

**COVID-19 and *Pneumocystis jirovecii* pneumonia: a diagnostic dilemma in HIV**

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## Case Report

During the rapidly evolving novel coronavirus disease (COVID-19) outbreak, more than a million cases have been diagnosed worldwide, however there has been limited reports of HIV and COVID-19 co-infection at the time of writing. We report a case highlighting the challenge of diagnosing COVID-19 and *Pneumocystis jirovecii* pneumonia (PJP) in an individual with HIV.

A 55-year-old male presented with a seven-day history of fevers, cough, and hypoxia. Co-morbidities include well-controlled HIV infection (diagnosed 2006, current CD4 count 422 cells/ $\mu$ L (35.6%), HIV-1 viral load <20 copies/ml), on emtricitabine/tenofovir disoproxil 200/245mg and raltegravir 1200mg once daily; and mild asthma. He had no prior history of PJP, was an ex-smoker, lived with his partner, and neither had recent travel histories nor contact with confirmed COVID-19 cases.

Chest CT (Figure 1.) showed extensive sub-pleural and para-mediastinal cystic changes, sub-pleural ground-glass changes bilaterally, most prominent in the upper lobes with relative sparing of the lung bases; consistent with PJP. Incidental interstitial lung fibrosis and paraseptal emphysema was also reported.

A lower respiratory tract induced sputum was tested for respiratory pathogens using multiplex polymerase chain reaction (PCR) and *P. jirovecii* DNA was detected. SARS-CoV-2 RNA was not detected by real-time PCR (RT-PCR) of an initial combined nose and throat swab (day 2). Investigations for other respiratory pathogens were negative.

PJP treatment was commenced with intravenous co-trimoxazole (120mg/kg/24hr) and oral prednisolone 40mg twice daily. He deteriorated three days into treatment and required critical care. A repeat throat swab (day 7) detected SARS-CoV-2 by RT-PCR.

He improved with high-flow oxygen not requiring intubation or ventilation. He was discharged (day 14) to complete 21 days oral treatment followed by long-term PJP prophylaxis.

## Discussion

We report the first case of *P. jirovecii* and SARS-CoV-2 detection in an individual with well-controlled HIV. At the time of writing only one other HIV/COVID-19 co-infection case has been published, with limited details of the individual's HIV status [1], and an European regional database of HIV/COVID-19 cases is currently under way [2]. We recommend further epidemiological data from HIV/COVID-19 cases to be collected and reported to understand the relationship between COVID-19, HIV and antiretroviral therapy.

Sensitivity of RT-PCR from throat swabs to detect SARS-CoV-2 RNA has been reported as 95% [3]. However retrospective studies comparing RT-PCR against combined clinical and radiographic criteria to diagnose COVID-19 in an epidemic setting reported lower sensitivities of RT-PCR at 70 - 80% [4]. Lower detection rates are associated with time from symptom onset, dropping from 100% to 40% if taken after day five of symptoms [5]. Retrospective testing of this patient's induced sputum, taken within 26 hours of the negative throat swab, confirmed the presence of SARS-CoV-2. Lower respiratory samples by induced sputum may aid diagnosis in the presence of negative upper respiratory samples [6].

The detection of *P. jirovecii* DNA in the induced sputum and initial negative SARS-CoV-2 result, in the presence of characteristic features of PJP formed the basis of the PJP diagnosis. The significance of detected *P. jirovecii* DNA using PCR alone remains uncertain and may represent colonisation of the respiratory tract. Immunofluorescent microscopy was not available in this case. The prevalence of

detectable *P. jirovecii* DNA in healthy immunocompetent adults has been reported between 0 - 20% [7, 8]. However, in 100% of lung autopsy samples from immunocompetent individuals with detectable *P. jirovecii* DNA, detailed immunoflorescent microscopy revealed both cyst and trophozoite forms suggestive of actively replicating *P. jirovecii* [9], suggesting mild PJP infection may be present even in immunocompetent adults with detectable *P. jirovecii*.

Clinically COVID-19 and PJP may present with similar features of dry cough, exercise desaturation and relatively normal chest auscultation. Common chest CT findings for both conditions include ground-glass pattern with interlobular septal thickening [10, 11]. Implications of missed COVID-19 diagnoses include missed opportunities for contact tracing and prevention of onward transmission in an epidemic setting. Clinical management of PJP and COVID-19 also differs, particularly high-dose corticosteroid therapy is recommended in severe PJP [12], however there is no evidence for corticosteroid therapy in COVID-19, and observational data suggest increased mortality and secondary infection rates in influenza, and impaired clearance of the closely related SARS-CoV and MERS-CoV viral infections [13].

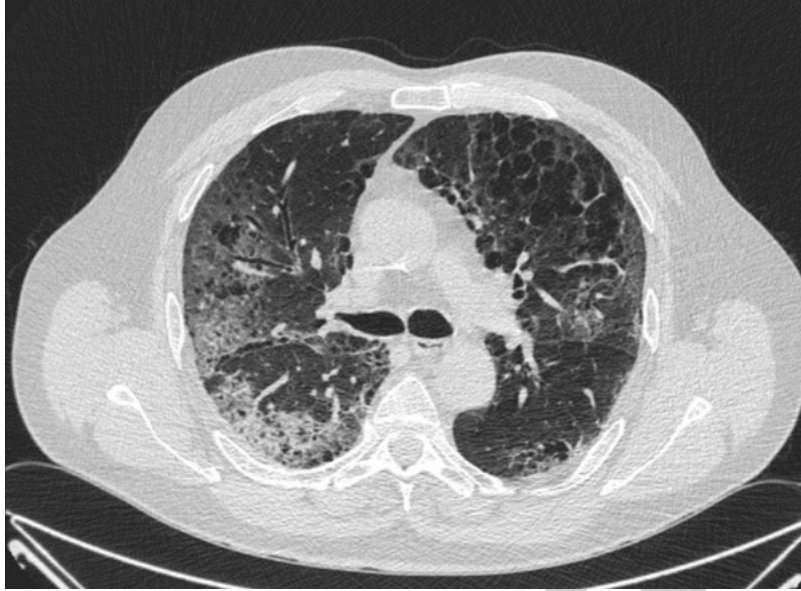
In conclusion, we report the first case of an individual living with HIV diagnosed and treated for both COVID-19 and PJP. Diagnosis of either conditions in the presence of both pathogens is challenging due to overlapping clinical and radiological features and limitations of current diagnostic assays, with clinical and public health implications in the current COVID-19 pandemic.

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**Figure 1:** Chest Computer Tomography image slice showing extensive sub-pleural and para-mediastinal cystic changes, sub-pleural ground-glass changes bilaterally.



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