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Post COVID 19 infections: A case series of 5 different pathogens

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Abstract

Secondary infections are commonly identified in viral respiratory infections and are an important cause of mortality and morbidity. Post Coronavirus disease 19 (COVID 19) infections significantly change the long-term outcome of COVID 19. The complexities of post COVID 19 infections are the diversity of pathogens encountered and high index of suspicion is needed to diagnose & manage these infections. But the significance of bacterial and fungal infection following COVID 19 has not been adequately elucidated in literature. We report five interesting cases of secondary infections in post COVID 19 patients which include *Pneumocystis Jirovecii* pneumonia; Mucormycosis; Pulmonary Tuberculosis; Pulmonary Nocardiosis and Pseudomonal lung abscess. We have highlighted the challenges imposed and management of such patients.

Keywords

post coronavirus disease 19; nocardia; tuberculosis; mucormycosis, *pneumocystis jirovecii*.

Introduction

Coronavirus disease 19 (COVID19) is an ongoing pandemic caused by the Severe Acute Respiratory Syndrome CoronaVirus 2 (SARS CoV 2). This virus commonly affects the lungs causing pneumonia with acute respiratory distress syndrome, type 1 respiratory failure, pulmonary thromboembolism and other organ systems. Severe complications include respiratory failure, sepsis, acute coronary syndrome, acute renal failure and secondary infections. Those who had COVID 19 develop two types of complications. First one is post-COVID 19 sequelae where in the patients have persisting hypoxia requiring oxygen support. The second one is the post COVID 19 infections. Risk factors for secondary infections included the use of broad-spectrum antimicrobials, glucocorticoids, severe pulmonary involvement and patients on immunosuppressant drugs for other conditions [1,2]. Review of literature has revealed reports of co-infection with various microorganisms during active COVID 19. There were no reports of infections following remission

of COVID 19. Here we report 5 such cases of post COVID 19 infection with different pathogens all occurring after remission from COVID 19.

Case I

A 63-year-old male known case of ischemic heart disease was treated for COVID 19. High resolution computerized tomography of (HRCT) lungs revealed CT severity index 14/25. He was treated with Remdesivir, Low molecular weight Heparin (LMWH), glucocorticosteroid. He improved and was discharged. One month after discharge, he presented with fever, breathlessness and cough for 10 days. On examination, he maintained 90% saturation in room air and had bilateral wheeze and crepitations. Complete Blood Count (CBC) showed white blood cell (WBC) count of 12,900 with 78% neutrophils and 10% lymphocytes. His renal function test (RFT) and liver function tests (LFT) were within normal limits. HRCT chest showed evidence of resolving atypical pneumonia. Bronchoalveolar Lavage (BAL) tested positive for Pneumocystis. jirovecii by Gomori Methenamine Silver (GMS) stain (Figure 1) and PCR. He was treated with Cotrimoxazole and prednisolone. He completely recovered after the treatment.

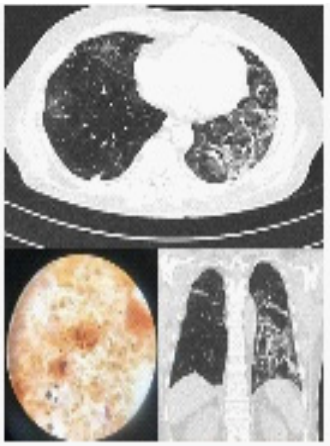

Figure 1: HRCT coronal and axial section of lung showing subtle ground glass densities with predominant interlobular septal thickening within with adjacent parenchymal strands and thin atelectasis in both lungs, predominantly in the peripheries, peri hilar regions and lower lobes. BAL- Gomori Methenamine silver staining shows cysts of *Pneumocystis Jirovecii.*

Case II

A 56-year-old male a known case of Type 2 Diabetes mellitus/ Systemic Hypertension who was treated for COVID 19 and discharged home 2 months back, presented with fever for more than 2 weeks. His vitals were stable and systemic examination showed bilateral crepitations. CBC showed a WBC count of 1,700 cells/cmm with 75% neutrophils, 19% lymphocytes and 5% monocytes. His RFT and LFT were within normal limits. Positron Emission Tomography (PET) scan showed features suggestive of COVID 19 sequelae in lungs and low metabolic activity at lymph nodes. BAL sample tested positive for *Mycobacterium Tuberculosis* (MTB) by XPERT MTB-Rifampicin (RIF) assay. He was started on Anti-Tubercular Therapy (ATT) with Rifampicin, Isoniazid, Pyrazinamide and Ethambutol. The patient gradually improved and was then discharged with ATT. On review, he had no further fever spikes and was symptomatically better.

Case III

A 61-year-old male, a known case of Type 2 Diabetes Mellitus/ Dyslipidemia, treated for COVID 19

one month back, presented with pain on the left half of the face with blurring of vision and protrusion of the left eye. On examination, he had proptosis of the left eye with left III, IV, V2, VI, VII cranial nerve palsies. CBC showed a WBC count of 8,500 with 56% neutrophils and 34% lymphocytes. RFT and LFT were within normal limits. MRI showed evidence of fungal sinusitis and orbital cellulitis. Diagnostic nasal endoscopy showed large posterior septal perforation with the involvement of the left maxillary sinus. He underwent left maxillary sinus debridement. He was started on intravenous Liposomal amphotericin B for 4 weeks and was switched to oral Isavuconazole. His tissue culture on Sabouraud dextrose agar and Lactophenol Cotton Blue stain revealed growth *Rhyzopus sp* (Figure 2). He was doing well on follow up.

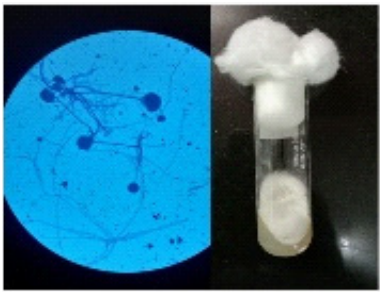

Figure 2: Tissue culture on Sabouraud dextrose agar showing black to grey tan cottony growth with salt and pepper appearance. Lactophenol Cotton Blue staining showed broad pauciseptate hyaline hyphae with right angled branching.

Case IV

A 54-year-old male known case of Type 2 diabetes mellitus had COVID 19 a month back, presented with non-productive cough and high-grade fever for 2 days. On examination, his vitals were stable and had reduced breath sounds in the left interscapular area. CBC showed a WBC count of 9,800 per cmm with 82% neutrophils and 12% lymphocytes. His RFT, LFT were within normal limits. Blood cultures were sterile. Chest x-ray showed a thick-walled cavity with an air-fluid level in the left middle and lower zone. BAL sample grew *Pseudomonas aeruginosa* (inducible AMPC). He was started on intravenous Meropenem. During the course of his stay, he developed proximal muscle weakness of all four limbs. Nerve conduction study showed demyelinating Polyradiculoneuropathy due to Guillain Barre syndrome. He was started on IV immunoglobulin and showed gradual improvement. On review, he was afebrile and chest X-ray showed complete resolution of the abscess.

Case V

A 58-year-old male with no co-morbidities admitted and treated for COVID 19 presented 2 weeks post-discharge with fever, dry cough and breathlessness for a week. On examination, he was afebrile and vitals stable. Systemic examination revealed bilateral basal crepitations. CBC showed a WBC count of 10,800 cells/cmm with 78% neutrophils and 12% lymphocytes. RFT and LFT were within normal limits. HRCT showed consolidation of the left lower lobe. BAL for modified Ziehl Neelsen stain for Nocardia was positive (Figure 3). He was started on Trimethioprim-Sulfamethoxazole. On review, the patient had no fever and was symptomatically better.

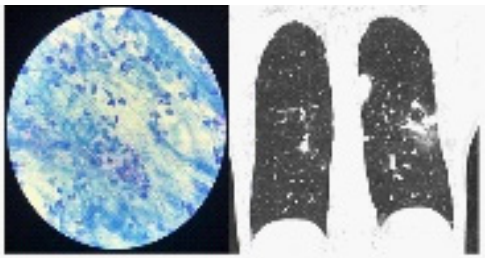

Figure 3: HRCT coronal section of lung showing consolidation in the left lower lobe. BAL – Modified Acid Fast Bacilli (AFB) stain showing the partially acid-fast beaded filamentous appearance of Nocardia.

Discussion

We report five cases of post COVID 19 sequelae that developed different secondary infections in a time span of two weeks to three months after active COVID 19 infection. All five patients were aged above 55 years and had similar severity of COVID 19 infection and treatment for the same. Four of these five patients had co morbidities.

Experiences from SARS, MERS and influenza outbreaks have evidenced co infection with other microorganisms in a subset of patients that frequently determines the morbidity and mortality [3,4]. A similar clinical pattern has been reported in COVID 19 pandemic, with concurrent secondary infections occurring during acute phase of COVID 19 infection. Lansbury L et al in their metaanalysis reviewed thirty studies and reported a pooled prevalence of 7% of co infections; most of them were of bacterial etiology [5]. Various other pathogens like invasive aspergillosis [6], Pneumocystis jirovecii [7], Mycobacterium tuberculosis [8] and mucormycosis [9] have also been implicated.

In our search through literature, we found no publications on secondary infections during the recovery phase of COVID 19 infection, similar to our report. More recently, studies have emerged in literature on the so called “Post COVID 19 syndromes” which elaborates on the clinical course after the acute phase of COVID 19 infection [10,11]. Even these studies have not commented on the incidence or characteristics of secondary infections occurring during the recovery phase of COVID 19 infection. In this context, indirect evidence comes from a study by Donnelly JP et al, who found that sepsis (8.5%) and pneumonia (3.1%) were common causes for readmission of COVID 19 patients within 60 days of discharge from initial hospitalization [12]. This study along with our report reiterates the importance of early diagnosis and management of post COVID 19 secondary infections.

Propensity for developing secondary infections ‘de novo” in late phases of COVID 19 infection could be explained by several factors like COVID 19 related damage to the lungs, immunomodulatory drugs, comorbidities etc. It is also possible that concurrent infections during acute phase of COVID 19 infection, might have remained undetected due to hesitancy for thorough microbiological evaluation using invasive “aerosol generating” procedures like bronchoscopy. Such undiagnosed concurrent infections potentiated by aforesaid factors, may have emerged in later course of recovery from COVID 19 infection.

Going by the potential impact of post COVID 19 secondary infections on morbidity and mortality, we strongly recommend future research in this subject. In an attempt to synchronize our efforts to understand this important entity we also recommend data repositories or registries to profile post COVID 19 infections. We believe that these efforts will help us evolve strategies towards better management of COVID 19.

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