CASE REPORT

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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 medijastinalnom 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 *Staphylococcus* 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.

Correspondence to: Biljana Lazović, Clinical Hospital Center Zemun, Vukova 9, 11 080 Belgrade, Serbia.
E-mail: lazovic.biljana@gmail.com

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 administration [1]. 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 body [6]. 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 pneumonia [7]. 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 research [8], but, on the contrary, the mortality rate from MRSA pneumonia decreased from 7.9% to 6.4% between 2009–2012 [7]. In addition to affecting infants and children [9], 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 years [10]. 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-

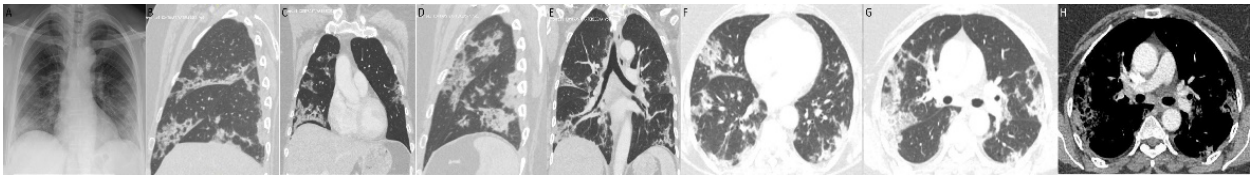

Fig. 1 – A) Chest X-rays of the presented patient: bilateral patchy areas of consolidation predominantly basal without pleural effusions; B-F) High-resolution computed tomography (HRCT), various radiological sections: bilateral diffuse patchy consolidations and subtle "ground-glass" opacities with the 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.

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