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Case Report

Methicillin-Resistant Staphylococcus aureus Co-infection in a Pakistani Patient with COVID-19: A Case Report

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ABSTRACT

Bacterial co-infections in patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pneumonia are not very common as the prevalence of co-infections with other respiratory viruses. The rate of bacterial co-infection in hospitalised patients infected with influenza is higher than 30%, whereas it is lower than 4% in hospitalised patients with SARS-CoV-2. Respiratory viral infections associated with bacterial co-infection have higher mortality and morbidity rates. The literature shows that most SARS-CoV-2 patients admitted to the hospital do not necessarily screen for bacterial infections and antimicrobial susceptibility. Therefore, clinicians' misdiagnosis of these co-infections can pose a significant risk to the lives of vulnerable patients with COVID-19. In that light, we presented a complicated case of methicillin-resistant *Staphylococcus aureus.*

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INTRODUCTION

Coronavirus disease-19 (COVID-19) was first reported in December 2019 in China's Wuhan city and then spread worldwide. Later on March 11, 2020, the COVID-19 pandemic was declared after being reported in many countries. Since the first COVID-19 pandemic, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected more than 370 million people, including over 5 million deaths. Both viral and bacterial respiratory infections substantially contribute to the burden of mortality and morbidity worldwide.[1] Bacterial co-infection is a life-threatening complication in many respiratory viral infections, contributing to the severity of the disease in the form of respiratory failure, shock, prolonged stay in the intensive care unit (ICU), and even death.[1,2] SARS-CoV-2 causes pneumonia and multi-organ failure, including myocarditis and thrombosis, as well as hypoxic-type respiratory failure.[3] SARS-CoV-2 infection makes the patients vulnerable to bacterial co-infections. However, the mechanisms of respiratory co-infection and the likelihood of bacteraemia favouring the respiratory tract epithelium are still unknown.[3]

The 1918 influenza pandemic data showed that nearly all deaths were caused by bacterial co-infection, including the most prevalent pathogens as *Streptococcus pneumoniae, Staphylococcus aureus (S. aureus), Beta-hemolytic streptococci,* and *Haemophilus influenza*.[4] Similarly, in the 2009 influenza pandemic, around 55% of the patient's autopsy samples were positive for bacterial co-infections.[5] The SARS-CoV-1 and Middle East Respiratory Syndrome (MERS-CoV) coronaviruses pandemic reported 20% and 30% of cases with bacterial co-infections.[6] However, research on the current pandemic has shown that patients with SARS-CoV-2 infection have lower than 4% of bacterial co-infections. Since bacterial co-infections with SARS-CoV-2 pneumonia have a known clinical impact, the disease might be missed diagnosed due to the low yield of diagnostic tests.[3]

For the benefit of public health, it is essential to assess the various uncertainties surrounding the effects of bacterial co-infections during the pandemic, particularly in intensive care settings. Here, we described a case of bacterial co-infection in a COVID-19 patient who was severely infected by methicillin-resistant *S. aureus* co-infection, along with their presentation, radiographic observation, and the outcomes.

CASE REPORT

A 90-year-old male patient who had previously been diagnosed with ischemic heart disease and hypertension was presented to the emergency room with several health complications, including shortness of breath, angina, fever, and a severe dry cough that had been going on for the previous six days. He was hospitalised in the intensive care unit (ICU) after being diagnosed with hypoxemic respiratory failure caused by COVID-19 pneumonia with oxygen saturating of 82% on room air. On admission to the emergency room, his widespread weakness, loss of appetite, taste, and smell were also noticed. He was breathing at a rate of 20 breaths per minute (bpm) with a heart

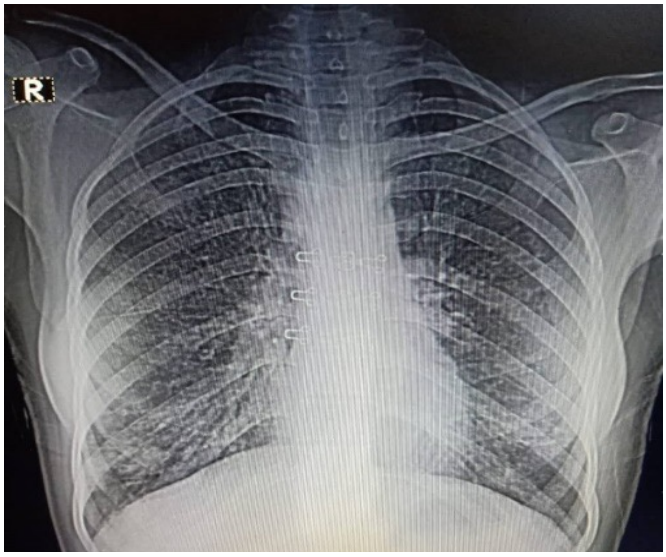

Figure 1. Chest X-ray showing bilateral infiltrates.

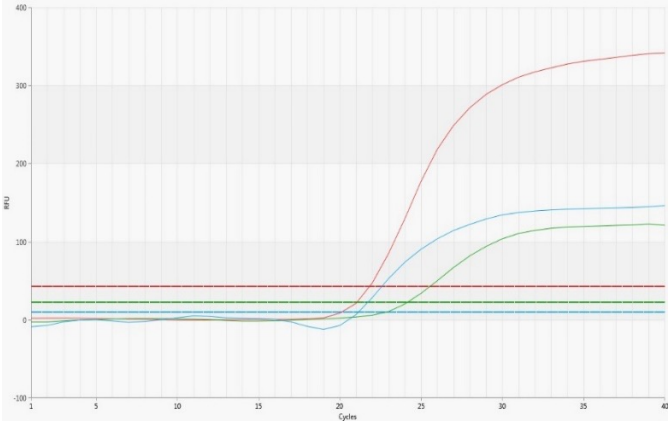

Figure 2. The graph illustrates reverse transcription PCR gene detection; red represents nucleocapsid, blue represents RNA-dependent RNA polymerase gene, and green represents internal control.

rate of 82 bpm and a temperature of 38.3 °C. He was found to have leukopenia with a leucocyte count of 5,700 mcL and a low neutrophil count of 88 mcL. The erythrocyte sedimentation rate (ESR) was elevated to 52 mm/h, with elevated interleukin-6 (IL-6) 12.7 pg/mL, C-reactive protein 3.2 mg/L, and procalcitonin (PCT) 0.4 µg/L, respectively. The chest radiograph showed multifocal pneumonia (Figure 1).

A rapid COVID-19 antigen test detected him as positive for COVID-19. Therefore, a nasopharyngeal sample was collected for further testing. Nasal cultures were collected from the patient using sterile cotton, plated on mannitol salt agar (MSA; Becton Dickinson Microbiology Systems), and incubated at 35 °C for 48 hours. We detected golden colour colonies on the MSA plate and subcultured on a trypticase soy agar supplemented with 5% sheep blood plates (Becton Dickinson Microbiology Systems) and incubated it at 35°C overnight. *S. aureus* was identified through colony morphology, a latex agglutination assay (Remel, Lenexa, KS), and a tube coagulase test using ethylenediaminetetraacetic acid (Becton Dickinson Microbiology Systems). *S. aureus* isolates were screened for methicillin resistance using the National Clinical and Laboratory Standards Institute disk diffusion method. Disk diffusion was conducted using a 1 µg oxacillin disk with Mueller-Hinton agar. The agar plates were incubated overnight at 35°C and measured the zone diameters.

He received both enteral and intravenous drugs with supplementary oxygen treatment. His PCR test showed positive results for the RNA-dependent RNA genes of SARS-CoV-2 on the second day of admission (Figure 2). He was treated primarily with remdesivir and hydrocortisone along with normal saline for the COVID-19 infection. Despite the high-flow nasal cannula's assistance (15 L/min), he was tachycardic and tachypneic. Therefore, he was intubated for further support on the third day of admission to the ICU. However, his repeated tests revealed an increase in the level of IL-6 of 33 pg/mL, PCT 0.6 µg/L, lactate dehydrogenase (LDH) 452 U/L, random blood sugar 141 mg/dL, total leukocyte count (TLC) 9,070/µL and platelets 32.7× 10^3/µL. Low levels of albumin and electrolytes were observed. However, alanine aminotransferase (ALT) and blood urea nitrogen (BUN) levels were raised to 55 U/L and 52 mg/dL, respectively. On culturing, it was revealed that he had bacteraemia and *S. aureus* co-infection. The culture of *S. aureus* was grown on differential media to confirm the isolates, and through Kirby Baur disk diffusion assay, the isolates showed resistance to oxacillin antibiotics (Figures 3 and 4). His therapy, antivirals, and supportive medication were further adjusted with piperacillin/tazobactam antibiotics for bacterial infections. Unfortunately, his health condition was severely exacerbated due to bacterial co-infection and finally expired on day seven of his post-hospital admission.

DISCUSSION

The patient presented to the ICU had a history of ischemic heart disease and hypertension. The patient had a productive dry cough with sputum production. A

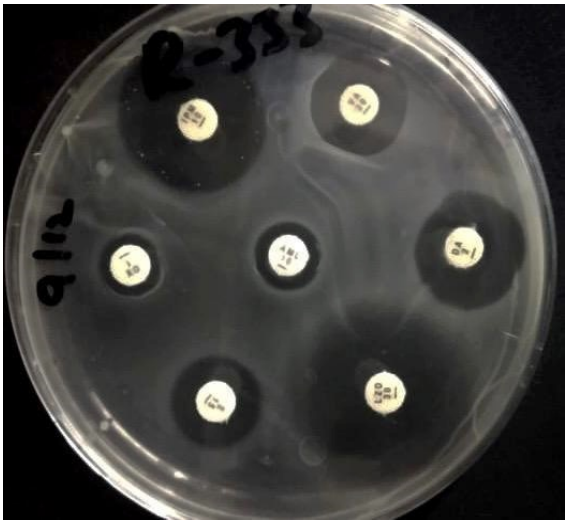

Figure 3. Antibiotic susceptibility pattern of methicillin-resistant S. aureus.

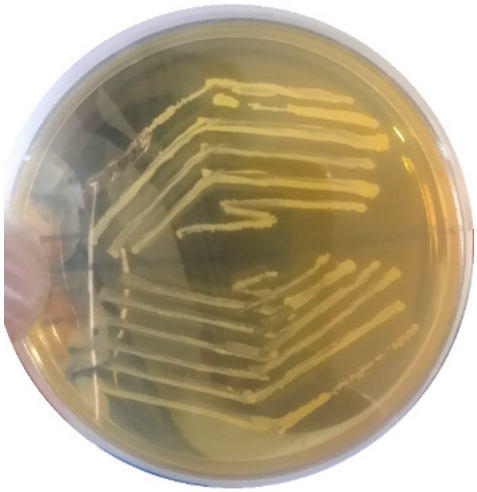

Figure 4. Growth of methicillin-resistant S. aureus on mannitol salt agar with characteristics of golden yellow colonies.

productive cough is not a unique finding for bacterial pneumonia because, according to a Zhou *et al*.[7] study, 50% of patients with SARS-CoV-2 infection had a similar presentation. The chest radiograph of the patient showed pneumonia with bilateral infiltrates. His rapid SARS-CoV-2 antigen test and PCR both were reported positive for COVID-19. Positive growth for *S. aureus* was seen in the sputum and nasopharyngeal swab cultures. The isolates showed resistance to oxacillin, one of the markers for methicillin-resistant *S. aureus* (MRSA) identification. According to the lab results, the patient had leukopenia and high ferritin, IL-6 and PCT levels.

Khilnani *et al*.[8] reported that immunocompromised, critically ill, and ICU patients were more susceptible to bacterial co-infections with increased usage of preventive or therapeutic antibiotics than non-invasive patients. Older people who live in nursing homes for long-term care also have a high risk of caring for *S. aureus*. Liu *et al*.[9] reported that the prevalence of MRSA in upper respiratory tract-infected patients was associated with high mortality ranging from 18.[9] to 30.0%. Co-infections can increase the severity of the disease and even mortality rates. According to Pacheco *et al*.[10], the overall co-infection rates in respiratory diseases can reach up to 68% of hospitalised patients co-infections could be explained by a possible dysregulation of the host immune response in case of infection with one pathogen, making the subsequent infection with the other pathogen more accessible. In previous viral pandemics, *S. aureus* was the leading cause of secondary bacterial infections, considerably increasing patient mortality rates. For influenza virus infection, mainly, *S. aureus* co-infection and bacteraemia were associated with mortality rates of nearly 50%, in contrast to the 1.4% mortality rates observed in influenza-infected patients alone.[10] A more similar phenomenon with reinfection and co-infection during the recent COVID-19 pandemic was recorded, which severely affected the hospitalised patients.[11]

Bacterial co-infections in respiratory viral infections are the leading cause of morbidity and mortality. According to Zhou *et al*.[7] and Lai *et al*., 12 studies on the 1918 influenza pandemic, between 20 and 60 million deaths were caused by bacterial co-infection rather than the virus itself. Although the rate of bacterial co-infection in COVID-19 is unclear, several studies reported that the rate is significantly lower than in prior pandemics.[7,12] Due to the lack of resources and the heavy burden on the healthcare system during a pandemic, COVID-19 patients are not being thoroughly diagnosed with co-infections.[7] In recent research, individuals with COVID-19 who also had *S. aureus* co-infection had the greatest fatality rate, at 61.7%.[12] The primary *S. aureus* co-infection diagnosis in individuals admitted to a medical facility suggests that the community serves as a favourable environment for the spread of pathogenic infections.[13] The mortality rate in *S. aureus* bacteraemia is associated with the severity of the disease, age, acute renal failure, length of mechanical ventilation, and antimicrobial resistance.[14] The patient's laboratory examination showed low albumin and electrolyte levels and increased ESR. He was given plenty of intravenous fluids, antivirals, antibiotics, anti-allergic, and hydrocortisone. Due to severe bacteraemia and COVID-19 complications, he expired on the seventh day of his post-hospital admission.

CONCLUSIONS

S. aureus is an opportunistic pathogen for humans and animals amongst the staphylococcal species with low guanine-cytosine content. It is also known as a commensal coloniser of the skin, nares and nasal cavity. It can enter the body through openings in the skin and cause various infections, from minor skin to life-threatening blood infections. The empirical anti-MRSA therapy methods were included with vancomycin hydrochloride or linezolid plus guideline-recommended standard antibiotics such as β-lactam, macrolide, or tetracycline hydrochloride, or extended-spectrum of quinolone.15 We propose that despite the low level of bacterial co-infection associated with COVID-19, it is important to investigate a severely ill patient for a possible co-infection. The role of evaluating empirically covering co-infections is very significant. Proper and timely evaluation of bacterial co-infection in high-risk patients may overcome the rate of morbidity and mortality.

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Conflict of Interests

The authors declare no conflict of interest.

Authors' Contribution

All authors participated in the literature and critical review for the case report preparation.

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