



Case report

COVID-19 infection and a repeated false positivity effect in HIV testing: A case report

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ABSTRACT

Several reports in the literature have described the association between SARS-CoV-2 infection and false positive HIV testing results. We present a case of a cisgender male who has sex with men with a false positive HIV test after fully recovering from COVID-19 14 days prior. Initial 4th generation HIV 1 and 2 antibody/antigen testing was positive twice, but confirmatory antibody testing was negative. HIV viral load was persistently undetectable. Most of the previously published case reports describe concurrent testing and positivity for HIV and COVID-19. Our report stands out due to the implication of a potentially prolonged association that could persist for several weeks.

Introduction

HIV testing has improved substantially since it was first commercially approved in 1985. Despite this, there have been recorded instances of false positive HIV test results due to infection with other pathogens including the Epstein-Barr Virus, influenza, and *Mycobacterium tuberculosis* [1,2]. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has already been reported to coincide with false positive HIV testing results [1,3–7].

Multiple theories can explain false positive HIV test results in COVID-19 patients. One hypothesis involves shared structural motifs between SARS-CoV-2 and HIV, potentially leading to HIV test interference due to a lack of strict homology in HIV testing platforms [4]. There is a documented higher occurrence of false positive results among individuals with detectable antibodies against Spike SARS CoV-2 proteins, lending support to this idea [3]. Furthermore, SARS CoV-2 is one of several pathogens capable of inducing non-specific polyclonal B-cell responses which may also contribute to false positive HIV testing [8]. In hospitalized COVID-19 patients, rheumatoid factor autoantibodies—known to interfere with diagnostic assays including HIV screening tests—were induced [9–11]. Others have suggested that hypergammaglobulinemia, associated with liver disease, acute or chronic inflammatory states, and autoimmune disorders, can contribute to false positive HIV serology [12]. A case report details an instance of false positive HIV serology in chronic granulomatous disease (CGD) in the setting of polyclonal hypergammaglobulinemia [13].

We present a case of a 20-year-old cisgender male who has sex with men with a false positive HIV test after recovering from COVID-19. This case adds to the handful of previous HIV and COVID-19 test cross-reactivity reports globally. Furthermore, it raises a new question: is COVID-19 infection associated with a persistent false HIV positivity effect?

Case

A healthy 20-year-old cisgender male college student was seen for a routine health visit at a Northeast US academic institution's pediatrician office. Family history was unremarkable. The patient reported rare tobacco and alcohol use, and no recreational drug use. He had a lifetime history of ten sexual partners and was sexually active exclusively with male partners. He denied any history of known sexually transmitted infections. The patient had no history of being on HIV pre-exposure prophylaxis (PrEP) and had tested negative for HIV six months before this visit. During this routine health visit, the patient inquired about repeat HIV testing.

The patient reported itching related to recently diagnosed scabies, which had been unresponsive to topical permethrin. Oral ivermectin, hydroxyzine 25 mg, and triamcinolone 0.1 % ointment were started. He had no other medications or known drug allergies.

Initial 4th generation HIV 1 and 2 antibody/antigen testing returned positive twice (separated by a 5-day interval), but confirmatory antibody testing was negative. 4th generation assay was performed on the

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Table 1
Summary of HIV testing.

	t = 0 days	t = 5 days	t = 20 days	t = 80 days	t = 257 days
HIV-1 antibody confirm	Negative		Negative		
HIV-1 band	No bands detected		No bands detected		
HIV-2 band	No bands detected		No bands detected		
HIV-2 antibody confirm	Negative		Negative		
Hep C antibody with reflex PCR	Negative				
HIV 1 and 2 antibody /p24 antigen, 4 th generation	Reactive	Reactive	Reactive	Negative	Negative
HIV 1 and 2 antibody confirmation/differentiation	Negative/no bands detected		Negative/no bands detected		
HIV 1 RNA quantitation		Undetected			
HIV RNA detection, qualitative		Undetected	Undetected		
Syphilis serology	Negative				Negative

Siemens Centaur XPT in both cases. The HIV viral load was undetectable. The infectious diseases consultant suggested repeat testing in four weeks.

On exam in the infectious disease clinic, the patient had stable vital signs, no rashes or skin lesions, no lymphadenopathy, and no other concerning findings. Further interview revealed that the patient was in a mutually monogamous relationship with a cisgender male partner in western Europe who had tested negative for HIV one and four months prior to engaging in condomless sex with the patient. The patient reported months had elapsed between his last sexual contact and the positive HIV testing results.

The patient also endorsed COVID-19 infection twice in the past year, including 14 days prior (per a home antigen test) to his initial positive HIV test result. At this time, the predominant variant circulating locally was “Omicron,” SARS-CoV-2 - BA.2 lineage [14]. The patient denied any COVID-19 symptoms when he was seen in the Infectious Disease clinic.

Additional lab testing results are shown in Table 1. All other lab values (CBC, lymphocyte subset, lipid panel, creatinine, and GFR) were normal.

Given that the patient’s sexual practices, signs/symptoms, and laboratory testing did not align well with a true diagnosis of acute HIV, his test results were attributed to recent COVID-19 infection and resulting cross-reactivity. No specific interventions were employed with the presumption that HIV reactivity should self-resolve.

Nearly three months after the patient’s initial reactive HIV testing, he received a negative HIV test, repeated at six months with negative results again. His scabies cleared after treatment with oral ivermectin. Approximately ten months later, the patient initiated HIV pre-exposure prophylaxis (HIV PrEP) with emtricitabine/tenofovir disoproxil fumarate (Truvada).

Discussion

This is not the first report of false positive HIV testing results in the context of co-infection or prior infection with SARS-CoV-2 [1,3–5,7].

The case reports above demonstrate concurrent testing and positivity for HIV and COVID-19. Our patient tested positive for HIV at least two weeks after COVID-19 recovery and in the absence of active symptoms. This too has been reported previously, and suggests the possibility of an enduring false positivity effect. Srivastava et al. reported on two patients at 12-day and 14-day intervals after initial COVID-19 infection who received false positive HIV results [15]. Moreover, Gudipati et al. generalize their conclusions only to active COVID-19 infection, yet inclusion criteria allowed a 2-week period in which both COVID-19 and HIV positives were present, potentially encompassing some recovered COVID-19 patients [4]. Papamanoli et al.’s HIV false positivity case details a patient exposed to COVID-19 a month prior who tested negative by PCR but positive for SARS-CoV-2 IgG antibodies to nucleocapsid and spike proteins [6].

Importantly, the negative results of confirmatory testing and ultimate conversion of HIV testing results to negative suggest that none of these patients are elite controllers [16] or infected with HIV-2 or other less common viral variants.

The published intervals between the most recent positive SARS-CoV-2 test result and the associated false positive HIV test result is illustrated in Fig. 1.

These case reports, particularly ours and the report by Papamanoli, suggest that infection with SARS-CoV-2 can generate persistently false positive HIV testing results. Until additional reports accrue it is impossible to know how long this post-COVID false HIV positivity window last on average. Given emerging evidence of COVID-related immune disruptions [17–19], durable false positivity of HIV tests (and tests for other pathogens) is plausible.

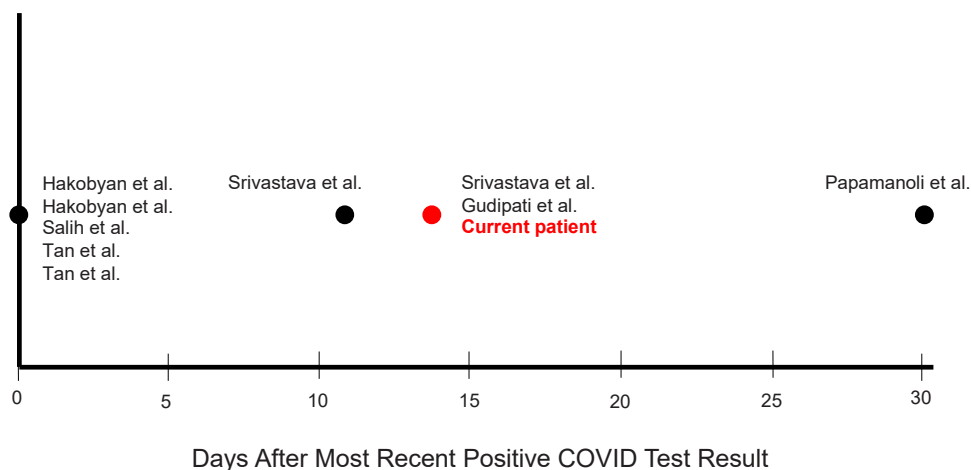


Fig. 1. Time Between False Positive HIV Testing and Related COVID-19 Infection. A graph depicting days between positive COVID test result and associated false positive HIV test result.

Distinguishing between coincidental positive results and a true association between test results will require formal investigation in large cohort studies. Until formally studied in large cohort studies, clinicians should be aware of this possible association and alert to the need to repeat testing over time to assure correct diagnosis.

Ethical approval

Approved.

Consent

Obtained.

Author statement

The authors confirm contribution to the paper as follows: study conception and design: A. Balasubramanian, D. Singh, T. Lahey; data collection: A. Balasubramanian; analysis and interpretation of results: A. Balasubramanian, D. Singh, T. Lahey; draft manuscript preparation: A. Balasubramanian, D. Singh, T. Lahey. All authors reviewed the results and approved the final version of the manuscript.

CRedit authorship contribution statement

Anupama Balasubramanian: conception of manuscript, acquisition of data, analysis and interpretation of data, writing of manuscript, editing of manuscript, final approval. **Devika Singh:** conception of manuscript, acquisition of data, analysis and interpretation of data, editing of manuscript, final approval. **Timothy Lahey:** conception of manuscript, analysis and interpretation of data, editing of manuscript, final approval.

Conflict of interest statement

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