


Letter to the Editor

False-negative nasopharyngeal severe acute respiratory coronavirus virus 2 (SARS-CoV-2) reverse-transcription polymerase chain reaction (RT-PCR) in immunocompromised patients resulting in healthcare worker exposures

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To the Editor—Exposure to coronavirus disease 2019 (COVID-19) infection will remain a concern in healthcare settings, even with increasing vaccination rates among healthcare staff and patient populations. This is particularly true for healthcare workers (HCWs) who are immunocompromised because they have been noted to have a lower response to available COVID-19 vaccines.^{1–6} Specific immunocompromised hosts, including hypo-gamma-globulinemic patients and those on anti-CD-20 inhibitors, are not only at risk for poor vaccine response but can also present with prolonged duration of symptoms and infection.

We describe 2 immunocompromised patients who were noted to have negative severe illness and acute respiratory coronavirus virus 2 (SARS-CoV-2) testing on nasopharyngeal (NP) swabs. Both patients were admitted for abnormal computed tomography chest findings, with associated respiratory symptoms of 42- and 100-day durations, respectively. Both cases occurred in immunocompromised individuals: a male aged 57 years with mantle cell lymphoma on rituximab and a female aged 59 years with history of follicular lymphoma on obinutuzumab therapy. Isolation precautions were discontinued once NP swab results returned negative. Both patients subsequently underwent bronchoscopy for bronchoalveolar lavage (BAL) sampling, and SARS-CoV-2 reverse-transcriptase polymerase chain reaction (RT-PCR) tests returned positive: one on day 26 of admission (cycle threshold value [Ct], 20.8), and the other on day 3 of admission (Ct, 31.8). Both patients received COVID-19-directed therapy with reported symptom improvement.

These 2 cases resulted in large exposure follow up investigations. In the first case, 10 HCWs were evaluated and 2 met significant-risk exposure criteria, both due to lack of eye protection in addition to a face mask when in close, prolonged contact with the unmasked patient [<2 m (6 feet) for >15 minutes]. The exposed HCWs were both fully vaccinated (complete vaccination

series plus 2 weeks) and were offered RT-PCR testing at baseline and days 5–7 following the exposure according to the institution's occupational health and safety recommendations. Neither case resulted in known patient exposure.

In the second case, the delay in diagnosis and use of high-flow oxygen therapy and an Aerobika breathing device throughout prolonged hospitalization resulted in an even larger exposure follow up. In total, 184 HCWs were reviewed for exposures, and 83 were identified as having significant-risk exposures going back 14 days prior to the positive test. Significant risk exposures were due to lack of eye protection when interacting with the unmasked patient and/or use of a face mask rather than a respirator during an aerosol-generating procedure or the postprocedure room clearance. Of the 83 exposed HCWs, 70 were fully vaccinated and were offered testing at baseline and day 5–7 following the exposure. Among these 83 HCWs, 13 (16%) were unvaccinated or were incompletely vaccinated, and serial PCR testing was arranged at baseline, day 5–7, and days 12–14 following the last exposure. HCWs who were not fully vaccinated and had a significant-risk exposure were issued work restrictions and were advised to quarantine at home following CDC and local public health guidelines.

In total, serial PCR testing was arranged for 85 HCWs with significant-risk exposures to 1 of the 2 immunocompromised patients. Fortunately, none of the HCWs contracted COVID-19 due to the exposures. This finding was largely attributed to the high vaccination rate among exposed HCWs, of whom 85% were fully vaccinated, with partial vaccination in some of the remaining HCWs.

These 2 cases highlight additional infection prevention and control considerations in caring for immunocompromised individuals with risk of persistent COVID-19 infection. Isolation precautions were prematurely discontinued following negative NP swabs in both scenarios, leading to large-scale exposure among HCWs. These cases also highlight the overall unknown potential infectivity of immunocompromised patients with prolonged symptoms, where transmission risk may be lower in cases with negative NP swab results and positive BAL sampling results with high Ct values, suggesting decreased overall viral burden. A threshold for Ct-value infectivity in such patients, however, has not been established. Clinicians and infection prevention and control specialists should be aware of possible false-negative NP swab results in profoundly immunosuppressed hosts until more research can be

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conducted to understand the infectivity of persistent COVID-19 infection in this population.

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