Infection with SARS-CoV-2 Omicron Variant 24 Days after Non-Omicron Infection, Pennsylvania, USA

Arlene G. Seid, Tigist Yirko, Sameera Sayeed, Nottasorn Plipat

Author affiliations: Pennsylvania Department of Health, Bureau of Epidemiology, Harrisburg, Pennsylvania, USA (A.G. Seid, N. Plipat); Bureau of Epidemiology, Lancaster, Pennsylvania, USA (T. Yirko); Bureau of Laboratories, Exton, Pennsylvania, USA (S. Sayeed

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A 42-year-old man, with up-to-date COVID-19 vaccination, experienced symptomatic SARS-CoV-2 infection in December 2021. Mutation tests suggested a non-Omicron variant. After his recovery, and 24 days after the first positive SARS-CoV-2 test, he had onset of symptomatic infection with the BA.1.1 (Omicron) variant, which was confirmed by whole-genome sequencing.

Repeated positive findings for SARS-CoV-2 infection within 90 days pose diagnostic challenges for public health professionals. Such results imply persistent viral shedding, reinfection, or coinfection, and each determination requires a different isolation and quarantine approach. When genetic sequencing resources are limited, healthcare professionals must base risk assessment decisions on such criteria as exposure history and community transmission levels. We describe a vaccinated healthcare worker who had positive SARS-CoV-2 tests 24 days apart. Each positive test was associated with a separate symptomatic illness.

On December 20, 2021, a 42-year-old otherwise healthy man, employed in a nursing home, had onset of nausea and emesis. He was up to date with COVID-19 vaccinations, having received the 2 initial doses of the Pfizer-BioNTech vaccine (https://www.pfizer.com), as well as a booster dose on October 11, 2021. He tested positive for SARS-CoV-2 by real-time reverse transcription PCR (RT-PCR) using Taqman assays (Thermo Fisher Scientific, https://www.thermofisher.com). The PCR test detected nucleocapsid 1 protein (cycle threshold [Ct] 33), nucleocapsid 2 protein (Ct 28), and spike protein (Ct 33) genes and did not detect the open reading frame 1ab gene. Further mutation tests by TaqMan Mutation Detection Assays (Thermo Fisher Scientific) showed the absence of delH69V70, suggesting the patient's infection was probably not caused by the Omicron BA.1 variant. The patient recovered within 1 week.

On January 12, 2022, the patient had new onset of fever, chills, myalgia, and cough. Four of his 6 household members were also sick and received positive results after administration of SARS-CoV-2 at-home antigen tests (Figure). The patient was tested at an urgent care clinic. The Quidel QuickVue SARS antigen test (Quidel, https://www.quidel.com) showed a positive result, and the BD Veritor influenza A/B antigen test (Thermo Fisher Scientific) showed a negative result. Negative findings from a multiplex RT-PCR for respiratory pathogens eliminated consideration of alternative diagnoses. The patient's specimen was sent to the Pennsylvania Department of Health Bureau of Laboratories (BOL) and tested by the CDC Influenza SARS-CoV-2 (FluSC2) Multiplex RT-PCR Assay. The test result was negative for Influenza A and B, but positive for SARS-CoV-2 (Ct 19). The whole-genome sequencing (Illumina, https://www.illumina.com) yielded Omicron variant BA.1.1. The patient tested negative by RT-PCR 1 week later.

Reinfection with a different virus variant is the most likely explanation for the positive antigen and PCR tests 24 days after this patient's initial SARS-CoV-2 infection diagnosis. We base this assumption on 3 facts: the symptomatic illnesses were separated by a full, albeit brief, recovery period; tests uncovered 2 genotypically distinct variants; and household exposure presented a likely route of transmission for the second infection during an Omicron surge.

Studies have described co-infections with 2 SARS-CoV-2 variants; however, those co-infections were noted either as contributors to a singular illness or as co-detected events in the same samples (*1*,*2*). Although persistent positive test results may follow an asymptomatic period, the onset of new symptoms and subsequent confirmation of a different variant by whole-genome sequencing makes that explanation unlikely for the patient we studied.

The frequency of coronavirus reinfection has been shown to depend on many variables: the studied population, the SARS-CoV-2 variants, time and place, and the defined duration between the initial and subsequent infections. The interval between infections of the same seasonal coronavirus could be <12 months (*3*). For SARS-CoV-2, the interval between reported infections of genetically distinct variants has ranged from 23 to >90 days (*4*).

Although this case appears to lend support to prior studies demonstrating the capacity of the Omicron variant to evade immunity, our findings also suggest that a fully protective humoral and cell-mediated immunity might take longer than 24 days to

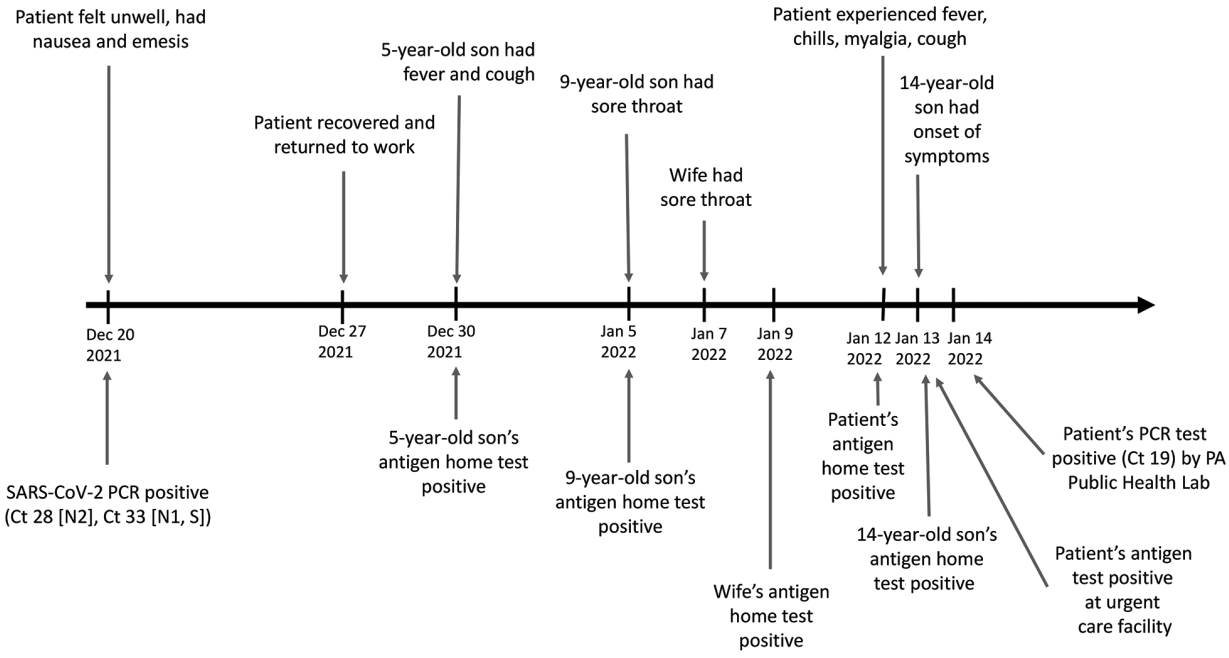

Figure. Timeline of a vaccinated healthcare worker who had positive viral tests for SARS-CoV-2 infection 24 days apart (December 20, 2021, and January 12, 2022), Pennsylvania, USA. Image shows symptoms and test results for the patient and household members. The patient and his wife were up to date with Pfizer-BioNTech (https://www.pfizer.com) SARS-CoV-2 vaccines (2 doses of primary series and 1 booster dose). Both eligible children (9-year-old and 14-year-old sons) were fully vaccinated against SARS-CoV-2. Ct, cycle threshold; N1, nucleocapsid 1 protein; N2, nucleocapsid 2 protein; PA, Pennsylvania; S, spike protein.

develop (*5*,*6*). Antibodies to SARS-CoV-2 infection may be present as early as 10 days postinfection, but the presence of antibodies alone is an incomplete predictor of protection (*7*). Cross-reactive immunity after COVID-19 illness and SARS-CoV-2 vaccination has been shown to confer broad protection against heterologous coronaviruses. This protection, however, might be variable depending on variants (*8*). When compared with ancestor and other variants, the Omicron variant has been shown to demonstrate reduced neutralization (*9*). Convalescent serum from infected patients largely did not neutralize the Omicron variant; conversely, serum from infected patients who were subsequently vaccinated and from patients who were vaccinated and had breakthrough infections did neutralize the Omicron variant, but to a lesser degree than for the Delta variant (*9*). In the patient we describe, immune response from 3 mRNA vaccines and COVID-19 infection did not prevent reinfection.

As documented in another study, household secondary attack rate by Omicron is higher (25%) than for the Delta variant (11%), even among booster-vaccinated persons (F.P. Lyngse et al., unpub. data, https://doi.org/10.1101/2021.12.27.21268278). In the patient we describe, it is more likely that household exposure led to the second infection. Still, given the short interval (24 days) between the 2 infections and the unavailable genetic sequencing data, we cannot rule out that this patient's initial infection might have been the source of the subsequent infections among members of the household. Full assessment of the clinical context, individual risk exposure, and community transmission level is essential in determining diagnosis and appropriate health intervention in patients who test positive again shortly after an initial positive viral test for SARS-CoV-2 infection.

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About the Author

Dr. Seid is a public health physician at the Pennsylvania Department of Health. Her research interests include vaccine-preventable diseases.

References

1 Francisco Junior RS, Almeida LGPd, Lamarca AP, Cavalcante L, Martins Y, Gerber AL, et al. Emergence of within-host SARS-CoV-2 recombinant genome after coinfection by Gamma and Delta variants: a case

report. Front Public Health. 2022;10:849978. https://doi.org/10.3389/fpubh.2022.849978
2. Samoilov AE, Kaptelova VV, Bukharina AY, Shipulina OY, Korneenko EV, Saenko SS, et al. Case report: change of dominant strain during dual SARS-CoV-2 infection. BMC Infect Dis. 2021;21:959. https://doi.org/10.1186/s12879-021-06664-w
3. Galanti M, Shaman J. Direct observation of repeated infections with endemic coronaviruses. J Infect Dis. 2021; 223:409–15. https://doi.org/10.1093/infdis/jiaa392
4. Roskosky M, Borah BF, DeJonge PM, Donovan CV, Blevins LZ, Lafferty AG, et al. Notes from the field: SARS-CoV-2 omicron variant infection in 10 persons within 90 days of previous SARS-CoV-2 delta variant infection—four states, October 2021–January 2022. MMWR Morb Mortal Wkly Rep. 2022;71:524–6. https://doi.org/10.15585/mmwr.mm7114a2
5. Pulliam JRC, van Schalkwyk C, Govender N, von Gottberg A, Cohen C, Groome MJ, et al. Increased risk of SARS-CoV-2 reinfection associated with emergence of the omicron variant in South Africa. Science. 2022;376:eabn4947. https://doi.org/10.1126/science.abn4947
6. Soleimanian S, Alyasin S, Sepahi N, Ghahramani Z, Kanannejad Z, Yaghobi R, et al. An update on protective effectiveness of immune responses after recovery from COVID-19. Front Immunol. 2022;13:884879. https://doi.org/10.3389/fimmu.2022.884879
7. Hueston L, Kok J, Guibone A, McDonald D, Hone G, Goodwin J, et al. The antibody response to SARS-CoV-2 infection. Open Forum Infect Dis. 2020;7:ofaa387.
8. Dangi T, Palacio N, Sanchez S, Park M, Class J, Visvabharathy L, et al. Cross-protective immunity following coronavirus vaccination and coronavirus infection. J Clin Invest. 2021;131:e151969. https://doi.org/10.1172/JCI151969
9. Rössler A, Riepler L, Bante D, von Laer D, Kimpel J. SARS-CoV-2 omicron variant neutralization in serum from vaccinated and convalescent persons. N Engl J Med. 2022;386:698–700. https://doi.org/10.1056/NEJMc2119236

Address for correspondence: Nottasorn Plipat, Division of Infectious Diseases Epidemiology, Pennsylvania Department of Health, 625 Forster St, Harrisburg, PA 17120, USA; email: nplipat@pa.gov

Pathogenesis and Transmissibility of North American Highly Pathogenic Avian Influenza A(H5N1) Virus in Ferrets

Joanna A. Pulit-Penaloza, Jessica A. Belser, Nicole Brock, Poulami Basu Thakur, Terrence M. Tumpey, Taronna R. Maines

Author affiliation: Centers for Disease Control and Prevention, Atlanta, Georgia, USA

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Highly pathogenic avian influenza A(H5N1) viruses have spread rapidly throughout North American flyways in recent months, affecting wild birds in over 40 states. We evaluated the pathogenicity and transmissibility of a representative virus using a ferret model and examined replication kinetics of this virus in human respiratory tract cells.

Highly pathogenic avian influenza (HPAI) A(H5Nx) viruses (clade 2.3.4.4, primarily H5N2 and H5N8 subtypes) were first detected along the Pacific flyway in 2014, resulting in outbreaks in wild bird and domestic poultry populations in North America (*1*). No human cases were associated with these outbreaks in the United States, but sporadic HPAI H5Nx virus human infections have been documented in other geographic locations, highlighting the potential of these viruses to jump species barriers during culling or sampling of infected birds (*2*). Despite reduced detection of H5Nx viruses in North America in recent years, clade 2.3.4.4b H5N1 virus, which emerged and displaced other H5Nx virus in Europe, Asia, and Africa, was detected in wild birds in North America in late 2021. Since then, the virus has been introduced into all 4 flyways of North America (*3*). The detection and spread of this virus in US commercial and backyard poultry pose substantial economic implications and concerns for human health, as evidenced by the first confirmed HPAI H5N1 human case, documented in the United States in April 2022 (*4*), underscoring the pandemic potential presented by continued circulation of viruses at the animal–human interface. To investigate the relative risk posed by these viruses, we examined the pathogenicity and transmissibility of a representative HPAI H5N1 virus, A/American Wigeon/SC/22-000345-001/2021 (aw/SC) by using a ferret model and assessed the capacity of this virus to replicate in a human respiratory cell line compared with seasonal H1N1 viruses.