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PULMONARY COMPLICATIONS OF COMMUNITY ASSOCIATED METHICILLIN RESISTANT *STAPHYLOCOCCUS AUREUS* (CA-MRSA) - CASE SERIES

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ABSTRACT

Community- associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) has received considerable attention in recent years as one of the important cause of infections among individuals in the community who do not have risk factors for MRSA infections such as hospitalization or prolonged contact with the medical system.

Recently community-associated (CA)-MRSA infections are detected more commonly and their incidence is increasing; there is risk of wider spread. These new CA-MRSA strains appear to behave differently to Hospital Associated-MRSA strains. Although predominantly causing skin and soft tissue infections, mainly as boils and abscesses requiring drainage, invasive infections including necrotising pneumonia can also occur. This case series presents three such case reports of necrotizing pneumonia caused by CA-MRSA in healthy individuals.

INTRODUCTION

Staphylococcus aureus, the most virulent, pluripotent pathogen, causing disease through both toxin-mediated and non-toxin-mediated mechanisms. It is a part of the normal human flora of healthy persons and persistently or transiently colonized in anterior nares, skin, vagina, axilla, perineum, and oropharynx. These colonization sites serve as reservoir for future infection [1, 2].

Staphylococcus aureus (S. aureus) infections, including methicillin resistant *Staphylococcus aureus* (MRSA), primarily involve skin and soft tissues. A new strain of MRSA, i.e, CA-MRSA is emerging and is associated with an increased risk of severe soft tissue infections and necrotizing pneumonia. Life threatening infections like necrotizing pneumonia, caused by this pathogen is in increasing trend. Resolution of staphylococcal pneumonia may be expected to follow a prolonged course [1,3]. Hence, early recognition and appropriate treatment of severe necrotizing pneumonia and sepsis caused by CA-MRSA is mandatory to improve the outcome of patients. Here, we are presenting with three such interesting case reports of CA-MRSA infections leading to necrotizing pneumonia.

CASE PRESENTATIONS

Case 1

A 65 years old female was admitted to medicine ward, presented with fever, cough with expectoration, wheezing, chest pain, loss of appetite, lethargy and anorexia for a period of 6 weeks. On physical examination she was febrile. Pallor, moist skin, facial puffiness and bilateral pitting pedal edema were observed. Other general physical examinations and vital signs were within normal limits. Respiratory system examination revealed reduced breath sounds in left lung fields and bilateral basal coarse crepitations.

Investigations: Her investigation findings were as follows- Hemoglobin-8.0 gm%, Total WBC count-16,800/mm^3, Differential count showed polymorphs- 85%, lymphocytes -10% and eosinophils -5%; erythrocyte sedimentation rate -12mm at end of 1hr, Plasma glucose-110mg/dL, Liver function test & Serum Electrolytes-Normal range. Serological test for HIV antibodies- Negative.

Chest X-ray on admission showed left lower lobe pneumonic consolidation with mild synpneumonic pleural effusion [Figure-1]. Chest x-ray after one week of admission showed consolidation with well defined thick walled cavitary lesion involving left lower lobe with moderate left pleural effusion.

The sputum was processed by Gram staining and was cultured on blood agar, chocolate agar and MacConkey agar. Gram staining of sputum smear showed presence of epithelial cells < 10/LPF, polymorphonuclear leukocytes >25/LPF and Gram-positive cocci in clusters [Figure-2] suggestive of *Staphylococci*, seen along with normal oropharyngeal flora. No acid fast bacilli were seen on Ziehl-Neelsen staining of the sputum smear. On blood agar, opaque β haemolytic colonies appeared after overnight incubation [Figure-3]. The isolate was confirmed as *Staphylococcus aureus* by standard biochemical tests. The antibiotic susceptibility pattern by Kirby-Bauer's disk diffusion method showed that the isolate was sensitive to ciprofloxacin, levofloxacin, cefotaxime, gentamicin and resistant to penicillin, amoxicillin-clavulanic acid and co-trimoxazole. The strain was resistant to oxacillin and later

on got confirmed as methicillin resistant *Staphylococcus aureus* (MRSA) by oxacillin screen agar and minimal inhibitory concentration (MIC) method according to clinical laboratory standard institute (CLSI) guidelines[3].

The patient was started on oral levofloxacin and was nebulised. Following the antibiogram report, IV Gentamicin was started. The fever subsided and the patient responded well to this line of treatment and got discharged after 7 days.

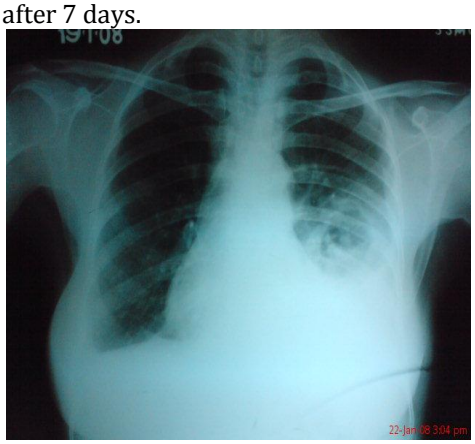

Figure-1 Chest X-Ray: showing pyogenic cavity in left lower zone

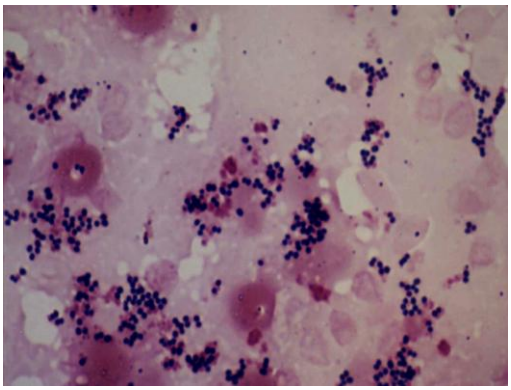

Figure-2-Gram stain smear of sputum smear showing gram positive cocci in cluster

Figure-2 Blood agar showing beta haemolytic colonies of *Staphylococcus aureus*

Case 2:

A 38 years old man was brought to the causality with right-sided chest pain, cough, hemoptysis, fever, and chills. He gave history of a furuncle over his right cheek for 6-7 days. On general physical examination patient had a temperature of 103°F, heart rate of 128bpm, respiratory rate
of 28 breaths/min, blood pressure of 130/70 mm of Hg. On auscultation, coarse crepitations were heard over the right lung base. Laboratory investigations like electrolytes, renal function and liver function tests were within normal limits. Complete blood count showed an increase in WBC count of 18,900 cells/µL. Initial chest X-ray showed patchy infiltrates in the right lower lobe.

The patient was admitted to the hospital, IV moxifloxacin was started and his sputum and blood samples were collected for culture. *Staphylococcus aureus* was isolated from sputum and blood culture. Isolate was confirmed by standard biochemical reactions. The antibiotic susceptibility pattern by Kirby-Bauer's disk diffusion method showed that the isolate was resistant to ciprofloxacin, moxifloxacin, cefotaxime, cefoxitine, penicillin, amoxicillin-clavulanic acid, gentamicin and sensitive to imipenem and vancomycin. The strain was confirmed as methicillin resistant *Staphylococcus aureus* (MRSA) by oxacillin screen agar and minimal inhibitory concentration (MIC) method according to CLSI guidelines. A follow-up chest X-ray was taken on 5th day after admission, showed cavitary pneumonia in the right lower lobe and bilateral minimal pleural effusions. Based on the antibiogram report, moxifloxacin was discontinued and IV vancomycin was started. On day 7, patient got discharged against medical advice.

Case 3:

A 59-year-old man presented with acute onset breathlessness, chills and a nonproductive cough to the emergency department. On general physical examination, he had a temperature of 38.0°C, pulse rate of 62/ min, blood pressure of 90/60 mm Hg and an oxygen saturation of 80%. Clinical examination revealed bilateral lower lobe crackles and chest x-ray showed bilateral pulmonary patchy infiltrates. His laboratory investigation showed marked leukocytosis. His sputum and blood samples were collected and sent for culture. The patient failed to respond adequately to oxygen supplementation. The patient was sedated, ventilated and started on ceftriaxone and azithromycin.

MRSA was isolated from sputum and blood cultures. Repeat chest X-ray taken on day 4 showed bilateral cavitary lesions in the lower lobes with moderate pleural effusion. The isolate was sensitive to vancomycin, co-trimoxazole, tetracycline, mupirocin, and clindamycin but resistant to oxacillin and erythromycin. Vancomycin was added to the patient's therapy.

The fever subsided and the patient started responding to the treatment and got discharged after 10 days.

DISCUSSION

All three case reports discussed above are in previously healthy individuals having a less complicated clinical course. All three cases are successfully treated due to early diagnosis and adequate treatment. However, many reported cases of CA-MRSA are associated with high mortality and morbidity. Probably these isolates of MRSA carried Panton-Valentine (leukocidin) genes [5]. However due to lack of facilities, *PVL* testing was not done for the above three isolates.

MRSA is growing in prevalence in the Indian scenario. Studies form different centers around the country estimate the prevalence to be between 20 and 40% and sometimes even higher[6] . Previously MRSA was known as a hospital pathogen, but now it is emerging independently as a community pathogen. The new strains of MRSA causing community-associated infections, called community-associated MRSA (CA-MRSA), are genetically very different from hospital strains of MRSA. [7] These new clones of MRSA carry virulence genes, including PVL, making infections

more severe. Infections may also occur in healthy adults and children without having any prior history of hospitalization[1, 5,7] . The clinical spectrum of patients with CA-MRSA necrotizing pneumonia includes an influenza-like prodrome, rapidly develop severe respiratory symptoms, hemoptysis, hypotension and a high fever. They also present with chest X-ray abnormalities like patchy lung infiltrates, cavitary lesions, pneumatoceles, pleural efffusion and lung abscesses[8,9,10] . These features are not specific to CA-MRSA but rather are consistent with PVL producing *S. aureus* and, therefore, can be applicable to some strains of MSSA (methicillin sensitive *Staphylococcus aureus*) also[10].

Therapeutic options for severe CA-MRSA infections are limited to vancomycin and linezolid.[5] In less severe infections, clindamycin, and doxycycline are available options. Fluoroquinolones are not recommended because resistance to these agents develops rapidly[11] .

Pneumonia when suspected on clinical spectrum should be confirmed by Chest X-ray findings. Severe pneumonia patients with recent history of skin or soft tissue infections, *S. aureus* should be considered as a possible etiological agent of Community Associated Pneumonia (CAP) and immediate admission and adequate treatment should be provided to avoid complications [5,12].

S. aureus is a part of the normal human flora of anterior nares, skin and oropharynx. It can enter the lung parenchyma either by microaspiration of the upper respiratory flora or by the hematogenous route. In cases 1 and 3, the source of *S. aureus may be* bacteremic seeding from upper respiratory tract and in case 2 from primary skin infection[13,14] .

CA-MRSA pneumonia can lead to formation of cavitary lung lesions due to tissue necrosis by ischaemia, direct toxic effects of the micro-organism or its products or indirect effect of host immune response (cytokines). Most common cause of cavitary pulmonary diseases are infectious diseases due to *Mycobacteria, Staphylococcus aureus*, gram negative bacilli and fungi resulting in lung necrosis and formation of cavities. Parapneumonic pleural effusion complicate Staphylococcal pneumonia in 40% of adult cases and one half of these effusions progress to empyema[15-16].

Sputum Gram stains showing gram positive cocci in clusters may be an early clue to the diagnosis of MRSA-CAP, thus allowing appropriate antibiotic coverage to be started sooner and antibiotic therapy can be supplemented or revised based on the antibiogram reports. These cases emphasize the importance of obtaining blood and sputum cultures in patients who are hospitalized with CAP and have cavitary infiltrates.

CONCLUSION

CA-MRSA is an important emerging cause of CAP in previously healthy adults. High mortality has been reported with CA-MRSA pneumonia; hence, there is a need for increased awareness.

History of recent or current skin infections may provide a clue about the underlying etiologic agent for CAP. Treatment for suspected cases of MRSA-CAP should include broad spectrum therapy, including coverage for MRSA while awaiting the results of cultures and antibiogram.

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