CASE REPORT

HIV and SARS-CoV-2 co-infection: The diagnostic challenges of dual pandemics

A Parker,[1,2] MB ChB, FCP (SA), MMed (Int Med), Cert ID (SA) Phys; **J Shaw,**[2] MB ChB, MMed (Int), FCP (SA), MPhil (Pulm), Cert Pulm (SA); **S Karamchand,**[2] MB ChB, BPharm, MSc (Med) (Clin Pharm); **S Lahri,**[3] MB ChB, FCEM (SA); **N Schrueder,**[2] MB ChB, FCP (SA); **M-Y Chothia,**[2] MB ChB, FCP (SA), MMed (Int Med), Cert Neph (SA); **A Mowlana,**[2] MB ChB, FCP (SA), MMed (Int Med); **U Lalla,**[4] MB ChB, FCP (SA), MMed (Int Med), Cert Crit Care (SA) Phys; **B W Allwood,**[5] MB ChB, FCP (SA), Cert Pulm (SA), PhD; **C F N Koegelenberg,**[5] MB ChB, FCP (SA), MMed (Int Med), FRCP (UK), Cert Pulm (SA), PhD; **J J Taljaard,**[1] MB ChB, MMed (Int Med), DTM&H

[1] *Division of Infectious Diseases, Department of Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University and Tygerberg Hospital, Cape Town, South Africa*
[2] *Division of Internal Medicine, Department of Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University and Tygerberg Hospital, Cape Town, South Africa*
[3] *Division of Emergency Medicine, Department of Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University and Tygerberg Hospital, Cape Town, South Africa*
[4] *Division of Critical Care, Department of Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University and Tygerberg Hospital, Cape Town, South Africa*
[5] *Division of Pulmonology, Department of Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University and Tygerberg Hospital, Cape Town, South Africa*

Corresponding author: *A Parker (aparker@sun.ac.za)*

The first critically ill patient admitted to our hospital in Cape Town, South Africa, during the COVID-19 pandemic was co-infected with HIV and SARS-CoV-2. *Pneumocystis jirovecii* pneumonia (PCP) and other respiratory opportunistic infections share many clinical features with severe COVID-19. Our understanding of the nuances of co-management of HIV and COVID-19 is evolving. We describe the diagnostic and therapeutic challenges presented by this case.

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Globally there are an estimated 37.9 million people living with HIV (PLHIV), with ~20.6 million (54%) in the eastern and southern Africa region, and 7.7 million (20%) in South Africa (SA).[1] The current best estimate for antiretroviral (ART) coverage in SA is 62% of PLHIV, with only 54% having suppressed viral loads, translating into a significant number of individuals at high risk of opportunistic infections such as *Pneumocystis jirovecii* pneumonia (PCP).[2] Exponential spread of COVID-19 in SA is anticipated, and at the time of writing there were >2 000 confirmed cases in the country.[3] While there is currently no evidence to suggest that HIV infection confers an increased risk of either contracting COVID-19 or developing severe disease, it certainly does confound the diagnostic assessment and management of these patients.

Case report

A 41-year-old HIV-positive man self-presented to our designated COVID-19 test and treatment centre in Cape Town, SA. He complained of a 12-day history of fever, a non-productive cough, myalgia, diarrhoea, and gradually worsening dyspnoea. He was employed as a taxi driver, and had provided transport to international travellers for up to a day prior to symptom onset. He was unable to recall whether any of his passengers had flu-like symptoms. Three days prior to admission, he had presented to his local community health centre specifically requesting a test for COVID-19. However, since he did not meet the case definition at the time, he was treated symptomatically.

The patient's medical history included ART since 2016 with a fixed-drug combination of tenofovir, emtricitabine and efavirenz. No recent CD4+ cell count was available, but the patient had an undetectable HIV viral load 6 months prior to this presentation, which was confirmed during his current admission. He had no history of tuberculosis (TB), AIDS-defining illnesses, or chronic cardiovascular or respiratory illnesses.

The initial clinical evaluation revealed that he was haemodynamically stable but had evidence of acute respiratory distress, including a peripheral oxygen saturation of 73% while breathing ambient air, and a respiratory rate of 28 breaths per minute. He was admitted directly to an isolation ward, where he was intubated under appropriate infection prevention and control measures and transferred to the intensive care unit.

Investigations

A chest radiograph (Fig. 1) demonstrated diffuse bilateral ground-glass infiltrates, with patchy areas of consolidation. A full blood count revealed lymphopenia (white blood cell count 0.56×10^9/L, normal range 1.4 - 4.2 $\times 10^9$/L) and a mildly reduced platelet count (166×10^9/L, normal range 171 - 388 $\times 10^9$/L), with an absolute CD4+ cell count of 78 cells/μL. The C-reactive protein level was 225 mg/L (normal <10 mg/L), and the procalcitonin (PCT) level 0.97 μg/L (normal <0.1 μg/L). He had mild hepatic transaminitis and normal kidney function.

Differential diagnosis

The differential diagnosis included PCP, influenza or another viral pneumonia, TB and atypical bacterial pneumonia. Owing to the

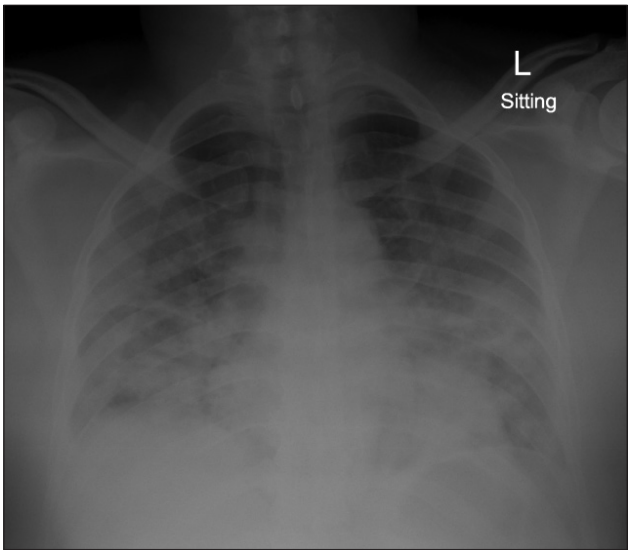

Fig. 1. Chest radiograph.

clinical picture of a severe acute respiratory illness, COVID-19 pneumonitis was included in the differential diagnosis.

Treatment

The patient was treated empirically with intravenous amoxicillin-clavulanic acid for severe community-acquired bacterial pneumonia and azithromycin for atypical bacterial pneumonia, as well as trimethoprim-sulfamethoxazole for presumed PCP. Empirical oseltamivir was withheld, as his symptoms had been present for >72 hours.

Subsequent testing of endotracheal aspirates confirmed a positive polymerase chain reaction (PCR) for SARS-CoV-2, with a negative multiplex respiratory virus panel, negative Xpert MTB/RIF Ultra for TB, negative bacterial staining and culture, and negative immunofluorescence for *P. jirovecii*. Owing to the low sensitivity of the latter, a serum beta-D-glucan assay was requested, which revealed a level of <31 μg/mL.

Specific therapy included changing his ART to lamivudine, zidovudine and lopinavir/ritonavir for ease of administration in the intensive care unit (ICU) setting and adding chloroquine 650 mg daily for 2 days, and then 600 mg daily for 3 days.

Ethics approval

Ethics approval for this case study was granted by the Health Research Ethics Committee of Stellenbosch University (ref. no. N20/04/005_COVID-19).

Discussion

Our patient presented relatively late in the course of disease, and in retrospect the initial case definition should have included people who have close contact with international travellers. It is unclear whether the severity of our patient's presentation can solely be attributed to the normal progression of COVID-19 in an immunocompromised patient or whether it was complicated by a bacterial infection (initial raised PCT which gradually dropped to 0.46 μg/L on antibiotic treatment). In a resource-constrained setting, it is common practice to ration access to intensive care, particularly in patients with HIV infection who are not established on ART and whose case is complicated by AIDS-defining illnesses, owing to their historical poor prognosis.[4] At present we do not know what the outcomes of critically ill HIV/SARS-CoV-2 co-infected patients will be. When there is widespread community transmission of SARS-CoV-2, with high numbers of severely ill patients requiring ICU care, distinguishing between COVID-19, PCP and other AIDS-defining illnesses at the outset will become of critical importance. In PLHIV and other immunocompromised populations, PCP remains an important differential diagnosis in patients with CD4+ cell counts <200 cells/μL who present with progressive lower respiratory tract symptoms, including a dry cough, shortness of breath, hypoxaemia and bilateral ground-glass infiltrates on radiological imaging. However, none of these features are specific for PCP, and they may also be consistent with COVID-19 pneumonitis. In our setting, the diagnosis of PCP in HIV-infected patients is made on clinical and characteristic chest radiographic features, without further extensive diagnostic testing. During the COVID-19 pandemic, we recommend further diagnostic testing when PCP is considered. This includes an expectorated sputum sample[5] (or a tracheal aspirate in the intubated patient) for PCR or immunofluorescence testing, and also a serum sample for beta-D-glucan. Owing to the potential for generating aerosols, obtaining an induced sputum sample for PCP testing is currently not advised.[6]

The World Health Organization clinical guideline[6] cautions against the routine use of corticosteroids in the management of COVID-19, outside the setting of a clinical trial. The rationale stems from evidence that corticosteroids conferred no survival benefit in other viral pneumonias such as severe acute respiratory syndrome (SARS), Middle Eastern respiratory syndrome (MERS) and influenza.[6] Conversely, withholding additional corticosteroids in HIV-infected patients with PCP and hypoxaemia is associated with worse outcomes.[7] On the available evidence at the time of submission, we do recommend initiating empirical corticosteroids in hypoxaemic patients with a high likelihood of PCP, and stopping them as soon as a COVID-19-positive result is confirmed and/or PCP test results are negative. These clinical dilemmas, along with other pertinent questions such as whether protease inhibitors offer some protection against SARS-CoV-2, or whether chloroquine, with potential ART drug interactions, has a role in the treatment of COVID-19 in PLHIV, should be explored in controlled clinical trials.[8] With increasing community transmission of SARS-CoV-2, our local case definition has evolved to include all patients presenting with a respiratory tract infection. In sub-Saharan Africa our resources are already constrained by the high burden of HIV-associated respiratory tract infections and TB. Adding the COVID-19 pandemic to the soup is potentially disastrous for our healthcare system and the community at large. The swift action by our government to contain the spread of the infection, and the dedication of the thousands of SA healthcare workers who are already experienced in the management of the complex clinical dilemmas presented by HIV, is reason for some hope in this crisis.

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1. Joint United Nations Programme on HIV and AIDS (UNAIDS). Fact sheet – World AIDS Day 2019. 1 December 2019. https://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf (accessed 3 April 2020).
2. Joint United Nations Programme on HIV and AIDS (UNAIDS). AIDS info. Country factsheets: South Africa 2018. https://aidsinfo.unaids.org (accessed 3 April 2020).
3. National Department of Health, South Africa. Update of COVID-19 (03 April 2020). https://sacoronavirus.co.za/2020/04/03/update-of-covid-19-03rd-april-2020 (accessed 3 April 2020).
4. Koegelenberg CF, Bulaya T, Balkema CA, Taljaard JJ, Irusen EM. Validation of a severity-of-illness score in HIV-positive patients requiring intensive care unit admission for mechanical ventilation. Q J Med 2016;109(6):434-435. https://doi.org/10.1093/qjmed/hcw061
5. Harris JR, Marston BJ, Sangrujee N, DuPlessis D, Park B. Cost-effectiveness analysis of diagnostic options for *Pneumocystis* pneumonia (PCP). PLoS ONE 2011;6(8):e23158. https://doi.org/10.1371/journal.pone.0023158
6. World Health Organization. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: Interim guidance. 13 March 2020. https://www.who.int/docs/default-source/coronaviruse/clinical-management-of-novel-cov.pdf (accessed 15 March 2020).
7. Ewald H, Raatz H, Boscacci R, Furrer H, Bucher HC, Briel M. Adjunctive corticosteroids for *Pneumocystis jiroveci* pneumonia in patients with HIV infection. Cochrane Database Syst Rev 2015, Issue 4. Art. No.: CD006150. https://doi.org/10.1002/14651858.CD006150.pub2
8. Decloedt E, Reuter H, Allwood B, et al. Benefit v. risk when using chloroquine in patients with severe COVID-19 disease. S Afr Med J 2020;110(5):336. https://doi.org/10.7196/SAMJ.2020.v110i5.14761

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