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CASE REPORT

# Concomitant Invasive Pneumococcal Disease in a Patient with COVID-19 – A Case Report from the Louisville Epidemiology Study

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## Abstract

A 60-year-old male presented to the Emergency Department (ED) with a one-two day history of confusion, headache, and subjective fever. Because he had met with a contact two days prior to admission who had recently traveled from the Bahamas, a COVID-19 nasopharyngeal (NP) and oropharyngeal (OP) polymerase chain reaction (PCR) test was ordered. He was diagnosed with bacterial meningitis based on presenting neurologic symptoms and the identification of *Streptococcus pneumoniae* from blood cultures. The COVID-19 NP and OP test returned positive, although he never developed shortness of breath, cough, other respiratory symptoms, diarrhea, abdominal pain, nausea, vomiting, or any change in sense of smell or taste. On day three of admission, the patient had improved clinically on intravenous (IV) antibiotics and was discharged home with instructions to self-quarantine. This case demonstrates the possibility of co-infections with COVID-19 and raises the possibility of an association between COVID-19 and patient susceptibility to invasive pneumococcal disease (IPD).

## Introduction

Previous literature has shown associations with both influenza and respiratory syncytial virus activity and the incidence of both IPD and pneumococcal meningitis. [1-5] Currently, no such association or examples have been provided with COVID-19 and IPD. With the rapid progression of COVID-19 prevalence and mortality, the documentation and characterization of potential complications and risks of COVID-19 are needed. This case describes concomitant pneumococcal meningitis in a patient positive for COVID-19 and discusses the potential role that COVID-19 may have in the pathogenesis of IPD and meningitis.

## Case Report

A 60-year-old male presented to emergency department with a one to two day history of confusion, headache, and subjective fever. His past medical history includes hypertension, hyperlipidemia, and arthritis, and has no vaccination history listed in his medical record. The patient's wife described the patient was in his baseline health the night prior to admission, which is alert and oriented times four. On the morning of admission, she noted that the patient was chilled and shaking, and asking for a blanket. At that time, he stopped talking and was noted to be extremely weak, unable to stand up without full assistance. She denied any recent illness, cough, shortness of breath, nausea, vomiting, or diarrhea. The patient's wife did report that the patient recently returned from a trip to Spain. No specifics on the trip were included in the patient's medical record (departure, return, duration, destinations, activities, etc.). The family also reported that the patient had contact with a friend two days prior to admission who had recently traveled from the Bahamas. The person who had traveled to the Bahamas had been back in the United States for about two weeks with no respiratory, gastrointestinal, or other infectious symptoms. No other known sick contacts or possible exposures were noted.

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**Table 1.** Vital Signs

| Day of Admission | Temperature (°F) | Heart Rate (bpm) | Respiratory Rate (breaths/min) | Blood Pressure (mm Hg) |
|---|---|---|---|---|
| Initial | 102 | 115 | 22 | 177/108 |
| Day 1 | 97.5-102 | 84-115 | 16-26 | 150-191/81-109 |
| Day 2 | 96.7-98.4 | 76-110 | 13-26 | 113-157/70-96 |
| Day 3 | 97.6-98.3 | 68-75 | 16-17 | 134-153/85-91 |

**Table 2.** Laboratory Values

| Day of Admission | WBC $10^3$ cells/μL | Lymphocyte % | T- Bili mg/dL | ALT U/L | AST U/L | Alk Phos U/L | PCT ng/mL | Lactic Acid mmol/L | CRP mg/dL | ESR mm/hr |
|---|---|---|---|---|---|---|---|---|---|---|
| Day 1 | 15.55 | 4.9 | 1.1 | 31 | 44 | 61 | – | 3.8 | – | – |
| Day 2 | 23.74 | 2.7 | – | – | – | – | 6.34 | 6.3 | – | – |
| Day 3 | 22.59 | 3.3 | – | – | – | – | – | – | – | – |
| (Day 7) | 9.26 | 15.2 | – | – | – | – | – | – | 2.5 | 31 |
| (Day 14) | 6.62 | 16.5 | – | – | – | – | – | – | 1.5 | 34 |

Initial vital signs were significant for a temperature of 39.1 °C (102.3 °F) and heart rate of 104 bpm (**Table 1**). The physical exam in the ED noted no nuchal rigidity and was unremarkable other than severely altered mental status and non-verbal status. Brudzinski's or Kernig's signs were not assessed. Significant labs on admission included an elevated WBC of 15.55 x $10^3$ cells/μL, elevated procalcitonin of 6.34 ng/mL, and an elevated lactic acid of 3.8 mmol/L (**Table 2**).

Chest X-ray reported no evidence of cardiopulmonary abnormality. A CT of the head, chest, abdomen and pelvis was obtained. The head CT without contrast demonstrated no mass lesion, hemorrhage or acute artifact. The chest CT without contrast was limited by motion artifact, but did not show any evidence of acute airspace disease or pleural effusion (**Figure 1**). Subsequently, an MRI of the brain with and without contrast was obtained (**Figure 2**). The report noted fluid with restricted diffusion layers dependently in the lateral ventricles without hydrocephalus consistent with ventriculitis. The image was limited by motion to assess for corresponding enhancement or leptomeningeal enhancement. Due to the noted travel history and contact, the patient was tested for COVID-19 disease by a combined nasopharyngeal/oropharyngeal swab sent for PCR and the patient was placed in appropriate isolation. Unfortunately, a lumbar puncture was not obtained due to COVID-19 isolation. Treatment was started with ampicillin 2 g IV q4 hours, ceftriaxone 2 g IV q12 hours, vancomycin 1750 mg IV q12 hours, and dexamethasone 10 mg IV q6 hours for suspected acute bacterial meningitis.

The patient significantly improved with antibiotics. Two of two blood culture sets resulted on day two of admission with gram-positive cocci in pairs and chains. *Streptococcus pneumoniae* was identified by the Verigene system (Nanosphere Inc., Northbrook, IL, USA). Susceptibilities identified a multidrug resistant *Streptococcus pneumoniae* on day three of admission. The *S. pneumoniae* MIC was 2 μg/mL to penicillin and 2 μg/mL to ceftriaxone. On the third day of admission, the SARS-CoV-2 PCR resulted positive. The patient remained without evidence of symptoms related to COVID-19 disease (respiratory, gastrointestinal) throughout his hospital admission. The patient received IV vancomycin after discharge for the duration of their meningitis therapy.

## Discussion

The pathogenesis of pneumococcal meningitis consists of bacterial colonization of mucous membranes, translocation into the bloodstream, survival in the bloodstream, and eventual entry and replication in the central nervous system. [6,7] Before *S. pneumoniae* can colonize, it first needs to adhere to mucosal surfaces, which it accomplishes through three different types of receptors: the platelet-activating factor receptor, laminin receptors, and the polymeric immunoglobulin receptor. After initial adherence, colonization is promoted by the evasion of secretory immune globulin A (IgA). Pathogen secretion of proteases helps to inactivate IgA. Although it widely varies from study to study, *S. pneumoniae* colonization of the nasopharynx is generally considered common even in healthy children and adults with its incidence reported anywhere from 8.6% - 33.2%. [8,9] After sufficient colonization of the pathogen, invasion of tissues and translocation into the bloodstream can occur. Although this occurs significantly less often than colonization, there are many factors that can facilitate translocation into the bloodstream including environmental factors, host factors, and pathogen virulence.

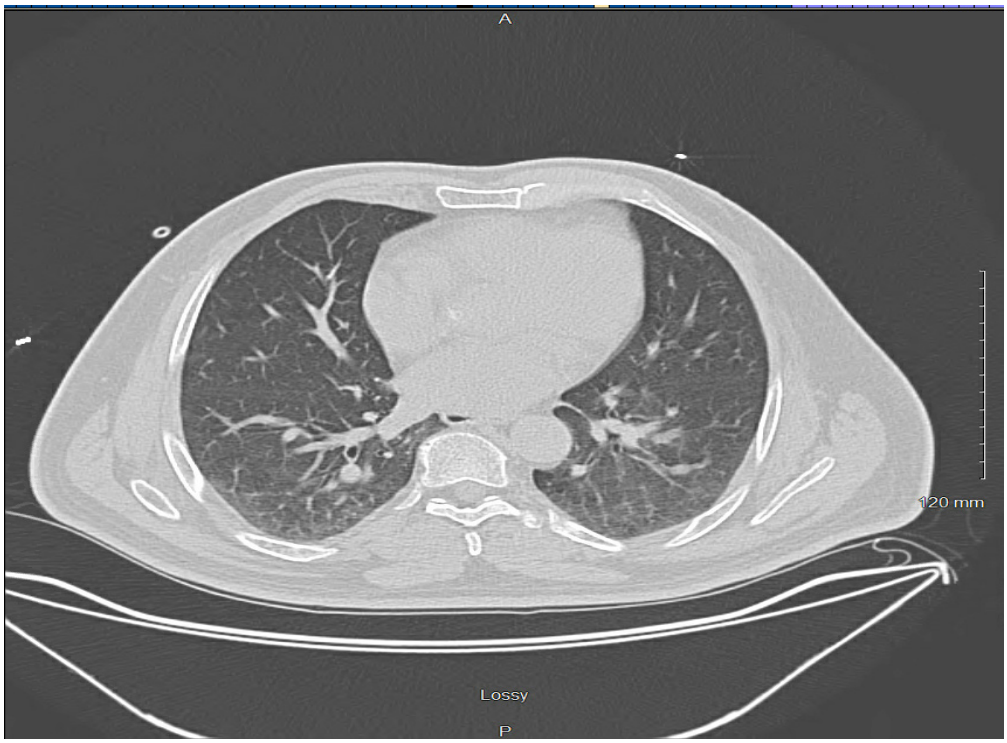


**Figure 1.** Chest CT: Computed tomography image of the chest with no evidence or findings of cardiopulmonary abnormalities.

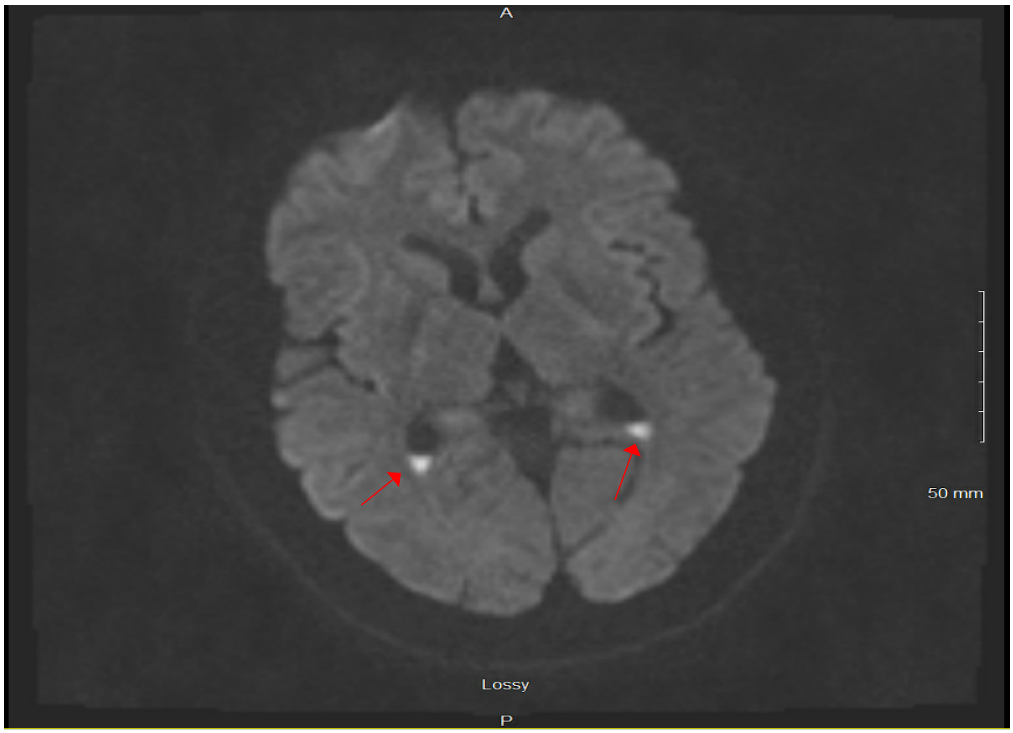


**Figure 2.** Brain MRI: Magnetic resonance image of the brain showing bilateral 6 mm x 4 mm collections layering in the posterior horns of the lateral ventricles (red arrows). The differential diagnosis includes ventriculitis versus mild subarachnoid hemorrhage.

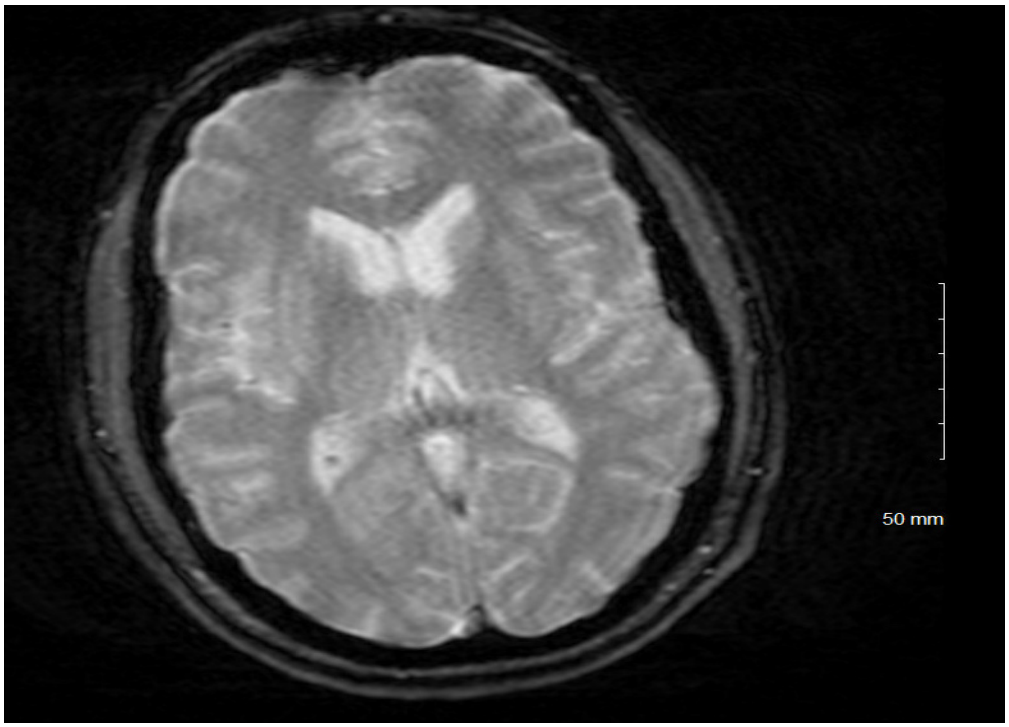


**Figure 3.** Brain MRI Gradient ECHO: Magnetic resonance image with normal signal suggesting low likelihood for subarachnoid hemorrhage.

The association between respiratory viruses and increased incidence of IPD and pneumococcal meningitis has been documented, which is a common example of environmental factors influencing pneumococcal disease. [10-13] Possible mechanisms of increased susceptibility to IPD include the respiratory viruses' ability to impair the host's innate immune system by recruiting inflammatory mediators and damaging mucosal and epithelial tissue. [11-14] Damage to these tissues and the resulting mucosal impairment and increased permeability of epithelia can facilitate bacterial pathogen adherence and promote translocation. This has been commonly used to explain the association between both influenza and RSV activity and the increased incidence of IPD and meningitis. Specific mechanisms have been described, including a synergistic activation of interferons from influenza virus and pneumococcal coinfection [12] as well as the stimulation of the platelet-activating factor receptor in the host defense against *S. pneumoniae* following influenza infections [13].

The primary route of entry for SARS-CoV-2 is thought to be through the nasopharynx, which can eventually progress into the airways and lower respiratory tract. [15] Similar to other viral pathogens, COVID-19 has been shown to recruit inflammatory cytokines including IL-1, IL-6, IL-7, IL-8, IL-9, IL-10, IFN-γ, and TNF-α among others. [16,17] These pro-inflammatory mediators that have been found in patients with COVID-19 are also known to cause tissue damage, and may provide a link to COVID-19 and increased host susceptibility to IPD.

This case provides an example of a patient that was either colonized or infected with SARS-CoV-2, and that developed concomitant pneumococcal meningitis. Interestingly, this patient did not demonstrate any signs or symptoms consistent with pneumonia from either *S. pneumoniae* or COVID-19. Although cause cannot be determined, this case demonstrates the ability of COVID-19 to co-habit with bacterial pathogens, and raises the question of whether COVID-19 can be involved in the pathogenesis of and susceptibility to IPD similar to what has been described with other respiratory viruses.

Another key point is the importance of epidemiology in screening and diagnosis of patients during an outbreak in addition to symptoms and radiographic evidence of disease. This patient would likely not have been screened without the mention of a possible sick contact and travel history, which may have resulted in further spread of COVID-19. Patients with known or high-risk exposure during an outbreak (such as sick contacts or travel history) should be tested for COVID-19 in order to decrease spread from persons with asymptomatic carriage or subclinical presentation.

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