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Case Report

Post Covid Pneumonia a Diagnostic Conundrum: Is it Fungal, Mycobacterial or May Be Both?

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Abstract

The SARS-CoV-2 was first detected and diagnose in several patients who had traveled to Wuhan city, China or went to a seafood market in Wuhan city, China. It is a highly pathogenic and transmissible coronavirus type that emerged in year 2019 and has caused a worldwide acute respiratory illness, named 'coronavirus disease 2019' (COVID-19), which leads to high morbidity and mortality. The specific medical countermeasures for these human coronaviruses are still under research. Sometimes spread of false information regarding these human coronaviruses are also seen worldwide which result in panic in general public regarding the infection. Post-Covid upper zone cavitating pneumonia represents a diagnostic challenge, specially between Tuberculosis and aspergillosis, notably in this part of the globe with resource constrained settings.

Keywords: Post COVID pneumonia, Covid-19, human coronaviruses.

Introduction

Coronavirus belongs to the subfamily *Coronavirinae* of the *Coronaviridae* family and based on genetic properties, it is further subdivided into four genera: α-coronavirus, β-coronavirus, γ-coronavirus and δ-coronavirus. In the last two decades, β-coronavirus genera have been a major virus of research due emerging and re-emerging infections and resulting in outbreak [1]. In past few decades three highly pathogenic and deadly human coronaviruses which have emerged, namely SARS-CoV-2, SARS CoV and MERS-CoV [2]. The SARS-CoV-2 was first detected and diagnose in several patients who had traveled to Wuhan city, China or went to a seafood market in Wuhan city, China. SARS- CoV-2 (Severe acute respiratory syndrome coronavirus 2) is a highly pathogenic and transmissible coronavirus type that emerged in year 2019 and has caused a worldwide acute respiratory illness, named 'coronavirus disease 2019' (COVID-19), which leads to high morbidity and mortality [3]. The specific medical countermeasures for these

human coronaviruses are still under research. Sometimes spread of false information regarding these human coronaviruses are also seen worldwide which result in panic in general public regarding the infection [4].

Post-Covid upper zone cavitating pneumonia represents a diagnostic challenge, specially between Tuberculosis and aspergillosis, notably in this part of the globe with resource constrained settings [5]. Bronchoscopy, NAAT test and galactomannan assays maybe helpful in this regard. Sometimes it may not be possible to differentiate between fungal and mycobacterial infections, necessitating an empirical administration trial of voriconazole and/or ATT to be given concomitantly or sequentially depending on the clinical response, imaging and laboratory parameters [6]. Here we reported a case of a patient with post covid pneumonia with detailed diagnosis, differential diagnosis, treatment and follow-up at our tertiary care center.

Case Report

A 48-year-old woman without any significant comorbidities was transferred to our Intensive care unit from another hospital. She has had COVID -19 pneumonia on her day 45, tracheostomized maintaining oxygen saturation at 92 % on Pressure controlled mode of mechanical ventilation. She had an indwelling left sided intercostal drain with underwater seal for 25 days with cheesy drainage of 200ml/day, related to a persistent left sided bronchopleural fistula. She had a pulse of 120 bpm, BP130/80 mmHg temperature 38C. Her laboratory parameters were as per table 1.

Table 1: Distribution of laboratory study parameters.

Parameters	Values
Hemoglobin	9g/dl
Total leucocyte count	19000/mm3
differential count	N81.3L12.7E0.5M4.7B0.15
Platelet count	3 lakhs/mm3
Serum bilirubin (total)	0.8mg/dl
Serum bilirubin Direct	0.2mg/dl
AST	15U/L
ALT	18U/L
total protein	5g/dl
albumin	2.8mg/dl
INR	1.3
Serum creatinine	0.2mg/dl
Blood urea	17.3mg/dl
Serum sodium	135 mmol/L
Potassium	3.5 meq/L
chlorides	99 mmol/l

Recent CT scan demonstrated moderate hydropneumothorax on left side with pneumomediastinum. In addition, multiple bilateral patches of consolidation and ground glass opacities as COVID19 pneumoniae sequelae. There was one moderate sized bulla on both lung apices, with an associated cavitating consolidation in the right lung apex. The Patient had received a cocktail of various antibiotics like meropenem, colistin, teicoplanin, vancomycin, piperacillin-tazobactam time to time depending on antibiotic sensitivity pattern, apart from methyl prednisolone and remdesivir at the referring hospital. However, despite all these supportive

measures, drain output remained high. In view of the refractory cavitating pneumonia on right side and the high persistent drain output on the left side, even after adequate antibiotic therapy, a strong suspicion of mycobacterial infection and fungal, especially aspergillosis was kept in the differential diagnosis. Gene X PERT nucleic acid amplification test of the tracheal aspiration and chest drain sample were negative for mycobacterium tuberculosis and KOH mount was negative for fungal elements. Bronchoscopy and galactomannan assay were not done due to logistical issues.

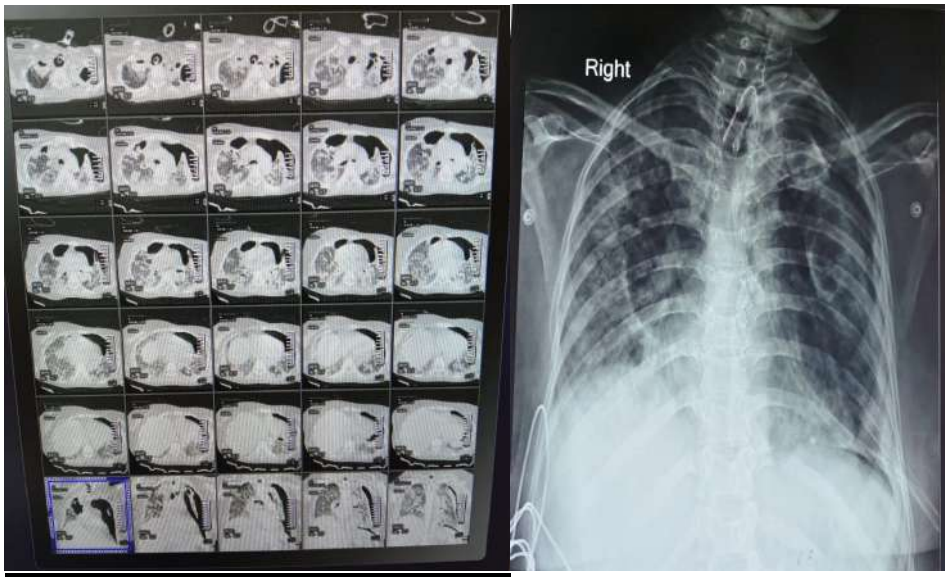

Figure 1: Findings on CT Scan and X-Ray imaging.

An antitubercular chemotherapy combination regime was started empirically based on rifampicin ethambutol, Isoniazid and Pyrazinamide. However, rifampicin was not tolerated due to the development of severe gastritis and drug-induced hepatitis. Therefore, the patient was further switched to a modified Antitubercular regimen with ethambutol, levofloxacin, Isoniazid and thrice weekly kanamycin. A significant improvement was seen within seven days with increase in appetite, sealing of the fistula on day 6, weaned off mechanical ventilation on day 8, furthermore the intercostal drain was removed on day 10 post- antitubercular therapy (ATT). The patient was successfully discharged on day 14 on 1 liter of oxygen, on modified ATT planned for one half to two years as the regimen was rifamycin free. In view of the strong suspicion of fungal infection, the patient was required for a weekly follow-up.

The patient was planned for perfenidone therapy in the near future, initially at a low dose, in view of the hepatotoxicity. The patient was recuperating well during the following 2 months when developed a spontaneous pneumothorax on the right side presumably related to ipsilateral bulla rupture, without any evidence of previously visualized cavitation and there was resolution of the right upper lobe consolidation. Repeated Imaging at this time also revealed complete expansion of the left lung.

In this second hospital admission, the patient required an intercostal drainage on the right side with underwater seal with improvement. In the near future, the patient may require bulla excision if development of recurrent spontaneous pneumothorax occurs, but meanwhile, the patient was kept under surveillance for high suspicion of fungal infection.

Figure 2: Showing intercostal drainage.

Discussion

Post-Covid upper zone cavitating pneumonia represents a diagnostic challenge, specially between Tuberculosis and aspergillosis, notably in this part of the globe with resource constrained settings [5]. Bronchoscopy, NAAT test and galactomannan assays may be helpful in this regard. These, in addition to CT chest findings such as infarct -shaped consolidations and smooth bronchial wall thickening-were more frequent in invasive pulmonary aspergillosis whereas mass-shaped consolidations and centrilobular nodules (<10mm, clustered) were more frequent in tuberculosis (which were present in our case) [7]. Imaging features that may favor mucormycosis over aspergillus infection in a neutropenic patient are bird nest sign, >10 pulmonary nodules, pleural effusion with presence of concomitant sinusitis and progression of infection despite voriconazole therapy [8].

Sometimes it may not be possible to differentiate between fungal and mycobacterial infections, necessitating an empirical administration trial of voriconazole and/or ATT to be given concomitantly or sequentially depending on the clinical response, imaging and laboratory parameters [9]. Hence, modified ATT without rifampicin and pyrazinamide may have to be considered in view of voriconazole's potential interaction withCYP3A4, CYP2C9, CYP2B6 andCYP2C19 cytochromes as it may act as both as a substrate and inhibitor, apart from the hepatoxicity potential of the concomitant therapy. Thus, L-Amb may be used instead, in the initial period, since, the administration of rifampicin could reduce serum concentrations of voriconazole while Isoniazid may increase voriconazole concentrations by inhibiting CYP2C19 [10].

On discharge, the patient may need to be shifted to Isavuconazole as it has demonstrated non inferiority to voriconazole with lower drug related hepatobiliary, ocular and skin side effects. It is the only triazole agent that shortens QTc hence no cardiac risk although its coadministration with rifamycin is contraindicated because of reduction in isavucanazole plasma concentration [11]. Similarly, when posoconazole coadministration with ATT for mucormycosis coinfection is being considered, Rifampicin is a strong cytP450 inducer while azoles are strong inhibitors, thus coadministration may lead to treatment failure. Rifampicin may be replaced by rifabutin although the interaction may still persist albeit at a lower frequency necessitating thrice weekly dosing [12,13].

Conclusion

We concluded from the present case study that in addition to CT chest findings, bronchoscopy, NAAT test and galactomannan assays may be helpful in

diagnosing post-Covid upper zone cavitating pneumonia to distinguish from Tuberculosis and aspergillosis. To round up, all delayed resolution pneumoniae in a post COVID patient are not necessarily fungal, a close clinical suspicion needs to be kept for mycobacterial and, even occasionally, in combination.

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