus.

Apstrakt

Uvod. *Staphylococcus (S.) aureus* je jedan od najprisutnijih i najopasnijih humanih patogena čija je glavna karakteristika stvaranje enzima koagulaze. Ova karakteristika omogućava identifikaciju i procenu patogenosti bakterije. Pored kožnih infekcija, endokarditisa, osteomijelitisa i infektivnog artritisa, čest je uzročnik pneumonije kako kod dece tako i kod odraslih. **Prikaz bolesnika.** Prikazana je žena starosti 65 godina, sa tegobama u vidu suvog kašlja i malaksalosti, sa rentgenskim nalazom mrljastih polja konsolidacije i promenama tipa „mlečnog stakla“ sa zadebljanjem bronhijalnog zida i jednostranom mediastinalnom limfadenopatijom na snimku grudnog koša dobijenom kompjuterizovanom tomografijom. Meticilin rezistentni *S. aureus* izolovan je iz bronhoalveolarnog aspirata uzorkovanog tokom bronhoskopije. Bolesnica je empirijski lečena azitromicinom, a kasnije, na osnovu rezultata antibiograma, isključen je azitromicin i uveden meropenem posle čega je usledilo poboljšanje zdravstvenog stanja bolesnice. **Zaključak.** Prikazan je redak slučaj pneumonije sa neubedljivom simptomatologijom, laboratorijskim i radiološkim nalazima. Neophodno je posvetiti više pažnje ovakvim slučajevima ubuduće, posebno na upotrebu antibiotika na koje stafilokoke sve više razvijaju rezistenciju.

Ključne reči:

antibiotici; bronhoskopija; koagulaza; meticilin, rezistencija; pneumonija; staphylococcus aureus.

Introduction

Coagulase-positive *Staphylococcus (S.) aureus* is one of the most omnipresent and dangerous human pathogens, both because of its virulence and capability to develop antibiotic resistance ¹. *S. aureus* is the only species of the genus *Staph-*

lococcus that produces coagulase, and this characteristic is used as one of the criteria for identifying and assessing staphylococcal pathogenicity ². Pneumonia, one of the diseases caused by *S. aureus*, is not so common except in patients on corticosteroid therapy, those who already have influenza, or those with chronic bronchopulmonary diseases.

Pneumonia can occur as a primary lung infection or by the hematogenous spread of a pathogen (as an intravenous catheter infection, endocarditis, or soft tissue infection), as well as a consequence of intravenous drug administration¹. According to the data in the literature, it is interesting that in some populations, *S. aureus* is the most common cause of hospital-acquired pneumonia (HAP), defined as an event that happens more than 48 hours after admission to the hospital^{1, 3, 4}. Methicillin-resistant *S. aureus* (MRSA) is becoming the pathogen that all the more often causes other forms of pneumonia: community-acquired pneumonia (CAP), healthcare-associated pneumonia (HCAP), and ventilator-associated pneumonia (VAP)⁵. Nowadays, according to some authors, community-associated methicillin-resistant *S. aureus* (CAMRSA) is the newest menace to patients hospitalized with pneumonia. The Center for Disease Control and Prevention (CDC) has set the following criteria for distinguishing CAMRSA from other hospital strains: a) a diagnosis of MRSA made in an outpatient setting or culture positive for MRSA 48 hours after hospital admission; b) no evidence of MRSA infection or colonization in the patient's medical history; c) for the last year the patient has not been hospitalized, stayed in a nursing home, received hospice care, underwent dialysis or surgery; d) the patient does not have a permanently applied catheter or another medical device that passes through the skin into the body⁶. As stated by multiple authors, the number of hospitalizations due to *S. aureus* pneumonia decreased by 24% from 2009–2012 in the USA, largely driven by a 19% decrease in MRSA pneumonia⁷. We herein described a case of a woman who came to our hospital with specific radiological findings, in whom *S. aureus* was isolated during hospitalization and later confirmed that the pneumonia was caused by MRSA.

Case report

A 65-year-old woman came to our hospital complaining of a dry cough and malaise lasting for several days. During the examination, on admission, the patient was afebrile, blood pressure was 120/70 mmHg, and auscultation breathing noise was weakened on both sides without any accompanying pathological findings. The patient submitted a chest X-ray, done outside of our hospital, showing bilateral patched areas of consolidation, predominantly basal without pleural effusion (Figure 1A), on the basis of which the attending physician decided to hospitalize the patient. Laboratory findings were within normal range, except for C-reactive protein

(CRP), which was elevated to 100 mg/mL. Sputum was sterile. Tumor markers like neuron-specific enolase (NSE), carcinoembryonic antigen (CEA), and the cytokeratin 19 fragmentation antigen (CYFRA 21-1) were also negative. The patient was prescribed azithromycin for seven days, after which the level of CRP was still increased. We then decided to do a chest high-resolution (HR) computed tomography (CT) HRCT, which showed bilateral diffuse patchy consolidations and subtle "ground-glass" opacities with predominantly subpleural and peribronchial distribution with present bronchial dilatation and wall thickening in the abnormal region, unilateral mediastinal lymphadenopathy without pleural effusion (Figure 1B - 1H). Since the diagnosis was not discernible, it was decided to perform a bronchoscopy, during which a bronchoaspirate was taken, seeded on an appropriate medium where a coagulase-positive *S. aureus* was later isolated. According to the antibiogram, the meropenem was administered intravenously for seven days. After the application of meropenem, the radiological changes were withdrawn, and the CRP decreased to 20 mg/mL, after which the patient was released for home treatment. During hospitalization, according to the protocol for sepsis, we made an additional cardiological ultrasound examination and a Doppler ultrasound of the legs, both of which were within normal range.

Discussion

In recent years, the prevalence of MRSA-induced pneumonia has declined among hospitalized patients in the United States. This fact is accompanied by mortality improvement and a shortened hospital stay. MRSA pneumonia prevalence constantly reduced from 2009 (75.6 cases per 100,000 releases) to 2012 (56.6 cases per 100,000 releases)⁷. Further along, some authors believe that CAP caused by *S. aureus* has a high mortality rate, around 16.6% according to their research⁸, but, on the contrary, the mortality rate from MRSA pneumonia decreased from 7.9% to 6.4% between 2009–2012⁷. In addition to affecting infants and children⁹, MRSA pneumonia is becoming more common in the elderly population. Our patient was 65 years old at the time of diagnosis; similar average data was obtained by different authors who reported that the median age for HAP was 68 years, and for HCAP, 74 years¹⁰. Dry cough and malaise were the main symptoms of our patient without the accompanying fever. Data from some studies show that cough is the most common symptom in 86% of cases, shortness of breath in 79%, spu-



Fig. 1 – A) Chest X-rays of the presented patient: bilateral patchy areas of consolidation predominantly basal without pleural effusions; B-F) High-resolution computed tomography (HRCT), various radiological sections: bilateral diffuse patchy consolidations and subtle “ground-glass” opacities with the predominantly subpleural and peribronchial distribution; G) HRCT: bronchial dilatation and wall thickening in inflammatory regions; H) HRCT: unilateral mediastinal lymphadenopathy, no pleural effusion.

tum production in 64%, while fever is recorded in 50%, and weakness in 43% of respondents ¹¹. In one study, on chest examination, doctors noticed the lower respiratory sound and sporadic rales at the base of both lungs, similar to our findings ¹². Laboratory findings were inconclusive, except for elevated CRP. A slight increase in leukocytes with the predominance of neutrophils in the proportion of 94% represented a significant laboratory result that indicated a bacterial infection. CRP and procalcitonin were also elevated at 14.2 mg/dL and 26.6 ng/mL, respectively ¹². In our patient, bacteria were not isolated by microbiological treatment of sputum; contrary to some studies where MRSA was isolated from sputum, we used bronchoalveolar lavage, and all our results were confirmed in blood culture ^{13,8}. Tumor markers were negative; furthermore, we could not find any research about the interconnection between MRSA pneumonia and changes in the levels of tumor markers. Radiological findings showed patched areas on both lungs; a similar description was given by other authors ¹³. One retrospective study described the percentage of individual changes in X-ray findings in MRSA pneumonia – the most commonly described were cavitation/necrosis (43.5%), lobar pneumonia (37.5%), multilobar pneumonia (31.2%), effusions/empyema (31.2%), and diffuse patchy (25%) infiltrates ¹⁴. In another case report, authors described CT findings as multiple consolidations in bilateral upper and lower lobes ¹³. According to data from another retrospective study, “ground-glass” attenuation was the most described finding on CT (79.4%), compared to bronchial wall thickening (60.3%), consolidation (58.8%), bilateral pleural effusion (51.5%), and bilateral lymph node enlargement (64.7%). The changes most commonly affected the lower lung fields ¹⁵. Most of the above-described changes were present on the CT of our patient. Bronchoscopically, we took an aspirate from which MRSA was isolated after cultivation, thus making the right diagnosis. Searching the literature, we came across only one study where bronchoscopy was used to take a bronchoalveolar lavage from which *S. aureus* was isolated in more than 100,000 bacteria per mL; thus, this finding was considered significant for diagnosis ¹⁶.

Prior to diagnosing MRSA pneumonia, based on the clinical picture and radiological findings, the patient was given azithromycin intravenously for seven days; the same antibiotic was empirically included by doctors in one local hospital, assuming it was CAP ¹². Based on the results of the antibiogram, we decided to change the antibiotic and administer meropenem. However, according to the results of the antibiogram and in accordance with their experience, some authors opted for linezolid ¹³, whereas others noted a significant decrease in CRP using tigecycline empirically ¹². According to new guidelines for empiric treatment of MRSA pneumonia, the treatment should include vancomycin or linezolid ¹⁷, although a few authors prefer linezolid because of its ability to inhibit bacterial toxin production. A randomized trial showed superiority in clinical outcomes but not in mortality after linezolid administration compared with vancomycin in HAP or HCAP MRSA pneumonia ¹⁸. Some authors also believe MRSA pneumonia should be treated with vancomycin, linezolid, or ceftaroline in resistant cases ¹⁹. Our patient was hospitalized for more than two weeks, while according to some researchers, the length of hospital stay for MRSA pneumonia was between 6.9–7.8 days ⁷.

Conclusion

We have presented a rare case of pneumonia caused by MRSA, with few symptoms and unconvincing laboratory and radiological findings. Timely thinking, adequate diagnostics, and antibiotic therapy will reduce morbidity and mortality rates of this type of pneumonia. A crucial problem today is the staphylococcal strain which is becoming increasingly resistant to the antibiotic therapy applied according to therapeutic protocols. Therefore, in the future, more rational use of antibiotics in treating infectious conditions must be taken into account.

Conflict of interest

The authors declare no conflict of interest.

R E F E R E N C E S

1. *Bush LM, Vasquez- Pertejo MT*. Staphylococcal infections. MSD MANUAL Professional version. Available from: <https://www.msmanuals.com/en-jp/professional/infectious-diseases/gram-positive-cocci/staphylococcal-infections#> [last modified March 2021].
2. *Berger-Jekić O, Dinić M, Đukić S, Jelesić Z, Kocić B, Kulauzov M*, et al. Medical bacteriology. Belgrade: Savremena administracija; 2008. (Serbian)
3. *McEachern R, Campbell GD Jr*. Hospital-acquired pneumonia: epidemiology, etiology, and treatment. *Infect Dis Clin North Am* 1998 Sep; 12(3): 761–79, x.
4. *Richards MJ, Edwards JR, Culver DH, Gaynes RP*. Nosocomial infections in medical intensive care units in the United States. National Nosocomial Infections Surveillance System. *Crit Care Med* 1999; 27(5): 887–92.
5. *Carleton HA, Diep BA, Charlebois ED, Sensabaugh GF, Perdreau-Remington F*. Community-adapted methicillin-resistant *Staphylococcus aureus* (MRSA): population dynamics of an expanding community reservoir of MRSA. *J Infect Dis* 2004; 190(10): 1730–8.
6. Center for Disease Control and Prevention. Community associated MRSA. Information from the US Centers for Disease Control and Prevention. Available from: http://www.cdc.gov/ncidod/hip/ARESIST/mrsa_comm_faq.htm [accessed 2005 July 31].
7. *Jacobs DM, Shaver A*. Prevalence of and outcomes from staphylococcus aureus pneumonia among hospitalized patients in the United States, 2009-2012. *Am J Infect Control* 2017; 45(4): 404–9.
8. *Santos JW, Nascimento DZ, Guerra VA, Rigo Vda S, Michel GT, Dalcin TC*. Community-acquired staphylococcal pneumonia. *J Bras Pneumol* 2008; 34(9): 683–9. (English, Portuguese)
9. *Carrillo-Marquez MA, Hulten KG, Hammerman W, Lambert L, Mason EO, Kaplan SL*. *Staphylococcus aureus* pneumonia in children in the era of community-acquired methicillin-resistance at Texas Children's Hospital. *Pediatr Infect Dis J* 2011; 30(7): 54550.

10. *Lewis SS, Walker VJ, Lee MS, Chen L, Moebring RW, Cox CE, et al.* Epidemiology of methicillin-resistant *Staphylococcus aureus* pneumonia in community hospitals. *Infect Control Hosp Epidemiol* 2014; 35(12): 1452–7.
11. *Moran GJ, Krishnadasan A, Gorwitz RJ, Fosheim GE, Alberth V, Limbago B, et al.* MERGENCY ID NET Study Group. Prevalence of Methicillin-resistant *Staphylococcus aureus* as an etiology of community-acquired pneumonia. *Clin Infect Dis* 2012; 54(8): 1126–33.
12. *Chen J, Luo Y, Zhang S, Liang Z, Wang Y, Zhang Y, et al.* Community-acquired necrotizing pneumonia caused by methicillin-resistant *Staphylococcus aureus* producing Panton-Valentine leukocidin in a Chinese teenager: case report and literature review. *Int J Infect Dis* 2014; 26: 17–21.
13. *Liu CW, Lin SP, Wang WY, Huang YH.* Influenza With Community-Associated Methicillin-Resistant *Staphylococcus Aureus* Pneumonia. *Am J Med Sci* 2019; 358(4): 289–93.
14. *Thomas R, Ferguson J, Coombs G, Gibson PG.* Community-acquired methicillin-resistant *Staphylococcus aureus* pneumonia: a clinical audit. *Respirology* 2011; 16(6): 926–31.
15. *Morikawa K, Okada F, Ando Y, Ishii R, Matsushita S, Ono A, et al.* Methicillin-resistant *Staphylococcus aureus* and methicillin-susceptible *S. aureus* pneumonia: comparison of clinical and thin-section CT findings. *Br J Radiol* 2012; 85(1014): e168–75.
16. *González C, Rubio M, Romero-Vivas J, González M, Pícaro JJ.* *Staphylococcus aureus* bacteremic pneumonia: differences between community and nosocomial acquisition. *Int J Infect Dis* 2003; 7(2): 102–8.
17. *File TM Jr.* Treatment of community-acquired pneumonia in adults who require hospitalization. Available from: <https://www.uptodate.com/contents/treatment-of-community-acquired-pneumonia-in-adults-who-require-hospitalization#H4033052510> [updated 2021 September 3].
18. *Wunderink RG, Niederman MS, Kollef MH, Shorr AF, Kunkel MJ, Baruch A, et al.* Linezolid in methicillin-resistant *Staphylococcus aureus* nosocomial pneumonia: a randomized, controlled study. *Clin Infect Dis* 2012; 54(5): 621–9.
19. *Kaysin A, Viera AJ.* Community-acquired pneumonia in adults: diagnosis and management. *Am Fam Physician* 2016; 94(9): 698–706.

Received on August 8, 2020
Revised on February 28, 2022
Accepted on March 1, 2022
Online First March 2022