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Multi-drug resistant community-acquired pneumonia, bacteraemia, and infective endocarditis: A case report

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Abstract

BACKGROUND

The prevalence of multidrug-resistant (MDR) bacteria has increased globally, with extensive drug-resistant (XDR) bacteria posing a threat to patients.

CASE SUMMARY

This case study describes a young man admitted for suspected tropical fever infections who experienced rapid deterioration in health. Despite negative results for tropical fever infections, he had neutrophilic leucocytosis, acute kidney injury, and chest imaging suggestive of bilateral consolidations. On day two, he was diagnosed with infective endocarditis with possible rheumatic heart disease and MDR methicillin-resistant *Staphylococcus aureus* bacteremia, and community-acquired pneumonia. Despite treatment with broad-spectrum antibiotics, he did not respond and succumbed to death on day five.

CONCLUSION

This case highlights that clinicians/public should be aware of MDR community-acquired pneumonia, bacteremia, and endocarditis which ultimately culminates in high rates of morbidity and mortality. Early identification of strain and prompt antibiotic treatment is a mainstay for the management and prevention of early fatalities.

Simultaneously, route cause analysis of community-acquired MDR/XDR pathogens is a global need.

INTRODUCTION

Antimicrobial drug resistance remains a global healthcare problem and poses a significant challenge to physicians worldwide, as the prevalence of multidrug-resistant (MDR), extensive drug-resistant (XDR), and pan-drug-resistant (PDR) bacteria has increased in many tertiary care centres globally [1-3]. XDR bacteria are the current threats to patients. XDR bacteria are typically isolated in nosocomial settings. However, community acquisition of these infections is less prevalent but increasing day by day. Community-acquired pneumonia is a common clinical illness caused by bacteria and other pathogens. When it is associated with XDR bacteria then it is a matter of concern as there is a high risk of complications such as bacteremia and infective endocarditis[4]. Staphylococcus aureus is one of the leading causes of bacteremia, both in the community and in the hospital setting, which can result in complicated or metastatic infections such as pneumonia, infective endocarditis, or sepsis with multi-organ dysfunction[5]. When compared with methicillin-sensitive S. Aureus (MSSA), MRSA is one of the leading causes of S. aureus bacteremia cases and is associated with significant mortality and morbidity and poor clinical outcomes[6,7]. There is a limited amount of literature specifically addressing the combination of MDR community-acquired pneumonia (CAP), bacteremia, and infective endocarditis.

The incidences of bacteremia in CAP patients are 4% to 18% and one prediction model predicts bacteremia in these patients with the help of variables like using recent antibiotic treatment, liver disease, and three vital-signs (Systolic blood pressure < 90 mmHg, Temperature < 35 C° or ≥ 40 C°, Pulse ≥ 125/min) and three laboratory abnormalities (Blood urea nitrogen ≥ 30 mg/dL, Sodium < 130 mmol/L, WBC < 5,000/mm³ or > 20,000/mm³)[8]. This pneumonia resulting bacteremia can lead to septicemia and other systemic complications like infective endocarditis, mostly due to

delayed antibiotic administration^[9]. Though this triad of pneumonia, bacterimia, and infective endocarditis is uncommon, but community-acquired MDR organism causing the triad is very rare.

Thereby, we report a case to raise public health concerns.

CASE PRESENTATION

Chief complaints

Fever and abdominal pain for 3days.

Vomiting, swelling in the lower limbs, and itching and rashes all over his body for 1day.

History of present illness

A young man in his 20s, previously healthy and with no substance abuse, suddenly felt ill. For the past three days, he had been experiencing an intermittent, documented, high-grade fever with associated chills that did not resolve despite taking medication. He also had abdominal pain for three days, initially as acute onset persistent nonprogressive dull aching pain in the right hypochondriac region, which later became diffuse without any aggravating or relieving factors. He experienced 3-4 episodes of non-bilious, non-blood-stained vomiting containing food particles. Additionally, he had bilateral symmetrical painless swelling in the lower limbs, without any decreased urine output, burning micturition, frothy urine, haematuria, or pyuria. He initially sought medical attention at a local hospital and took some medication, but approximately 30 minutes later, he developed skin itching and rashes all over his body, which was suspected to be a drug reaction. Further evaluation revealed deranged renal function, and he was subsequently referred to our centre.

History of past illness

Non-contributory.

Personal and family history

Non-significant.

Physical examination

Upon presentation, he was fully conscious of tachycardia and tachypnoea and maintained saturation at room air. A general physical examination did not reveal any major findings, except for bilateral pitting edema. Per abdominal examination showed diffuse tenderness and guarding without any rigidity, distension, or palpable organomegaly. The patient was intubated due to acute hypoxic respiratory failure and was subsequently shifted to the intensive care unit. On day two of admission, the patient demonstrated high-grade fever, accompanied by subconjunctival dot haemorrhages, erythematous skin and non-blanching hemorrhagic petechiae, mucosal and skin erosions, splinter haemorrhages, Janeway lesions, and bilateral pitting pedal oedema with pan systolic murmur at the mitral area, it is possible that the murmur might have been missed due to subjective variations in the examiner's assessment on the first day of examination (Fig 1).

Laboratory examinations

The patient's initial laboratory tests showed an increase in neutrophilic white blood cells with a decrease in platelet count, along with an elevated level of procalcitonin at 38 ng/mL (normal range, <0.05) (a marker for bacterial infection) and acute kidney injury (Table 1). A peripheral blood smear revealed normocytic normochromic cells with toxic granules, indicating toxic changes in the white blood cells. Further investigations revealed disseminated intravascular coagulation, as evidenced by elevated levels of prothrombin time/international normalized ratio (INR), activated partial thromboplastin clotting time, and D-dimer. As per institution policy and surviving sepsis guidelines 2021, the patient had clinical and biochemical evidence of definitive sepsis hence 2 sets of blood cultures were sent before administration of antibiotics. Workups for tropical fever infections such as COVID-19, H3N2, H1N1, Dengue,

Malaria, Scrub typhus, Leptospira, and Typhoid were negative. Arterial blood gas analysis showed normal anion gap metabolic acidosis with lactic acidosis and acute hypoxic respiratory failure.

Blood cultures were sent for suspected infective endocarditis, and after 48 h of incubation, two sets of blood cultures revealed MDR methicillin-resistant *Staphylococcus Aureus* (MRSA), which was sensitive to linezolid, vancomycin, clindamycin, tigecycline, but resistant to penicillin, ciprofloxacin, levofloxacin, erythromycin, co-trimoxazole, and gentamicin. On the fourth day of admission, nested multiplex PCR (BioFire[®]) test of an endotracheal aspirate revealed the presence of *Pseudomonas aeruginosa*, *Staphylococcus aureus*, Human Rhinovirus, and Enterovirus but sterile on culture. Microbial gene testing detected the presence of mec A/C (Methicillin-resistant *Staphylococcus aureus* (MRSA) cassette, which confers resistance to methicillin and other beta-lactam antibiotics) and MREJ (Mobile RmtE/J group genes, which encode rRNA methyltransferases that confer resistance to aminoglycoside antibiotics) genes. The urine culture was sterile.

Imaging examinations

Ultrasonography of the abdomen showed hepatosplenomegaly, and an X-ray of the abdomen did not reveal any acute surgical emergencies. Chest X-ray showed bilateral areas of opacity in the middle and lower lobes with air bronchograms. High-resolution computed tomography (HRCT) of the thorax revealed consolidation and air bronchograms in bilateral lung areas, along with interspersed ground glass opacities and bilateral pleural effusions (Fig 2). A 2D echocardiography was done due to high suspicion of infective endocarditis, which revealed findings suggestive of rheumatic heart disease: moderate mitral regurgitation, moderate mitral stenosis, mild aortic regurgitation, thickened anterior mitral leaflet with hockey stick sign with restricted leaflet motion, dilated left atrium, vegetations on the mitral valve, and a left ventricular ejection fraction of 50%.

MULTIDISCIPLINARY EXPERT CONSULTATION

Based on the presentation and baseline investigation, two differential diagnoses were considered. The first was a pulmonary-renal syndrome, characterized by diffuse alveolar haemorrhage and glomerulonephritis, which can be caused by any underlying autoimmune disorder. This often presents with new onset bleeding from the respiratory tract, respiratory distress with hypoxia, and bilateral confluent opacities seen on the HRCT thorax. However, severe thrombocytopenia and bilateral effusion, which are not typical findings of vasculitis, did not support this diagnosis. Furthermore, these opacities could be explained by community-acquired pneumonia as the patient's endotracheal aspirate bio-fire test was positive for *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Antinuclear antibodies (ANA) tested were negative by indirect immunofluorescence assay (IFA), so further serological workup for autoimmune conditions was not pursued.

The second differential diagnosis was ⁵ Severe Fever with Thrombocytopenia Syndrome (SFTS), an acute febrile illness characterized by fever, thrombocytopenia, leukopenia, and gastrointestinal symptoms. It is transmitted to humans by tick bites, primarily from *Haemaphysalis longicornis*, *Ixodes nipponensis*, *Rhipicephalus microplus*, and *Amblyomma testudinarium*. This syndrome is associated with a high fatality rate and can lead to multiple organ failure and death^[8]. However, the patient tested negative for other endemic tick-borne diseases like scrub typhus.

FINAL DIAGNOSIS

Other investigations revealed that the patient had community-acquired pneumonia associated with methicillin-resistant *Staphylococcus aureus* (MRSA), bacteremia, and infective endocarditis, hence the differential was not considered.

TREATMENT

The diagnosis of ineffective endocarditis was made according to the modified Dukes' criteria, in addition to community-acquired pneumonia, sepsis with multi-organ

dysfunction syndrome, shock, encephalopathy, severe acute respiratory distress syndrome, acute kidney injury, and disseminated intravascular coagulation. Intravenous (IV) vancomycin 15 mg/kg every 12 h, gentamicin 1mg/kg every 8 h, and meropenem 1gm every 8 h were started as empirical antibiotics. Ventilator settings were optimized according to the ARDS protocol, and sedation and neuromuscular blockade were administered. Prone positioning was also done. Dual vasopressor support was implemented to maintain a mean arterial pressure above 65mmHG. Approximately 14 units of fresh frozen plasma and 10 units of random donor platelets were used to treat continuous endotracheal bleed and Ryle's tube bleed. Antipyretics were given to control fever spikes, and therapeutic hypothermia measures were also followed. After the culture reports, the injection of meropenem was stopped, and ceftazidime-avibactam and aztreonam were started in their place. Gentamicin was stopped, vancomycin was continued, and colistin was administered through nebulization. The patient rapidly progressed to septic shock and multiorgan dysfunction. Despite being on 100% FiO₂ hypoxia and saturation levels worsened, leading to severe acute respiratory distress syndrome (ARDS).

OUTCOME AND FOLLOW-UP

Despite aggressive treatment, the patient's bacteremia did not respond and had a fulminant course, eventually succumbing to death on the fifth day of admission due to severe ARDS.

DISCUSSION

Community-acquired multi-drug resistant (CA-MDR) infections are infections that are acquired outside of healthcare settings and are caused by microorganisms that are resistant to multiple types of antibiotics. CA-MDRs are a significant public health concern, particularly in developing countries where inadequate healthcare facilities, poor sanitation, and limited access to antibiotics contribute to the spread of these infections. CA-MDR infections can be transmitted through direct contact with

contaminated surfaces or through person-to-person contact, and risk factors include overuse and misuse of antibiotics, poor sanitation and hygiene, lack of access to clean water, crowded living conditions, poor infection control practices in healthcare settings, immunosuppression, chronic illnesses, and malnutrition.

India is one of the countries where CA-MDR is a significant public health concern. Several studies and reports have highlighted the high prevalence of CA-MDR in India, as well as the challenges in addressing this issue. Of particular concern is the emergence of community-acquired MRSA infections in patients with no apparent risk factors at the community level, as seen in our case^[10]. Community acquisition of MRSA infection is associated with significant morbidity and mortality, similar to nosocomial MRSA infection. Person-to-person transmission of community-associated MRSA has been reported^[11]. Numerous studies, systematic analyses, and meta-analyses conducted in India have revealed a progressive rise in the incidence of MRSA and changes in resistance patterns. A systematic review and meta-analysis found that the prevalence of MRSA in India was relatively high at 27%, with a higher proportion observed among men aged >18 years^[12]. However, all MRSA isolates in India were found to be sensitive to vancomycin and teicoplanin. Resistance to cotrimoxazole, erythromycin, gentamicin, and other penicillins and cephalosporins appeared to be common features of MRSA isolates in India, consistent with other Indian studies and our patient^[13]. Another study conducted in a tertiary care centre in southern India also revealed a high level of resistance among MRSA isolates, with Linezolid, Piperacillin/tazobactam, and Tetracycline found to be effective agents against MRSA^[14]. CA-MRSA (Community-acquired methicillin-resistant *Staphylococcus aureus*) isolates are now being increasingly reported from India. D' Souza *et al* studied 412 confirmed cases of MRSA and found that 54 per cent were true CA-MRSA possessing the SCCmec (Staphylococcal Chromosomal Cassette mec) IV and SCC mec V genes. These were mainly isolated from SSTIs. CA-MRSA isolates also showed variable resistance to ciprofloxacin, erythromycin, clindamycin and tetracycline^[15]. Chatterjee *et al* found the overall

prevalence of *S. aureus* nasal colonization was 52.3 per cent and that of MRSA was 3.89 per cent in the community^[16].

Addressing the issue of CA-MDR infections in India requires collaboration between healthcare providers, policymakers, and the public to promote responsible antibiotic use, improve infection control practices, and ensure effective treatment of infectious diseases.

Global analysis of burden of bacterial AMR in 2019: a systematic analysis The analysis has shown AMR caused an estimated 1.27 million deaths and was associated with an estimated 4.95 million deaths worldwide in 2019, with drug resistance in lower respiratory and bloodstream infections having the greatest impact. Among the 23 pathogens studied, drug resistance in six (*E. coli*, *S. aureus*, *K. pneumoniae*, *S. pneumoniae*, *A. baumannii*, and *P. aeruginosa*) alone led directly to 929,000 deaths and was associated with 3.57 million deaths. Resistance to fluoroquinolones and beta-lactam antibiotics accounted for over 70% of deaths caused by AMR. The health impact of pathogens varied widely based on location, with high-income countries most affected by *S. aureus* and *E. coli*, while in Sub-Saharan Africa, *K. pneumoniae* and *S. pneumoniae* caused the most deaths. The study emphasized the need for improved global data collection to address the most pressing challenges posed by antimicrobial resistance^[17]. Preventing community-acquired MDR infections requires a multifaceted approach that involves improving sanitation and hygiene practices, promoting responsible antibiotic use, improving infection control practices in community settings, and increasing access to healthcare for vulnerable populations. This includes educating the public about the importance of appropriate antibiotic use and supporting initiatives to reduce the overuse and misuse of antibiotics, as well as implementing effective infection control measures in community settings and providing access to affordable and quality healthcare for all individuals. Additionally, developing new antibiotics and alternative treatments, monitoring and tracking CA-MDR infections, and educating healthcare providers and the general public on CA-MDR and its risks are essential.

Overall, CA-MDR infections represent a significant public health concern, and addressing this issue requires collaboration between healthcare providers, policymakers, and the public to promote responsible antibiotic use, improve infection control practices, and ensure effective treatment of infectious diseases.

CONCLUSION

There is a growing threat of multi-drug resistant (XDR) bacteria in the community setting in patients with no apparent risk factors. The presence of a CA- MDR MRSA strain increases the risk of treatment failure and further spread of infection and associated complications. Better surveillance, infection control measures, and antibiotic stewardship programs are urgently needed in the community.

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