

Pearls and pitfalls: Two contrasting HIV diagnoses in the COVID-19 era and the case for screening

The risk of coronavirus disease 2019 (COVID-19) to people living with HIV (PLWH) remains poorly understood. There have been over 400 reported cases of COVID-19 and HIV coinfection reported throughout Europe. The majority consist of those with an established HIV diagnosis, receiving antiretroviral therapy (ART).

Two cases of previously undiagnosed HIV presenting to secondary care with respiratory symptoms are detailed in this series, with a view to extrapolate lessons on blood-borne virus (BBV) screening in the COVID-19 era.

The first patient, a fit and well white Scottish 38-year-old man, with a body mass index (BMI) of 24.6, presented after 5 days of dyspnea and a productive cough. His temperature was 38°C and SpO₂ was 89% on room-air. Investigations were remarkable for a lymphocyte count of $0.7 \times 10^9/L$, a C-reactive protein (CRP) of 242 mg/L and a chest radiograph demonstrating subtle bibasal consolidation. Subsequently, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was present on polymerase chain reaction (PCR) from a viral swab. He rapidly deteriorated with progressive respiratory failure requiring intubation and ventilation. Whilst intubated, a routine BBV screen on day four of admission demonstrated HIV seropositivity. There were no discernible clinical or lifestyle risk factors for this diagnosis of bar disease severity. At diagnosis, the viral load was 6.35 log₁₀ and CD4⁺ was 220 cells/mm³. ART (emtricitabine/tenofovir and dolutegravir) and cotrimoxazole, for pneumocystis jiroveci pneumonia (PJP) prophylaxis (PCR negative), were commenced via nasogastric tube. He went on to make a full recovery and was discharged on day 17 of admission.

The second patient was a white Scottish 51-year-old man with a BMI of 23.6. He had a background of herpes zoster, weight loss, oral candidiasis, and pernicious anemia. He presented with dyspnoea and diarrhea. The examination was unremarkable save oral candidiasis. He was afebrile, tachycardiac at 120 bpm, mildly dyspneic at 23 bpm, and oxygen saturations were 96% on air. Bilateral consolidation on chest radiograph was reported as indeterminate for COVID-19. Blood investigations demonstrated a lymphocyte count of 0.4×10^9 , a CRP of 27 mg/L and D-dimer of 720 ng/mL. It was felt that COVID-19 was a likely diagnosis. A computed tomography pulmonary angiogram was performed, ruling out a pulmonary embolus but demonstrating bilateral ground-glass changes that were reported as atypical for COVID-19. Despite these findings and two negative swabs for SARS-CoV2 PCR, COVID-19 remained the clinical diagnosis until day 6 of admission when a BBV screen confirmed HIV seropositivity with a viral load of 5.28 log₁₀ and CD4⁺ 25 cells/mm³. A subsequent

sputum sample was positive for PJP on PCR for which he was started on treatment dose cotrimoxazole. He was started on ART (emtricitabine/tenofovir and raltegravir) before discharge. He was discharged on day 19 with follow-up by infectious diseases.

The current scientific consensus is that PLWH receiving treatment is at no greater risk of severe COVID-19.¹⁻⁴ However, the evidence base in the published literature pertains to stable patients with a suppressed viral load. To the best of our knowledge only seven patients diagnosed with HIV at presentation with acute COVID-19 have been reported (see Table 1).^{5,6} There is an inference of higher disease severity and younger age at presentation, however, conventional risk factors such as obesity or respiratory disease impart significant variability.^{15,16} Case 1 is the first to our knowledge requiring intubation.

These cases confer salient lessons. First, HIV and COVID-19 coinfection was diagnosed in the absence of risk factors, prompted by high disease severity in an atypically young and fit patient. On the second case, a classic presentation of PJP, a COVID-19 mimic, was initially missed in the context of the pandemic, due to similarities in clinical presentation, radiographic changes, and blood parameters.

There are approximately 7500 patients living with undiagnosed HIV in the UK.⁷ They are considered immunosuppressed, under the assumption that this may correlate with a severe COVID-19 phenotype.¹ Previous case series have observed a nonsignificant correlation between a low CD4⁺ count and increased disease severity (Table 1), but this is inconsistent.⁹ Without other risk factors for COVID-19, the severe presentation in case one supports this assertion. This also supports previous findings of a lower age requiring hospitalization.^{2,3,8,14} Larger studies in high-prevalence settings are required to explore these associations further.

The British HIV Association recommends HIV screening for community acquired pneumonia presentations.¹¹ However, there is currently no extension of this to patients with COVID-19. A systematic review published in July 2020 states that HIV testing should be offered to anyone presenting with a clinical picture of viral pneumonia.³

Active patient screening is required to extend our knowledge of the role of HIV as a risk factor for COVID-19. Undiagnosed PLWH represent a vulnerable patient group and advocating routine BBV screening is essential for those requiring hospitalization with COVID-19. The additional benefit of this would be prompting the early diagnosis of mimics such as PJP, seen in the second case, which conveys a high mortality and requires aggressive treatment.

TABLE 1 A summary of notable case series published to date of HIV/COVID-19 coinfections

Mean age	Patient numbers (n)	Origin	ART	Detectable viral load (n)	New diagnoses (n)	Main findings
60	31	US	All on ART	0	0	Similar rate of hospitalization and severity to controls. ¹
53	51	Spain	All on ART	1	0	Nonsignificant association between significant disease and a lower CD4 count. Mean age lower than general population. Increased prevalence of comorbidities in HIV/COVID-19 coinfecting than HIV controls. ⁸
58	9	US	All on ART. Three poorly compliant	0	0	Nonsignificant association between significant disease and a lower CD4 count. ⁹
53	18	UK	All on ART	0	0	Substantial increase in morbidity and mortality for PLWH even if on ART. Most cases were from black, Asian, and minority ethnic groups. ¹⁰
51	2	China	One on ART and one ART naïve	1	1	Both patients recovered without invasive ventilation. ⁶
48	33	Germany	All on ART	0	0	No evidence of increased morbidity or mortality. Suggestion of a lower mean age of hospitalization. ²
51	47	Italy	All on ART	3	0	Lower mean age of hospitalization but no increase severity or mortality. ⁴
38	5	Spain	Four on ART and one ART naïve	1	1	The patient newly diagnosed with HIV had concomitant PJP and bacterial pneumonia. ⁵
50-59	236	Spain	All on ART	Unspecified; estimated at 95% of patients	0	Lower prevalence of COVID-19 in PLWH established on ART but higher mortality. ART may be protective. ¹²
28	1	Tokyo	ART naïve	1	1	Mild/moderate COVID-19 severity in a young ART naïve patient (oxygen requirement). ¹³
31	2	China	ART naïve	2	2	Young patients demonstrating a longer disease course and more severe symptoms than comparable HIV-negative data. ¹⁴
37	4	Turkey	Three on ART and one noncompliant	1	0	One death in obese comorbid patient on ART. Young cohort. Emphasis on conventional comorbidities. ¹⁵
32	3	UK	Two on ART and one ART naïve	1	1 (lost to follow-up)	Emphasis on comorbidities. Comparable disease severity in patient ART naïve. ¹⁶
37	1	China	ART naïve	1	1	Long disease course. High severity COVID-19 requiring high flow oxygen. ¹⁷

Note: Basic demographics included country of origin and clinical characteristics of the cases. In addition to a precis of the main findings of the article. Abbreviations: ART, antiretroviral therapy; COVID-19, coronavirus disease 2019; PJP, pneumocystis jiroveci pneumonia; PLWH, people living with HIV.

Capacity in virology laboratories may preclude mass testing, however it should be advocated for in high-prevalence areas and in younger patients with atypically severe presentations. There may be a role for point of care HIV-antibody tests depending on local epidemiology and resources.

ACKNOWLEDGMENT

The authors had full access to all the data in the study and had final responsibility to submit it for application.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

FB-M and PD both conceived the idea of this correspondence and participated equally to its writing. Written informed consent was obtained for both patients.

Francisca Bartilotti Matos 

Peter Davies

Infectious Diseases Department, Monklands University Hospital,
Airdrie, UK

Correspondence

Francisca Bartilotti Matos, Infectious Diseases Department,
Monklands University Hospital, Flat 2, 46 Addison Road,
Glasgow G120TT, UK.

Email: francisca.bartilottimatos@nhs.net

ORCID

Francisca Bartilotti Matos  <http://orcid.org/0000-0001-6088-829X>

REFERENCES

- Shalev N, Scherer M, LaSota E, et al. Clinical characteristics and outcomes in people living with HIV hospitalized for COVID-19. *Clin Infect Dis*. 2020. <https://doi.org/10.1093/cid/ciaa635>
- Härter G, Spinner CD, Roeder J, et al. COVID-19 in people living with human immunodeficiency virus: a case series of 33 patients. *Infection*. 2020. <https://doi.org/10.1007/s15010-020-01438-z>
- Cooper TJ, Woodward BL, Alom S, Harky A. Coronavirus disease 2019 (COVID-19) outcomes in HIV/AIDS patients: a systematic review. *HIV Med*. 2020. <https://doi.org/10.1111/hiv.12911>
- Gervasoni C, Meraviglia P, Riva A, et al. Clinical features and outcomes of HIV patients with coronavirus disease 2019. *Clin Infect Dis*. 2020. <https://doi.org/10.1093/cid/ciaa579>
- Blanco JL, Ambrosioni J, Garcia F, et al. COVID-19 in patients with HIV: clinical case series. *Lancet HIV*. 2020;7(5):e314-e316. [https://doi.org/10.1016/S2352-3018\(20\)30111-9](https://doi.org/10.1016/S2352-3018(20)30111-9)
- Wu Q, Chen T, Zhang H. Recovery from COVID-19 in two patients with coexisted HIV infection. *J Med Virol*. 2020. <https://doi.org/10.1002/jmv.26006>
- O'Halloran C, Sun S, Nash S, et al. *HIV in the United Kingdom: Towards Zero 2030*, December 2019, Public Health England, London.
- Vizcarra P, Perez-Elias MJ, Quereda C, et al. Description of COVID-19 in HIV-infected individuals: a single-centre, prospective cohort. *Lancet HIV*. 2020. [https://doi.org/10.1016/S2352-3018\(20\)30164-8](https://doi.org/10.1016/S2352-3018(20)30164-8)
- Suwanwongse K, Shabarek N. Clinical features and outcome of HIV/SARS-CoV-2 coinfecting patients in The Bronx, New York city. *J Med Virol*. 2020. <https://doi.org/10.1002/jmv.26077>
- Childs K, Post FA, Norcross C, et al. Hospitalized patients with COVID-19 and human immunodeficiency virus: a case series. *Clin Infect Dis*. 2020. <https://doi.org/10.1093/cid/ciaa657>
- UK National Guidelines for HIV Testing 2008, British HIV Association (BHIVA). September 2008. <https://www.bhiva.org/file/RHNUJgIseDaML/GlinesHIVTest08.pdf>. Accessed July 6, 2020.
- Del Amo J, Polo R, Moreno S, et al. Incidence and severity of COVID-19 in HIV positive persons receiving antiretroviral treatment. *Ann Intern Med*. 2020;26:M20-3689. <https://doi.org/10.7326/M20-3689>
- Nakamoto T, Kutsuna S, Yanagawa Y, et al. A case of SARS-CoV-2 infection in an untreated HIV patient in Tokyo, Japan. *J Med Virol*. 2020. <https://doi.org/10.1002/jmv.26102>
- Li W, Ma Q, Wang X, Tang M, Lin J, Xiao B. The characteristics of two patients coinfecting with SARS-CoV-2 and HIV in Wuhan, China. *J Med Virol*. 2020. <https://doi.org/10.1002/jmv.26155>
- Aydin OA, Karaosmanoglu HK, Yasar KK. HIV/SARS-CoV-2 coinfecting patients in Istanbul, Turkey. *J Med Virol*. 2020. <https://doi.org/10.1002/jmv.25955>
- Toombs JM, Van den Abbeele K, Democratis J, Merricks R, Akj M, Missouriis CG. COVID-19 in 3 people living with HIV in the United Kingdom. *J Med Virol*. 2020. <https://doi.org/10.1002/jmv.26178>
- Wang M, Luo L, Bu H, Xia H. One case of coronavirus disease 2019 (COVID-19) in a patient co-infected by HIV with a low CD4 + T-cell count. *Int J Infect Dis*. 2020;96:148-150. <https://doi.org/10.1016/j.ijid.2020.04.060>