Bacterial Pneumonia Co-Infection in COVID-19 Patients

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Abstract

The objective of this study was to highlight the emergence of COVID-19 bacteria pneumonia co-infections in patients infected with SARS-Cov-2 and risk factors related to its incidence and outcomes. We reported two cases of elderly patients with multiple comorbidities infected with SARS-Cov-2 and developed COVID-19 bacterial pneumonia requiring admission to intensive care unit (ICU) with one mortality preceded by septicemic shock and multi-organ failures. Observing the potential risk factors for being infected with SARS-Cov-2 and developing COVID-19 bacterial pneumonia we strongly advocate for rapid detection of COVID-19 bacterial pneumonia in SARS-Cov-2 infected patients and rapidly characterized the bacterial involved for a better outcome and importantly for efficient antimicrobial stewardship. COVID-19 bacterial pneumonia is an emerging disease requiring rapid detection and bacterial characterization with the ongoing management for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

Keywords: COVID-19, bacterial pneumonia, acute respiratory syndrome

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Introduction

Having Covid-19 bacterial pneumonia in a patient who is infected with SARS-COV-19 will significantly increase the severity of the illness and worsen the morbidity and mortality risk. However, the exact mechanisms by which SARS-CoV-2 precipitate Covid-19 bacterial pneumonia and lead to septicemic shock with multi-organ failure are still not well understood. We hope that by rapid detection of potentially high-risk patients and early identification of bacterial involved in Covid-19 bacterial pneumonia would improve patients’ treatment and management. Further, this will reduce the morbidity and mortality and most importantly can improve antimicrobial stewardship in Covid-19 bacterial pneumonia throughout the course of SARS-CoV-2 infection worldwide.

CASE REPORT

Case 1

This is a 74-year-old gentleman with underlying hypertension, stage 3 chronic kidney disease and gouty arthritis. He developed symptoms to suggest viral infection which were fever, dry cough, myalgia, and lethargy two days after attending a mass gathering with almost 1500 participants in Sarawak. Without seeking any treatment, his symptoms did not improve and on day 6 of illness he sought therapy at our hospital. Treated with the risk of COVID-19 infection, the patient was admitted to COVID general ward with the impression of SARS-CoV-2 infection with the differential diagnosis of viral fever and atypical pneumonia. Nasopharyngeal swab COVID-19 screening done on the day of admission revealed a positive result for SARS-CoV-2 infection stage 3B. Clinically the patient was not in any respiratory or cardiovascular distress with the blood pressure of 140-160/80-90 mmHg, normal heart rate, not tachypneic, body temperature of 37.4 to 37.9 °C and normal blood sugar monitoring. Blood investigations showed Hb 14.1 g/dL, platelet count of 168 x 10^9/L and white cell count of 4.5 x 10^9/L. His CRP was 50mg/L with normal renal profile and no evidence of coagulopathy, liver derangement and electrolyte imbalances. His initial chest radiograph demonstrated heterogenous opacity at the lower zone (Figure 1). However, his subsequent chest radiograph showed worsening pneumonia patch on the right lower zone of his lung. The patient was decided to be transferred to ICU on the same day of his admission to our hospital for close monitoring and observation for impending respiratory distress.

In ICU, he was prescribed with oral Augmentin (Amoxicillin Clavulanate) 1.2g tds, oral Azithromycin 500mg tds, and oral Tamiflu (oseltamivir phosphate) 75mg bd. However, later the day he was further prescribed with oral Kaletra (lopinavir 400mg/ritonavir 100mg) bd and oral hydrochloroquine 200mg bd.

In ICU, patient demonstrated a worsening hypoxemia which was responded with oxygen supplement via nasal prong and later with venturi mask 40% oxygen delivery. Clinically, patient was not tachypneic with a respiratory rate of 16-18 breaths per minute with a good blood pressure. Three days in ICU, the patient remain stable with no evidence of respiratory distress and good oxygenation via nasal prong oxygen supplement and was transferred to general ward. After being discharged from ICU, patient was remained stable in the general ward for the first 3 days and not requiring oxygen supplement. However, on the 4th day in the general ward, patient demonstrated signs of respiratory distress by the evidence of mild tachypneic, oxygen saturations of 92% in room air. Physical examination revealed bilateral lungs crepitations up to the midzone with a sub normal body temperature. Arterial blood gases (ABG) revealed type one respiratory failure with the arterial oxygen of 54.7 mmHg on room air. Repeated chest radiograph revealed a worsening pneumonic patch.

Sputum culture and sensitivity taken on the day of his admission grew Streptococcus Pneumoniae while his blood culture remained no growth. Therefore, for his second ICU admission he was started with antibiotic ceftriaxone 2gm daily to cover for concomitant bacterial infection. Repeated nasopharyngeal swab for SARS-Cov-2 screening on day 6 of his hospitalization remain positive. Patient was transferred to ICU for the second time for close observation on day 7 of his hospitalization in view of worsening respiratory symptoms. In ICU, oxygen supplement was continued via venti-mask with 60% oxygen delivery.

He progressed well in the ICU without endotracheal intubation and mechanical ventilation. He was discharged back to general ward after 4 days in ICU. After a total of 14 days of hospital admission, he was discharged home with a negative result of repeated SARS-Cov-2 screening.

Case 2

This is a 69-year-old gentleman who has multiple medial problems which were hypertension, gouty arthritis, chronic kidney disease stage 5 and hyperlipidemia. He started to develop fever, productive cough of white sputum, poor oral intake and lethargy after 12 days attending a mass gathering Ijtima’ Tabligh which lasted for 5 days. He went to a district hospital after 5 days of unresolving fever and productive cough. Screening and investigations from his sputum yielded positive SARS-CoV-2 infection (stage 5) with superimposed community acquired pneumonia. Apart from having temperature,
physical examination was unremarkable, and patient was hemodynamically stable and not in any distress. However, on day 3 of hospitalization, his clinical condition was deteriorating with increasing tachypnea, persistent spike of temperature and worsening tissue oxygenation requiring oxygen supplement via venti-mask with 40% oxygen delivery. Patient was sent to ICU with the diagnosis of SARS-CoV-2 infection (stage 5) with acute on chronic kidney disease with metabolic acidosis. (Creatinine: 288 μmol/L, Arterial blood gases: pH of 7.27, pCO2 of 29.3 mmHg and HCO3 of 14 mEq/L).

10 hours after admission to ICU, patient developed severe respiratory distress with hypoxemia requiring emergency endotracheal intubation, persistent hypotension despite aggressive fluid therapy and in metabolic acidosis. Auscultation of his lungs revealed bilateral coarse crepitations and his arterial blood gases revealed respiratory failure type one with worsening metabolic acidosis requiring hemodialysis. Chest radiograph demonstrated heterogenous opacity at the lower and middle zone of the lungs which suggest for severe pneumonic patch in both lungs (Figure 2). Patient was treated for septicemic shock with multi-organ failure and was covered with broad spectrum antibiotic of intravenous cefepime 2g daily plus continuation of treatment for COVID-19. However, despite aggressive treatment and renal replacement therapy, his condition worsened with persistent refractory hypotension despite on maximum noradrenaline and vasopressin support and aggressive fluid therapy and worsening metabolic acidosis. Patient succumb to death on day 3 of ICU admission and his blood culture and sensitivity revealed the presence of *Staphylococcus lugdunensis* while his sputum culture and sensitivity showed predominant presence of *Streptococcus pneumoniae*.

**DISCUSSION**

Clinical presentations following any viral infections are basically caused by virus-induced damage to the infected host’s cells and by the reaction of host’s immune response. The host’s immune system used antibodies to control virus infection by neutralizing the free virus, whereas virus-infected cells are identified and destroyed by cytotoxic T lymphocytes. Clinically, the severity of organ dysfunction following viral infection is depending on the extent of the cell destruction and many factors may influence the outcome of viral infection, such as the initial viral load, pre-existing host’s immunity and also the virulence of the virus itself. It is known that a highly virulence virus can replicate better, modify the host’s immune response and able to spread more rapidly. Covid-19 bacterial pneumonia is on rise in parallel with pandemic infection of SARS-CoV-2 virus. The concept of excessive morbidity and mortality associated with multi-organ failures from bacterial co-infection during or shortly after viral infection is well documented. However, the precise mechanisms by which SARS-CoV-2 causes severe bacterial co-infection pneumonia in human is still under researched. Latest findings revealed 50% mortality from SARS-CoV-2 was due to secondary bacterial infection and the current death rate from Covid-19 bacterial pneumonia itself was approximately 4%. Furthermore, a study involving 1099 patients in China with confirmed SARS-CoV-19 infection reported that total of 173 cases with severe condition were found to be associated with comorbidities of hypertension (23.7%), diabetes mellitus (16.2%), coronary heart disease, (5.8%), and cerebrovascular disease (2.3%). Meanwhile, study done by Zhang et al (2020) demonstrated that among those who were admitted with Covid-19 disease, 30% and 12% had hypertension diabetes mellitus respectively. In this case report, we would like to show possible correlation between co-morbid conditions and severity of SARS-CoV-2 infection among elderly patients.

It is known that SARS-CoV-2 virus binds to the target cells in the host through angiotensin-converting enzyme 2 (ACE 2) which is readily expressed by epithelial cells of the lung, intestine, kidney, and blood vessels. Therefore, the expression of ACE 2 by the epithelial cells will certainly increase (up-regulation of ACE 2) in patients who are treated with ACE inhibitors and angiotensin II type-I receptor blockers (ARBs) for their diabetes and hypertension, in which will facilitate the infection of SARS-CoV-2 and adding the risk of developing severe condition of Covid-19 among patients.

A study on the predictors of mortality for patients with Covid-19 bacterial pneumonia caused by SARS-CoV-2 infection identified four main risk factors which include age (≥65 years), pre-existing concurrent cardiovascular disease or cerebrovascular diseases, CD3+ T-cells (≤75 cellsμL-1) and cardiac troponin I (≥0.05ng/mL). The latter two factors were found to be the predictors for mortality of Covid-19 bacterial pneumonia patients. The significant decreased in the number of CD8 cell counts in the peripheral blood in patients with Covid-19 bacterial pneumonia may suggest a progressive immune-associated injury with inadequate adaptive immune responses as the possible mechanism by which SARS-CoV-2 infection causes severe illness, including septicemic shock and multi-organ failure with a significant fatal outcome. A study related to the clinical features of patient infected with SARS-CoV-2 revealed a much higher concentration of certain cytokines and chemokines, especially in patients with severe Covid-19 bacterial pneumonia than those with mild disease, which might suggest that SARS-CoV-2 infection may damage human body system and result in a systemic inflammatory response.

The interplay of virus infection and bacteria co-infection in a host involved a complex process and the prognosis of the patient depends on multiple contributors, including modulation of innate response resulting in delayed
The clearance of bacteria, hypersensitization of infected cells leading to enhanced immune-mediated lung damage, and modulation of bacterial adherence (Okamoto et al, 2004)9. Furthermore, the increase in bacterial adherence to host cells might be due to the exposure of the novel binding sites for bacteria on the epithelial surface, which can be due to the expression of highly glycosylated viral proteins or by the alteration of a bacterial receptor expression pattern9. Surprisingly, it was shown that human coronavirus HCoV-NL63 infection resulted in an increase adherence of Streptococcus pneumoniae to virus-infected cell lines and fully differentiated primary human airway epithelium cultures10. It was proven that respiratory viral infections will always predispose to bacterial co-infection which commonly contributed to increased disease severity and clinical outcomes. Bacterial pathogens predominantly involved in secondary infection of the respiratory tract are commonly recruited from natural respiratory tract pathogens, including Streptococcus pneumoniae, Haemophilus influenza, Pseudomonas aeruginosa and Staphylococcus aureas. However, during influenza outbreak in 1918, most fatalities were due to subsequent bacterial co-infection, particularly with Streptococcus pneumoniae organisms. In 2009, during H1N1 influenza pandemic, poor outcomes of the patient were always associated with bacterial co-infections and among those reported of hospitalized bacterial co-infection cases with confirmed pneumonia, revealed a mean of 19% positive for bacteria with 54% of them were related to Streptococcus pneumoniae11. Golda et al. (2011) concluded that infection with human coronavirus NL63 enhanced streptococcal adherence to epithelial cells10. In accordance, sputum culture and sensitivity of our patients revealed presence of Streptococcus pneumoniae. Golda and colleagues also concluded that viral infection showed no effect on adherence of other bacteria tested, and they assumed there was a specific synergistic interaction between Streptococcus pneumoniae and HCoV-NL6310. However, there is no evidence based for this finding to be related with SARS-CoV-2 infection.

CONCLUSION

Elderly with underlying comorbidities of cardiac diseases, hypertension, and diabetes on ACE 2 - stimulating drugs (namely ACE inhibitors and ARBs) have higher expression of ACE 2 on the epithelial cells of lung, intestine, kidney, and blood vessels. This will facilitate the infection of SARS-CoV-2. For the area that need to be explore further, there is a possibility of an increase in bacterial adherence to the epithelial cells leading to bacterial co-infection in patients with SARS-COV-19. Importantly, rapid detection of Covid-19 bacterial pneumonia due to SARS-CoV-19 infection and early identification of the bacterial involved are crucial for prompt treatment and prognosis of the patients.

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REFERENCES


Figure 1: Chest radiograph demonstrated heterogeneous opacity at the lower zone of the lungs which suggest for bilateral lower zone pneumonic patch.

Figure 2: Chest radiograph demonstrated heterogeneous opacity at the lower and middle zone of the lungs which suggest for severe pneumonic patch in both lungs.