Case Report

A rare coexistence of methicillin-resistant *Staphylococcus aureus* pneumonia with chronic necrotizing pulmonary aspergillosis in a not-so-sick patient:A case report

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ABSTRACT

We present a case of a 68-year-old female, a known case of diabetes who presented with a short history of fever and cough. Failure to respond to oral antibiotics led to further investigations which revealed the coexistence of methicillin-resistant *Staphylococcus aureus* pneumonia and chronic necrotising pulmonary aspergillosis. Dual infection with unusual pathogens in a not-so-sick patient with a short history of illness makes the case worth reporting. It highlights that, in people living with diabetes, rare and unusual presentations are common; hence keeping a high degree of suspicion, detailed workup including tissue diagnosis aids in early diagnosis and good clinical outcomes.

Key words: Chronic necrotising pulmonary aspergillosis, Coinfection, Methicillin-resistant *Staphylococcus aureus* pneumonia

Diabetes, advanced age, and underlying lung conditions can make one vulnerable to severe infections or unusual clinical presentations. One of the unusual presentations is the coexistence of two different organisms. It is important to identify the organisms correctly and quickly so that early and correct treatment can be initiated, especially if there is a coexistence of bacterial and fungal infections. Missed or delayed diagnosis can lead to poor patient outcomes. Failure to respond to conventional initial treatment should prompt detailed workup and aggressive investigation in these patients.

Our case report highlights one such case with coinfection of methicillin-resistant *Staphylococcus aureus* (MRSA) and aspergillosis. Diligent and aggressive workup led to quick diagnosis and treatment.

CASE DESCRIPTION

A 68-year-old lady person, who is a homemaker, came to the outpatient department (OPD) in the 1st week of May 2024 with complaints of moderate-grade fever for 5 days. She also had a cough with minimal mucoid expectoration. She was seen by a general practitioner near her house and was on treatment with oral amoxicillin plus clavulanate (375 mg) twice a day for the preceding 3 days along with oral paracetamol 650 mg on as and when required basis. Other than minimal throat discomfort that she had experienced at the onset of fever for a day, she gave no other significant history.

On general examination, she was moderately built and well nourished, conscious, coherent, and oriented to place, person, and time. There was no pallor, jaundice, peripheral lymphadenopathy, and pedal edema. Her temperature was 98.7° F, her blood pressure was 126/80 mmHg, and her pulse rate was 104/beats/min. On systemic examination, very minimal decreased air entry was noted in the right infraclavicular area. She was advised to undergo blood tests and chest imaging, increase the dose of amoxicillin to 625 mg thrice a day, and was advised admission for which she was not willing. She denied any history of travel, trauma, palpitations, giddiness, or sweating. She is a known case of hypertension (well controlled on antihypertensives), type 2 diabetes mellitus (well controlled on oral antidiabetics), primary hypothyroidism (at present euthyroid) for 20 years, and chronic obstructive pulmonary disease (COPD) for 10 years for which she was on inhaled bronchodilators and steroids. There was a history of admission 3 months before the present episode for lower respiratory tract infection, for which she had received injectable ceftriaxone for 7 days.

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On initial workup, white blood cells (WBC) were 13.6 thousand with neutrophils of 76%, and C-reactive protein (CRP) was markedly elevated at 328.2. The patient and relatives were informed about the report and counseled about the need for admission for further workup. They agreed and she was admitted. In hospital, 3 episodes of fever were observed. Her electrocardiogram showed sinus tachycardia and chest radiography revealed haziness in the right upper zone (Fig. 1).

She was started on injectable piperacillin - tazobactum and moxifloxacin along with supportive medications. In view of the persistent fever, the second episode in 3 months and markedly raised CRP and findings on chest X-ray, contrast-enhanced computed tomography (CECT) of the thorax was done, which was reported as showing a well-defined irregular shaped, heterogeneously enhancing, soft tissue density lesion with central non-enhancing necrotic area within in the right hilar region involving the apical and posterior segment of the right lung and upper lobe along the right horizontal fissure suggestive of probably a malignant lesion, for which she was advised histopathological correlation. Enhancing nodule involving the lateral basal segment of the right lower lobe was also noted (Fig. 2).

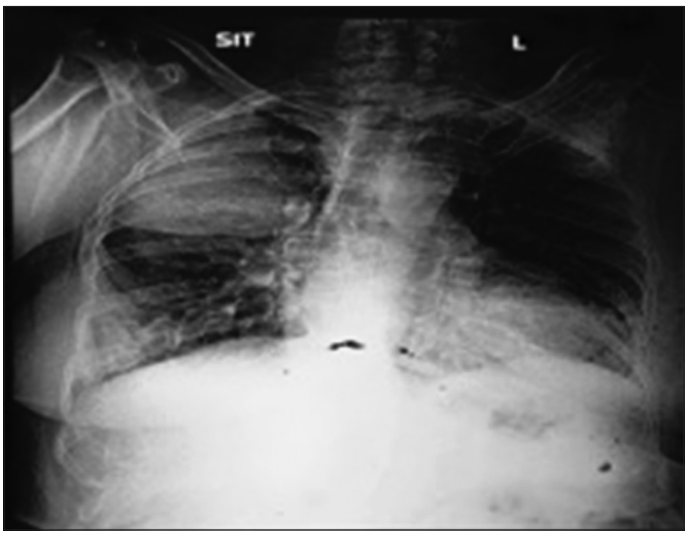

Figure 1: Chest X-ray of the patient

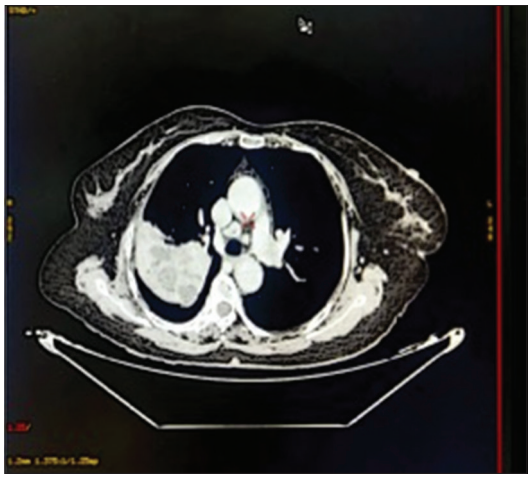

Figure 2: Contrast-enhanced computed tomography thorax of the patient

Sputum sample culture grew colonies of MRSA and the patient was started on Clindamycin. It was decided to perform Bronchoscopy and bronchoalveolar lavage (BAL). It was performed and the samples were sent for Gram stain, culture, Acid-Fast Bacilli stain, cartridge-based nucleic acid amplification test- gene expert, galactomannan, and biopsy.

The histopathology report did not reveal any changes of malignancy but the BAL culture also grew MRSA in view of which linezolid was added (considering Panton-valentine leukocidin). The other reports – including the gene expert was negative and the biopsy showed no evidence of malignancy/ granuloma/evidence of fungal infection. The BAL sample tested positive for *Aspergillus* (galactomannan Ag- 3.79 index ≥0.5 is positive) for which she was started on oral voriconazole. The patient tolerated the medications well. Voriconazole trough levels after 2 days of starting the drug were adequate.

The patient's length of stay in the hospital was 12 days and she was discharged with advice to continue and repeat CECT after 3 weeks. Her repeat blood tests revealed a normal WBC count with a CRP of 3.

DISCUSSION

In our case report, we presented a middle-aged female with MRSA pneumonia and aspergillosis who presented as a walk-in patient to the OPD with minimal symptoms and clinical signs. If not for the high CRP and the X-ray findings, she probably would not have been investigated aggressively. If not for the sputum culture, MRSA would not be considered as the causative pathogen. If not for the Bronchoscopy and BAL, the presence of *Aspergillus* could be missed. Missing the above would lead to delay in treatment, inadequate or wrong choice of antibiotics and prolonged duration of the illness can lead to complications or worsening. Our case is one of the rare entities of the coexistence of MRSA pneumonia and *Aspergillus* in a patient with minimal symptoms and clinical signs.

Bacterial and fungal coinfections are not rare but occur more commonly in certain clinical scenarios and patients with pre-existing lung conditions. They are also associated with longer hospitalization and poor patient outcomes, often resulting in delaying the diagnosis and hence treatment. *Pseudomonas aeruginosa* and *Aspergillus fumigatus* are the most common bacterial and fungal species present in cystic fibrosis airways, respectively, and coinfection worsens the clinical course [1]. Severe COVID-19 patients with secondary infections required longer hospitalization and had a higher risk of death and early diagnosis was important to design the right interventions to reduce mortality [2]. There are reported fatal cases of invasive Aspergillosis and MRSA associated with influenza A infection [3]. Allergic bronchopulmonary aspergillosis (ABPA), caused by complex immunological reactions to *A. fumigatus* usually warrants the use of long-term glucocorticoids, hence increasing the risk of acquiring secondary infections making it another clinical scenario conducive for co-infections. There is a reported case of ABPA complicated with *S. aureus* and *Nocardia* infection [4]. Accentuation of zonal differences in ventilation and

perfusion in these patients makes them susceptible to *S. aureus* infection and subsequent damage. *S. aureus* may have a tendency to infect lungs with upper lobe damage which coincidentally occurs in both conditions [4].

Studies have explored the factors associated with coinfections in invasive aspergillosis and have found them to be allogeneic hematopoietic stem cell transplantation, other hematological malignancies, other underlying diseases, lymphopenia, fever, CRP >180 mg/dL, tracheal intubation, isolation of two or more *Aspergillus* species and the presence of a non-nodular lesion on Chest computed tomography [5]. The above study also noted that coinfections were independently associated with higher mortality at week 12.

In the above cases with coinfections, it may be noted that the patients were sick, had pre-existing lung conditions, were hospitalized at presentation, and investigated aggressively in view of their clinical presentation or failure to improve with treatment. Our patient on the contrary attended the OPD as a walk-in with very minimal symptoms and signs and it was the disproportionate rise in CRP that led us to investigate further.

Aspergillus, a mold can lead to different clinical presentations-invasive pulmonary Aspergillosis (IPA) occurs primarily in severely immunocompromised patients or those with chronic lung diseases. Chronic necrotizing aspergillosis is a locally invasive disease described in those with chronic lung disease or mild immunodeficiency. Aspergilloma is found in patients with previously formed cavities in the lungs and ABPA is a hypersensitivity reaction to *Aspergillus* antigens, seen mostly in patients with asthma, atopy, or cystic fibrosis. Although *Aspergillus* species are widespread in the environment, pulmonary disease is mainly caused by *A. fumigatus* [6]. Considering the clinical course and presentation, our patient fits into chronic necrotizing aspergillosis. Our patient was not severely immunocompromised and presentation was not very typical. The high degree of suspicion and radiological findings helped in leading the investigation in the right direction and early diagnosis.

Community-acquired MRSA pneumonia historically affects younger patients, follows influenza infection, and is often severe, requiring hospitalization and causing the death of a significant proportion of those affected [7]. While it is important to identify these patients early and initiate correct antimicrobial therapy, reliance on the concept of healthcare-associated pneumonia to guide antimicrobial therapy leads to overutilization of broader spectrum antibiotics [8]. Multiple MRSA-specific scores are hence designed to identify patients at risk of MRSA. One such score is the Shorr score for MRSA pneumonia which identifies patients at low risk for MRSA pneumonia [8]. Our patient scored 2 points on the score indicating that she was at intermediate risk with advice to use clinical judgment. On another score, the drug resistance in pneumonia (DRIP) score predicts the risk for community-acquired pneumonia due to drug-resistant pathogens [9]. Our patient's score was 1, indicating that she was at lower risk of having a drug-resistant organism with advice to treat without extended-spectrum antibiotics. Clinical severity at presentation also guides treatment and CURB- 65 score, a simple severity assessment tool for pneumonia severity estimates mortality in community-acquired pneumonia to help determine inpatient versus outpatient treatment [10]. Our patient had a CURB-65 score of 1, indicating that she was in a low-risk group, with advice to consider outpatient treatment.

This highlights that there were no clinical indicators or scores to suspect or consider MRSA pneumonia in this patient.

CONCLUSION

Hereby, we conclude that our case represents an unusual presentation of MRSA pneumonia coinfection with chronic IPA, presenting with very minimal symptoms and signs, but disproportionately high levels of CRP that led to suspicion and search for underlying cause. When evaluating any patient, clinical presentation, blood tests, and imaging should be used to guide clinical decisions and the reason for any unexplained finding should be pursued. It should be noted that coinfections and infections with resistant organisms can occur in community-origin pneumonia amongst the elderly, and patients with diabetes and COPD, hence investigations should be done in that direction.

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