We present a case of a critically ill patient with coronavirus disease 2019 (COVID-19) found to have acquired immune deficiency syndrome and *Pneumocystis jirovecii* pneumonia (PCP). Coronavirus disease 2019 and PCP co-occurrence is increasingly reported and may complicate diagnostic and therapeutic strategies. Patients with severe COVID-19 should be screened for underlying immunocompromise and coinfections should be considered.

**Keywords.** coinfection; COVID-19; HIV; *Pneumocystis*; SARS-CoV-2.

With mounting global cases of coronavirus disease 2019 (COVID-19), there has been increasing recognition of fungal coinfection complicating COVID-19 care. Although *Aspergillus* spp appears to be the predominant fungal pathogen in persons with COVID-19 pneumonia [1], there are emerging reports of *Pneumocystis jirovecii* pneumonia (PCP) co-occurring with or after COVID-19.

In this study, we present a case of a patient hospitalized with hypoxic respiratory failure attributed to COVID-19 and was found to have a new diagnosis of acquired immune deficiency syndrome (AIDS) and PCP. We review all published literature to date of co-occurring COVID-19 and PCP.

**CASE REPORT**

A 36-year-old man with no known past medical history presented to an emergency room complaining of shortness of breath, fever, nausea, and diarrhea for 3 weeks. Additional review of systems was positive for chills, sinus congestion, sore throat, and cough. He denied anosmia and chest pain. He was Hispanic and lived with 2 relatives who were asymptomatic. He worked in construction and reported close contacts with coworkers with similar symptoms.

On admission, his temperature was 38.7°C, heart rate 121 beats per minute, blood pressure 94/59 mmHg, respiratory rate 40 breaths per minute, and oxygen saturation 89% on 15L high flow nasal cannula, improved in prone positioning. He was ill-appearing, in respiratory distress, and without abnormal lung sounds. The white blood cell count was 8600/μL (reference range, 4800 to 10 800); absolute lymphocyte count was 400/μL (reference range, 1200 to 3400); absolute neutrophil count was 7800/μL (reference, 1400 to 6500); C-reactive protein was 197.72 mg/L (reference, <10); ferritin was 1276.1 ng/mL (reference range, 10–300); lactate dehydrogenase was 789 IU/L (reference range, 100–220); and procalcitonin was 1.87 ng/mL (reference, <0.50). A swab for influenza A and B viruses was negative. An oropharyngeal swab for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction (PCR) was positive. Chest radiograph showed diffuse hazy pulmonary opacifications. A contrasted computed tomography angiography of the chest showed diffuse upper and lower lobe ground-glass alveolar airspace disease without pulmonary embolism.

The patient was admitted to intensive care and started on remdesivir, as well as cefepime and vancomycin for possible bacterial pneumonia. Over the next 48 hours he experienced persistent hypoxemia requiring intubation and transfer to our facility. As part of our institutional protocols for patients admitted with COVID-19 at the time of this encounter, routine screening with a fourth-generation human immunodeficiency virus (HIV)-1/2 antigen/antibody test was performed and reactive. Reflex HIV ribonucleic acid testing revealed a viral load of 578 876 copies/mL. His absolute CD4 cell count was <10 cells/μL and 2% of lymphocytes. Due to the patient's critical illness and clinical condition, additional social and medical history was unobtainable, but medical record review did not report a history of HIV and noted no outpatient medications. A new chest radiograph was reported as heterogeneous bilateral lung opacities with scattered air bronchograms (Figure 1), but treating providers felt the opacities were less dense than expected for COVID-19 and for his level of hypoxemia. He continued remdesivir via emergency use authorization, received a transfusion of COVID-19 convalescent plasma, and antibacterial medications were narrowed to ceftriaxone and azithromycin.

Given the patient's prolonged, subacute symptoms and x-ray findings, an evaluation for PCP was undertaken and...
he was started on empiric trimethoprim-sulfamethoxazole and prednisone. A tracheal aspirate acid-fast stain, bacterial culture, and *P. jirovecii* direct fluorescent antibody stain (DFA) were all negative. Positive serological studies included (1→3)-β-d-glucan >500 pg/mL as well as a weakly positive serum histoplasma antigen that was below the level of quantification. A QuantiFERON-TB Gold test was indeterminate. Urine histoplasma antigen and blood cultures for bacteria and molds were negative. On hospital day 7, he underwent bronchoscopy with bronchial alveolar lavage that yielded positive *Pneumocystis* DFA and PCR tests, positive SARS-CoV-2 PCR, and bacterial, fungal, and mycobacterial cultures that remain negative to date.

The patient completed a course of remdesivir. He received a 21-day course of trimethoprim-sulfamethoxazole and prednisone for PCP, and he started dolutegravir with combination tenofovir alafenamide/emtricitabine for HIV. His course was complicated by ventilator-associated pneumonia due to *Pseudomonas aeruginosa*, labial ulcer due to herpes simplex virus type 1, persistent hypoxemia, and ongoing fevers. He was evaluated for extracorporeal membrane oxygenation but deemed not to be a candidate due to his prolonged ventilation and his immunocompromised state. He continued to experience refractory hypoxemia despite maximal ventilator settings, paralytic agents, and prone positioning. On hospital day 26, he developed asystolic cardiac arrest and died. No autopsy was performed.

**Patient Consent Statement**

Consent was unable to be obtained from the patient due to patient being intubated and altered throughout his hospitalization. No family or next of kin was available, and, if they had been, obtaining consent would have risked potentially unwanted disclosure of the patient’s HIV status. All identifying details of the patient have been removed in accordance with our institutional policy and Oxford University Press publishing policy. Ethical board approval was not believed to be indicated because this did not involve human subjects research.

**Literature Review**

A literature search of Medline with the string “[COVID-19 and pneumocystis] or [SARS-COV-2 and pneumocystis] or [COVID-19 and PJP] or [SARS-COV-2 and PJP] or [COVID-19 and PCP] or [SARS-COV-2 and PCP]” was conducted in September 2020. This search yielded 28 results (Supplementary Figure 1). Thirteen articles were case reports, 5 of which were case reports of patients with both COVID-19 and PCP (Table 1). Of these, 3 were also HIV positive. Two cases were in people newly diagnosed with HIV, underscoring the need for HIV testing in individuals hospitalized for COVID-19 who would not be expected to have a severe course of illness. In one case, the patient was diagnosed with COVID-19, treated with tocilizumab and glucocorticoids, and later diagnosed with PCP, raising the possibility that immunomodulatory treatment for COVID-19 contributed to the development of PCP [2]. The other 8 case reports described cases of either PCP or COVID-19 and the challenge in distinguishing between them.

**DISCUSSION**

This case emphasizes that PCP and COVID-19 can present as co-occurring disease processes and a broad differential should be maintained, especially in immunocompromised patients. *Pneumocystis jirovecii* is an opportunistic fungal pathogen that primarily causes disease in immunocompromised individuals. Although historically associated with advanced HIV, PCP now often impacts persons who are immunosuppressed for other reasons as well, including malignancy [3], organ transplant [4], and those requiring other immunosuppressive drugs, particularly corticosteroids [5]. All 5 previously reported cases of COVID-19 and PCP coinfection identified during our literature review had a documented immunocompromising condition. It is notable that none of the other cases of COVID-19 and PCP died. This may be attributable to extent of immunosuppression in our patient as well as his late presentation to care. *Pneumocystis jirovecii* pneumonia and moderate-to-severe COVID-19 share many clinical characteristics, making them difficult to distinguish. Both often present with fever, cough, and hypoxia [6] and can have a wide range of radiographic findings including diffuse ground-glass opacities [7]. The similarities in presentation may be due to similar underlying mechanisms of pathogenicity between the 2 infections and their interaction with pulmonary surfactant [8]. Given these similar findings, there is a growing recognition of PCP as a COVID-19 mimicker in severely ill patients [9].
Table 1. Case Reports of PCP and COVID-19 Coinfection

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age/Sex</th>
<th>Comorbidities</th>
<th>Immune Suppression</th>
<th>Method of PCP Diagnosis</th>
<th>Clinical Course</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cai et al [2]</td>
<td>72/Female</td>
<td>Rheumatoid arthritis</td>
<td>HCQ, leflunomide</td>
<td>High-throughput sequencing</td>
<td>Diagnosed with COVID-19, treated with steroids and tocilizumab, initially improved then worsened over several weeks. Repeat COVID-19 RNA PCR negative, but high-throughput testing positive for <em>Aspergillus fumigatus</em> and PCP. Treated with steroids and antimicrobials.</td>
<td>Recovered, discharged from hospital</td>
</tr>
<tr>
<td>Bhat et al [24]</td>
<td>25/Male</td>
<td>HIV</td>
<td>HIV, new diagnosis, CD4 32 cells/μL on admission. HIV RNA not reported</td>
<td>PCP antigen testing on BAL</td>
<td>Intubated, treated with remdesivir, TMP/SMX, and steroids.</td>
<td>Extubated, discharged from hospital</td>
</tr>
<tr>
<td>Menon, et al [25]</td>
<td>83/Female</td>
<td>Ulcerative colitis, asthma, mitral valve prolapse</td>
<td>Budesonide, sulfasalazine</td>
<td>1.3-β-D-glucan 305 pg/mL, positive PCP PCR from tracheal aspirate</td>
<td>Intubated, treated with TMP/SMX</td>
<td>Extubated, discharged</td>
</tr>
<tr>
<td>Mang et al [26]</td>
<td>52/Male</td>
<td>HIV</td>
<td>HIV, new diagnosis, CD4 12 cells/μL on admission, HIV RNA 360 000 copies/mL</td>
<td>BAL fluid positive for PCP, method of detection not specified</td>
<td>Intubated, bronchial aspirate positive for multiple bacteria. Blood cultures positive for vancomycin-resistant <em>Enterococcus faecium</em> and <em>Staphylococcus epidermidis</em>. Blood PCR positive for CMV infection. Treated with linezolid, meropenem, TMP/SMX, prednisone, ganciclovir.</td>
<td>Extubated, improving but remained hospitalized at time of publication</td>
</tr>
<tr>
<td>Coleman et al [9]</td>
<td>55/Male</td>
<td>HIV, asthma</td>
<td>Well controlled HIV, last CD4 422 cells/μL before admission, HIV RNA &lt;20 copies/mL</td>
<td>Induced sputum positive for PCP by PCR</td>
<td>Diagnosed first with PCP, then with COVID-19 on hospital day 3. Treated with TMP/SMX, steroids.</td>
<td>Recovered and discharged</td>
</tr>
<tr>
<td>Current case</td>
<td>36/Male</td>
<td>HIV</td>
<td>HIV, new diagnosis, CD4 &lt;10 cells/μL, HIV RNA 578 000 copies/mL</td>
<td>BAL positive for PCP DFA and PCR testing. Serum 1,3-β-D-glucan &gt;500 pg/mL</td>
<td>Diagnosed with COVID-19, intubated, started on remdesivir and antibiotics. Transferred to our hospital and diagnosed with HIV and PCP. Started on TMP/SMX and steroids, completed 5 days of remdesivir, and received COVID-19 convalescent plasma. Developed <em>Pseudomonas aeruginosa</em> VAP.</td>
<td>Cardiac arrest and death</td>
</tr>
</tbody>
</table>

Abbreviations: BAL, bronchoalveolar lavage; CMV, cytomegalovirus; COVID-19, coronavirus disease 2019; DFA, direct fluorescent antibody stain; HCQ, hydroxychloroquine; HIV, human immunodeficiency virus; PCP, *Pneumocystis jirovecii* pneumonia; PCR, polymerase chain reaction; RNA, ribonucleic acid; TMP/SMX, trimethoprim/sulfamethoxazole; VAP, ventilator-associated pneumonia.
In the case of our patient, the 3-week symptom duration before presentation was atypically long for COVID-19. For comparison, a large series of patients with COVID-19 alone reported a median 7 days of symptoms preceding hospitalization [10]. Coinfection with both SARS-CoV-2 and P jirovecii can lead to diagnostic dilemmas. Although COVID-19 testing is now readily available via nasopharyngeal swabs with fast turnaround time by most hospital laboratories [11, 12], PCP is less easy to diagnose. Bronchial alveolar lavage fluid remains the gold standard for PCP diagnosis due higher sensitivity [13], but performing a bronchoscopy to obtain a bronchial alveolar lavage specimen is an invasive procedure that cannot always be readily performed in severely hypoxic patients, and it requires additional procedural caution due to the risk of aerosolization of SARS-CoV-2. Although the serum fungal marker 1,3-β-d-glucan can be used to aid in the diagnosis of PCP [14], additional testing and a compatible clinical presentation are required to confirm the diagnosis. Colonization with P jirovecii is common in patients with COVID-19, a finding that may further impact challenging diagnostic scenarios. A recent study of 108 critically ill patients with COVID-19 found that 9% had a positive PCR test for P jirovecii on bronchial alveolar lavage [15]. The use of corticosteroids for severe COVID-19 may further delay diagnosis of co-occurring PCP, because such patients may theoretically experience transient improvement, given the known beneficial effect of steroids in severe PCP. As targeted immunomodulators are studied in COVID-19, physicians should be mindful of the risk they may pose for PCP. For example, the anti-interleukin-6 monoclonal antibody tocilizumab, which was pursued as a potentially promising therapy for COVID-19, has been associated with PCP in the treatment of rheumatoid arthritis (0.28 events per 100 patient-years) [16].

Finally, this case of COVID-19 and AIDS in a Latinx male highlights the disparities intertwined with both COVID-19 and HIV in the United States. Coronavirus disease 2019 has disproportionately affected the Latinx and black communities in the United States [17]—populations that experience a greater incidence and prevalence of HIV, have a high rate of progression to AIDS, and encounter barriers to HIV testing and care [18–21]. The HIV testing efforts and the continuity of care among these vulnerable populations may be disrupted as healthcare resources are shifted toward the pandemic and traditional models of healthcare delivery are redesigned [22, 23]. However, the pandemic also presents new opportunities to engage patients in HIV screening and other preventive care as they seek COVID-19 testing or treatment. Incorporating HIV screening of all patients admitted for COVID-19 into institutional protocols is a sensible approach that would benefit individual patients and impact public health disparities.

CONCLUSIONS

In summary, there is increasing recognition of PCP co-occurring with or succeeding severe COVID-19, primarily in immunocompromised individuals. Diagnostic uncertainty and anchoring biases can potentially delay diagnosis due to substantial overlap in the clinical presentation. Providers caring for patients with severe COVID-19 should retain a broad differential diagnosis if the clinical syndrome is atypical for COVID-19 or in patients with immunocompromising conditions. It is sensible to consider routine testing of HIV in all patients admitted with COVID-19 as a means of mitigating this diagnostic dilemma and benefitting our public health efforts.

Supplementary Data

Supplementary materials are available at Open Forum Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Acknowledgments

Financial support. A. J. S. is funded by the National Institute on Drug Abuse (K23DA049946). K. T. is funded by the National Institute of Health T32 Grant (2T32AI007151).

Potential conflicts of interest. J. B. P. receives grant support from the World Health Organization and Gilead Sciences and nonfinancial support from Abbott Diagnostics, outside the scope of the manuscript. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References


