

Cross-reactivity of SARS-CoV-2 with HIV chemiluminescent assay leading to false-positive results

HIV may be considered as a differential diagnosis for patients who present with prolonged fever and respiratory symptoms. During the COVID-19 pandemic, several patients from our institution have had a simultaneous screening test for serum HIV antigen/antibodies as well as a nasopharyngeal swab for SARS-CoV-2 real-time reverse transcription PCR (rRT-PCR) on presentation to the hospital. While the molecular results often have a delayed turnaround time in light of increased testing volume, HIV screen performed as a chemiluminescent immunoassay on our Abbott Architect platform (Abbott Laboratories, Abbott Park, Illinois, USA) has a testing time of only 30 min. Herein, we retrospectively reviewed and identified two positive COVID-19 cases on rRT-PCR who concurrently tested reactive for HIV on the Architect, with further confounding results.

Both patients were admitted and tested in the same month. Our first patient was a man in his early 20s who had no significant medical history, presenting with a persistent fever for 2 days, dry cough and pharyngitis. He was not on any long-term medications. His initial laboratory investigations revealed white blood cells of $5.85 \times 10^9/\text{litre}$ (3.84–10.01), haemoglobin 144 g/L (131–166), haematocrit 43.7% (40.3–50.3), platelet $233 \times 10^9/\text{L}$ (164–387), sodium 137 mmol/L (135–145), potassium 4.1 mmol/L (3.5–5.0), C reactive protein $<5 \text{ mg/L}$ (0–10), ferritin $126 \mu\text{g}$ (20–300) and CareUS Dengue Combo kit was negative for NS1, IgM and IgG. His chest X-ray was otherwise normal. His first nasopharyngeal swab tested positive for SARS-CoV-2 and a concurrent HIV serological test on the Abbott Architect platform using the chemiluminescent immunoassay was reactive at 28.76 s/CO (sample relative light unit/cut-off relative light unit). Specimens with S/CO values of ≥ 1 are considered reactive. The second patient was a male in his early 70s who had a history of benign prostatic hyperplasia taking alfuzosin. He was a close contact of his wife who was recently diagnosed with COVID-19 and thence presented with high fever, dry cough and pharyngitis to the hospital. Chest X-ray revealed significant lower left zone atelectasis. His initial laboratory investigations revealed a white

blood cell count of $13.89 \times 10^9/\text{L}$ (3.84–10.01), haemoglobin 150 g/L (131–166), haematocrit 43.6% (40.3–50.3), platelets $202 \times 10^9/\text{L}$ (164–387), C reactive protein of 132 mg/L (0–10), ferritin $142 \mu\text{g}/\text{L}$ (20–300), sodium 136 mmol/L (135–145) and potassium 3.9 mmol/L (3.5–5.0). His first nasopharyngeal swab similarly tested positive for SARS-CoV-2 and a concurrent HIV test on the Abbott Architect platform was reactive at 1.11 s/CO. Neither of the patients reported previous blood transfusions, intravenous drug use or drug therapies, which may interact with testing.

These two patients' serum samples were repeated on a different Abbott Architect platform in a separate institution, which continued to show reactivity on the HIV chemiluminescent immunoassay. Their sera were then followed up by testing on a fourth generation, VIDAS HIV duo assay (BioMérieux, Durham, North Carolina, USA), an enzyme-linked fluorescent assay, which combines the detection of anti-HIV-1 (groups M and O) and anti-HIV-2 total immunoglobulins with HIV-1 p24 antigens. Both sera were negative for this duo assay. Confirmatory testing was then performed on the MP Biomedicals HIV immunoblot, which was negative in both sera.

This article underscores several important learning points. We have shown for the first time that there is cross-reactivity of SARS-CoV-2 antigen/antibodies with commercial chemiluminescent immunoassays leading to a false-positive result. Kliger and Levanon via sequence analysis had shown that HIV and SARS-CoV viral proteins shared sequence motifs that construct their active confirmation, which may explain a certain degree of homology in their proteins.¹ The limitation of HIV chemiluminescent assays must be emphasised. Liu and colleagues had previously demonstrated the susceptibility of fourth-generation p24 HIV antigen/antibody tests to false positivity from an array of pathogens, including that of Epstein-Barr virus and metastatic cancer.² Other centres have also reported interfering substances such as rheumatoid factor, anti-hepatitis C virus, liver cirrhosis and autoimmune disease.³ Further, although literature has reported specificity of HIV chemiluminescent immunoassays to be 99% or better, clinicians should be cognizant to the fact that discordant COVID-19 and HIV results necessitate professional laboratory consult in view of potential analytical error, where patient safety may be compromised if treatment is initiated prematurely.⁴ The limitation of our report is that the patients' attending physicians

had not sent a sample for HIV nucleic acid testing, which would be definitive. To further investigate cross-reactivity, a study for spiked SARS-CoV-2 antigen/antibodies on healthy sera should be performed to verify performance of HIV chemiluminescent immunoassays.

Shaun S Tan , **Ka Lip Chew, Sharon Saw, Roland Jureen, Sunil Sethi**

¹Department of Laboratory Medicine, National University Hospital, Singapore

Correspondence to Dr Shaun S Tan, National University Hospital, Singapore 119074, Singapore; shaun_sy_tan@nuhs.edu.sg

Handling editor Tahir S Pillay.

Contributors SST and KLC drafted the initial manuscript. SSa, RJ, SSe critically reviewed and approved of final submission.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The institutional ethics review board approved our study (DSRB: 2020/00407).

Provenance and peer review Not commissioned; internally peer reviewed.

This article is made freely available for use in accordance with BMJ's website terms and conditions for the duration of the covid-19 pandemic or until otherwise determined by BMJ. You may use, download and print the article for any lawful, non-commercial purpose (including text and data mining) provided that all copyright notices and trade marks are retained.

© Author(s) (or their employer(s)) 2020. No commercial re-use. See rights and permissions. Published by BMJ.



To cite Tan SS, Chew KL, Saw S, et al. *J Clin Pathol* Epub ahead of print: [please include Day Month Year]. doi:10.1136/jclinpath-2020-206942

Received 14 July 2020
Accepted 25 August 2020

J Clin Pathol 2020;0:1.
doi:10.1136/jclinpath-2020-206942

ORCID iD

Shaun S Tan <http://orcid.org/0000-0003-4100-0165>

REFERENCES

- 1 Kliger Y, Levanon EY. Cloaked similarity between HIV-1 and SARS-CoV suggests an anti-SARS strategy. *BMC Microbiol* 2003;3:20.
- 2 Liu P, Jackson P, Shaw N, et al. Spectrum of false positivity for the fourth generation human immunodeficiency virus diagnostic tests. *AIDS Res Ther* 2016;13:1.
- 3 Weber B, Gürtler L, Thorstenson R, et al. Multicenter evaluation of a new automated fourth-generation human immunodeficiency virus screening assay with a sensitive antigen detection module and high specificity. *J Clin Microbiol* 2002;40:1938–46.
- 4 Ly TD, Ebel A, Faucher V, et al. Could the new HIV combined p24 antigen and antibody assays replace p24 antigen specific assays? *J Virol Methods* 2007;143:86–94.