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...
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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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
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 virus using a ferret model and assessed replication kinetics of this virus in human respiratory tract cells.