



Case Report

False-positive HIV in a patient with SARS-CoV-2 infection; a case report



Rawezh Q. Salih^{a,b}, Gasha A. Salih^{c,d}, Berwn A. Abdulla^{a,b}, Abdulla D. Ahmed^a,
Hawbash R. Mohammed^{a,b,c}, Fahmi H. Kakamad^{a,b,e,*}, Abdulwahid M. Salih^{a,e}

^a Smart Health Tower, Madam Mitterrand Street, Sulaimani, Kurdistan, Iraq

^b Kscien Organization, Hamdi Str, Azadi Mall, Sulaimani, Kurdistan, Iraq

^c Gaziosmanpasa University, Faculty of Medicine, Tokat, Turkey

^d University of Human Development, College of Health Science, Sulaimani, Kurdistan, Iraq

^e University of Sulaimani, College of Medicine, Madam Mitterrand Street, Sulaimani, Kurdistan, Iraq

ARTICLE INFO

Keywords:

SARS-CoV-2

COVID-19

HIV

Cross-reactivity

False-positive

ABSTRACT

Introduction: A small portion of Corona Virus disease-2019 (COVID-19) cases associated with co-infections, however occasionally they turn out to be false positive due to possible cross-reactivities. The current report aims to present a rare case of false-positive human immunodeficiency virus (HIV) in a COVID-19 patient.

Case report: A 32-year-old female complaining from thyroid problems referred for thyroid operation. She had mild symptoms of COVID-19. Her preoperative laboratory findings were normal, except for HIV screening test which was repetitively positive. RNA PCR was performed to confirm the diagnosis of HIV, it revealed a negative result. The patient underwent thyroidectomy as planned and was given the required supportive treatment to recover from COVID-19. Two-month follow up revealed that she was negative for COVID-19 on PCR testing, and HIV immunoassay test was no longer positive.

Discussion: Due to structural similarities between the spike protein chains of SARS-CoV-2 and some other viruses such as dengue, Zika, and other closely related coronaviruses (SARS-CoV, MERS-CoV), the protein can potentially interfere with the immunoassay tests. Although HIV immunoassay tests have high sensitivity and specificity, false-positive results have been reported, such as in the case of Epstein Barr virus, Influenza vaccination, and the Australian COVID-19 vaccination.

Conclusion: Similarity between HIV and SARS-CoV-2 spike proteins can lead to antibody cross-reactivities, yielding false-positive results on immunoassay screening tests.

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel viral pathogen that causes the coronavirus disease-2019 (COVID-19), it first emerged from Wuhan, China in late 2019, and became a pandemic soon after [1]. The infection is highly transmissible and primarily spreads through sneezing, coughing, or talking within close proximities, hence it caused major social distancing in populated areas [2]. Even though the majority of COVID-19 cases are asymptomatic or have mild symptoms (such as, dry cough and fever), a minority of the cases (14%) can develop acute respiratory distress syndrome (ARDS), especially in the presence of the risk factors including; old age, hypertension, and diabetes [1]. It is regarded as a systemic disease and involves several organs of the body [3]. Amongst COVID-19 cases, 7.2% are reported to be associated with other bacterial, fungal, or viral

pathogens, which in turn can affect survivability and the approach used to treat these cases [4,5]. However, false-positive results of co-infections and misdiagnosis in the setting of COVID-19 have been occasionally reported in the literature, such as Dengue virus, indicating potential cross reactivity between SARS-CoV-2 and some other pathogens [6]. It is important to consider false-positive results in these cases, as they might result in unsuitable management and infection control [7]. False-positive result of human immunodeficiency virus (HIV) with SARS-CoV-2 infection is highly unique with only a few reported cases being present in the literature [8].

The current paper aims to present an exceedingly rare case of false-positive HIV with confirmed SARS-CoV-2 infection. SCARE 2020 guidelines have been taken into account in the writing of this report [9].

* Corresponding author.

E-mail address: Fahmi.hussein@uniuvsul.edu.iq (F.H. Kakamad).

<https://doi.org/10.1016/j.amsu.2021.103027>

Received 21 September 2021; Received in revised form 3 November 2021; Accepted 4 November 2021

Available online 6 November 2021

2049-0801/© 2021 The Authors. Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY license

(<http://creativecommons.org/licenses/by/4.0/>).

2. Case presentation

Patient information: A 32-year-old married female working as a housewife was referred for total thyroidectomy as she had been diagnosed as a case of papillary thyroid carcinoma (PTC).

Clinical findings: Upon examination, the patient had an ill-defining anterior neck mass, she also had common mild symptoms of COVID-19, such as coughing, dyspnea and fever.

Diagnostic approach: Preoperative laboratory findings showed normal levels of blood glucose, CBC, TSH, calcium, and blood urea. Polymerase chain reaction (PCR) for the nasal swab confirmed the diagnosis of COVID-19. However, anti-HIV antibody titer using Roche Cobas E411 analyzer was positive (repeated 3 times). To confirm the diagnosis of HIV, RNA-PCR test was performed which surprisingly revealed a negative result.

Therapeutic intervention: With full viral precaution, under general anesthesia, the patient underwent total thyroidectomy as planned and was given the required supportive treatment to recover from COVID-19. The histopathological examination of the specimen confirmed the diagnosis of the papillary thyroid cancer.

Follow-up and outcome: The patient was followed up after two months, PCR testing showed that she was negative for COVID-19 and her HIV immunoassay test was no longer positive.

3. Discussion

COVID-19 is considered as a systemic disease as it affects different parts of the body, with a small percentage of these cases being presented with other microbial co-infections which can further complicate the condition [4]. However, some reports have indicated that these infections can sometimes be a false-positive, such as in the case of dengue and zika viruses [10]. False-positive result of HIV in the setting of COVID-19 is extremely rare with only 3 cases being reported in the literature [8,11].

SARS-CoV-2 is an enveloped RNA virus belonging to the Coronaviridae family, they possess transmembrane crown-like glycoprotein spikes (S) on their outer surfaces that have a crucial role in host cell recognition and penetration, and can trigger host humoral immune response, hence trigger the production of their antibody counterparts [12]. The spike protein has a large surface area and consists of an S1 receptor binding domain (RBD) and an S2 non-receptor binding domain (non-RBD) that promotes viral fusion [13]. This spike protein or at least only the RBD domain has been utilized in enzyme-linked immunosorbent assays for COVID-19 testing [14].

Due to structural similarities between the spike protein chains of SARS-CoV-2 and some other viruses such as dengue and Zika, the protein can mediate antibody cross-reactivity between SARS-CoV-2 and these viruses, as a result, it can potentially interfere with immunoassay tests and lead to false-positive diagnosis [10]. Hicks and colleagues also demonstrated that the spike protein of SARS-CoV-2 can lead to antibody cross-reactivities with other closely related coronaviruses in which they all possess the spike proteins on their outer surfaces, such as SARS-CoV, MERS-CoV, and some seasonal embecoviruses (HCoV-OC43 and HCoV-HKU1), with the former two having the highest level of cross-reactivity with SARS-CoV-2 [14].

Generally, patients with COVID-19 present with fever, dyspnea, and coughing [2]. However, prolonged fever and respiratory symptoms may also be indicative of HIV [11]. Hence, laboratory tests are required to confirm the diagnosis of the condition, or to determine the presence of co-infection as HIV which in the setting of COVID-19 has a prevalence of 1.22% [15]. Meanwhile, in 2020 Tan et al. reported 2 cases of false-positive HIV with SARS-CoV-2 infection, they used Abbot Architect multiple times for the diagnosis of HIV and still achieved the same result. On the other hand, immunoblot test was negative in both cases [11]. And later in 2021, Papamanoli and associates reported another false-positive case, again they used the Abbot Architect in their

diagnosis [8]. Marking the current case, the 4th of this kind which was diagnosed via Roche Cobas E411 immunoassay testing platform.

This antibody cross-reactivity between the two viruses may be likely because the spike protein of HIV-1 shares astonishing similarity to that of SARS-CoV-2 [16]. To further support this argument, Yamaniha et al. have reported the exact opposite of the current case by presenting a false-positive SARS-CoV-2 antigen test in a patient with acute HIV infection [17].

Among population, the incidence of false-positive HIV result is between 0.0004% and 0.0007%, this is mostly determined by the specificity and sensitivity of the used diagnostic approach [18]. Although HIV immunoassay tests have been reported to have a high sensitivity and specificity of more than 99%, false results should still be considered in order to avoid unnecessary or unsuitable treatment as they do occasionally occur and can cause psychological distress in the patient [19]. Besides SARS-CoV-2, other agents have also been reported in the literature that have caused false-positive result in HIV screening tests, such as Epstein Barr virus, Influenza vaccination, and also the Australian COVID-19 vaccination which also led to its abandonment [18,20,21]. In order to avoid mismanagement, more specific confirmatory diagnosis of HIV is required in cases with possible SARS-CoV-2 infection, such as Western Blot, nucleic acid test, or RNA PCR testing [18].

In conclusion, HIV has a similar spike protein to that of SARS-CoV-2 which can lead to antibody cross-reactivities between the two viruses and cause false-positive results on immunoassay screening tests. Medical practitioners should be aware of the possibility of false-positive results in order to avoid mismanagement and avoid psychological distress to the patient.

Patient consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Source of funding

None is found.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Annals of medicine and surgery

The following information is required for submission. Please note that failure to respond to these questions/statements will mean your submission will be returned. If you have nothing to declare in any of these categories then this should be stated.

Please state any conflicts of interest

There is no conflict to be declared.

Please state any sources of funding for your research

No source to be stated.

Ethical approval

Approval is not necessary for case report in our locality.

Consent

Consent has been taken from the patient and the family of the

patient.

Author contribution

Rawezh Q.Salih: biologist diagnosing the case, follow up the patient, and final approval of the manuscript. Gasha A.Salih, Berwn A.Abdulla, Abdulla D.Ahmed, Hawbash R.Mohammed, Fahmi H.Kakamad, Abdulwahid M.Salih: literature review, writing the manuscript, final approval of the manuscript.

Registration of research studies

According to the previous recommendation, registration is not required for case report.

Guarantor

Fahmi Hussein Kakamad is the Guarantor of submission.

Declaration of competing interest

None to be declared.

References

- [1] H.M. Abdullah, H.H. Hama-Ali, S.N. Ahmed, K.M. Ali, K.A. Karadakhly, S. O. Mahmood, et al., Severe refractory COVID-19 patients responding to convalescent plasma; A case series, *Annals of medicine and surgery* 56 (1) (2020) 125–127.
- [2] A.A. Amin, A.H. Awakhti, L.A. Hussein, F.H. Fattah, H.O. Baba, F.H. Kakamad, et al., Survived COVID-19 patient presented with death on arrival: a case report, *International Journal of Surgery Case Reports* 81 (1) (2021) 1–3.
- [3] A. Baram, F.H. Kakamad, H.M. Abdullah, D.H. Mohammed-Saeed, D.A. Hussein, S. H. Mohammed, et al., Large vessel thrombosis in patient with COVID-19, a case series, *Annals of Medicine and Surgery* 60 (1) (2020) 526–530.
- [4] F.H. Kakamad, S.O. Mahmood, H.M. Rahim, B.A. Abdulla, H.O. Abdullah, S. Othman, et al., Post covid-19 invasive pulmonary Aspergillosis: a case report, *International journal of surgery case reports* 82 (1) (2021) 1–3.
- [5] Shwan A. Ahmad, Karokh H. Salih, Shaho F. Ahmed, Fahmi H. Kakamad, Abdulwahid M. Salh, Marwan N. Hassan, et al., Post COVID-19 transverse myelitis; a case report with review of literature, *Annals of Medicine and Surgery* 69 (2021) 1–3.
- [6] Y. Lustig, S. Keler, R. Kolodny, N. Ben-Tal, D. Atias-Varon, E. Shlush, et al., Potential antigenic cross-reactivity between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and dengue viruses, *Clin. Infect. Dis.* 2 (2020) 1–6.
- [7] T. Ogawa, T. Fukumori, Y. Nishihara, T. Sekine, N. Okuda, T. Nishimura, et al., Another false-positive problem for a SARS-CoV-2 antigen test in Japan, *J. Clin. Virol.* 131 (1) (2020) 1.
- [8] A. Papamanoli, G. Psevdos, False-positive HIV screening test in a patient with pulmonary embolism because of severe acute respiratory syndrome coronavirus 2 infection, *AIDS* 35 (9) (2021) 1521–1522.
- [9] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, A. Kerwan, A. Thoma, et al., The SCARE 2020 guideline: updating consensus Surgical Case Report (SCARE) guidelines, *Int. J. Surg.* 84 (1) (2020) 226–230.
- [10] Á.A. Faccini-Martínez, R. Rivero, E. Garay, A. García, S. Mattar, Y. Botero, et al., Serological cross-reactivity using a SARS-CoV-2 ELISA test in acute Zika virus infection, Colombia, *Int. J. Infect. Dis.* 101 (1) (2020) 191–193.
- [11] S.S. Tan, K.L. Chew, S. Saw, R. Jureen, S. Sethi, Cross-reactivity of SARS-CoV-2 with HIV chemiluminescent assay leading to false-positive results, *J. Clin. Pathol.* 1 (1) (2020) 1.
- [12] D. Mannar, K. Leopold, S. Subramaniam, Glycan reactive anti-HIV-1 antibodies bind the SARS-CoV-2 spike protein but do not block viral entry, *Sci. Rep.* 11 (1) (2021) 1–9.
- [13] A.C. Walls, Y.J. Park, M.A. Tortorici, A. Wall, A.T. McGuire, D. Velesler, Structure, function, and antigenicity of the SARS-CoV-2 spike glycoprotein, *Cell* 181 (2) (2020) 281–292.
- [14] J. Hicks, C. Klumpp-Thomas, H. Kalish, A. Shunmugavel, J. Mehalko, J.P. Denson, et al., Serologic cross-reactivity of SARS-CoV-2 with endemic and seasonal Betacoronaviruses, *J. Clin. Immunol.* 41 (1) (2021) 906–913.
- [15] P. Ssentongo, E.S. Heilbrunn, A.E. Ssentongo, S. Advani, V.M. Chinchilli, J. J. Nunez, et al., Epidemiology and outcomes of COVID-19 in HIV-infected individuals: a systematic review and meta-analysis, *Sci. Rep.* 11 (1) (2021) 1–2.
- [16] C. Zhang, W. Zheng, X. Huang, E.W. Bell, X. Zhou, Y. Zhang, Protein structure and sequence reanalysis of 2019-nCoV genome refutes snakes as its intermediate host and the unique similarity between its spike protein insertions and HIV-1, *J. Proteome Res.* 19 (4) (2020) 1351–1360.
- [17] K. Yamaniha, T. Kinjo, M. Akamine, M. Setoguchi, M. Tateyama, J. Fujita, False-positive for SARS-CoV-2 antigen test in a man with acute HIV infection, *J. Infect. Chemother.* 27 (7) (2021) 1112–1114.
- [18] L. Kavallierou, F. Bazigou, A. Cheropoulou, Acute EBV infection and HIV antibody cross-reactivity in a first Time donor, *Hematology & Transfusion International Journal* 1 (4) (2015) 100–102.
- [19] T.D. Ly, A. Ebel, V. Faucher, V. Fihman, S. Laperche, Could the new HIV combined p24 antigen and antibody assays replace p24 antigen specific assays? *J. Virol Methods* 143 (1) (2007) 86–94.
- [20] C.P. Erickson, T. McNiff, J.D. Klausner, Influenza vaccination and false positive HIV results, *N. Engl. J. Med.* 354 (13) (2006) 1422–1423.
- [21] P. McIntyre, Y.J. Joo, C. Chiu, K. Flanagan, K. Macartney, COVID-19 vaccines—are we there yet? *Aust. Prescr.* 44 (1) (2021) 19–25.