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Rapid elimination of SARS-CoV-2 in a fully vaccinated patient

SHORT CASE REPORT

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High SARS-CoV-2 viral loads in respiratory secretions detected by PCR technique are usually an indicator of high transmission risk, but not always. In this article, we present the case of a fully-vaccinated patient with rapid clearance of the alpha variant of the virus.

A middle-aged woman tested negative for SARS-CoV-2 upon arrival after an international flight. She had been vaccinated with two doses of mRNA vaccine several weeks before and was routinely quarantined together with two of her children travelling together. On day 7 she tested positive by PCR with a very high virus load (Ct value 13.4, > 10^7 copies/ml), and antibodies against the spike protein increased rapidly from 3703 U/ml to 9447 U/ml on day 15. Subgenomic mRNA was detected, indicating active virus replication, and typical virus particles were observed by EM directly from a nasopharyngeal specimen. However, viral culture was negative, and the virus (Alpha variant B.1.1.7) was not transmitted to the other family members. Eight days later (day 15), still asymptomatic, she was PCR-negative, indicating a very efficient elimination of the virus. In this case, two doses of mRNA vaccine protected against clinical symptoms as well as household transmission of SARS-CoV-2.

A fully-vaccinated woman in her forties was placed in quarantine on returning home to Norway after travelling abroad. She tested negative for SARS-CoV-2 at the airport and had no respiratory symptoms. On day 7 following arrival, she had a positive result on nasopharyngeal polymerase chain reaction (PCR) testing (Alinity m, Abbott). A high viral load was detected in the specimen, with a cycle threshold (CT) of 13.4, corresponding to > 10^7 copies/mL (information from the manufacturer), although she was still asymptomatic.

Total levels of antibodies to the spike protein (Elecsys, Roche), which develop following infection as well as following vaccination, were high (3703 U/mL) on day 9 following arrival. Testing for antibodies to the SARS-CoV-2 nucleocapsid (Elecsys, Roche), which are only produced by current or past infection, was negative. On day 15, another nasopharyngeal specimen was taken, which was negative on PCR testing. A blood sample taken at the same time found that

antibody levels to the spike protein had increased to 9447 U/mL. Antibodies to the nucleocapsid antigen were not detected until day 22, with levels rising rapidly on subsequent days.

Two of the patient's unvaccinated adult children travelled abroad with her and were also quarantined in the same house as their mother. They had four negative PCR tests and one negative antibody test, the last being eight days after their mother had tested positive for SARS-CoV-2.

The virus detected was an alpha variant (B.1.1.7), which gave a negative viral culture result in Vero-E6 cells (1). A PCR test was also performed, which was positive for mRNA, indicating active viral replication (2, 3). Transmission electron microscopy of the specimen revealed several round particles of a typical size (60–140 nm), with spike-like structures on the surface (Figure 1).

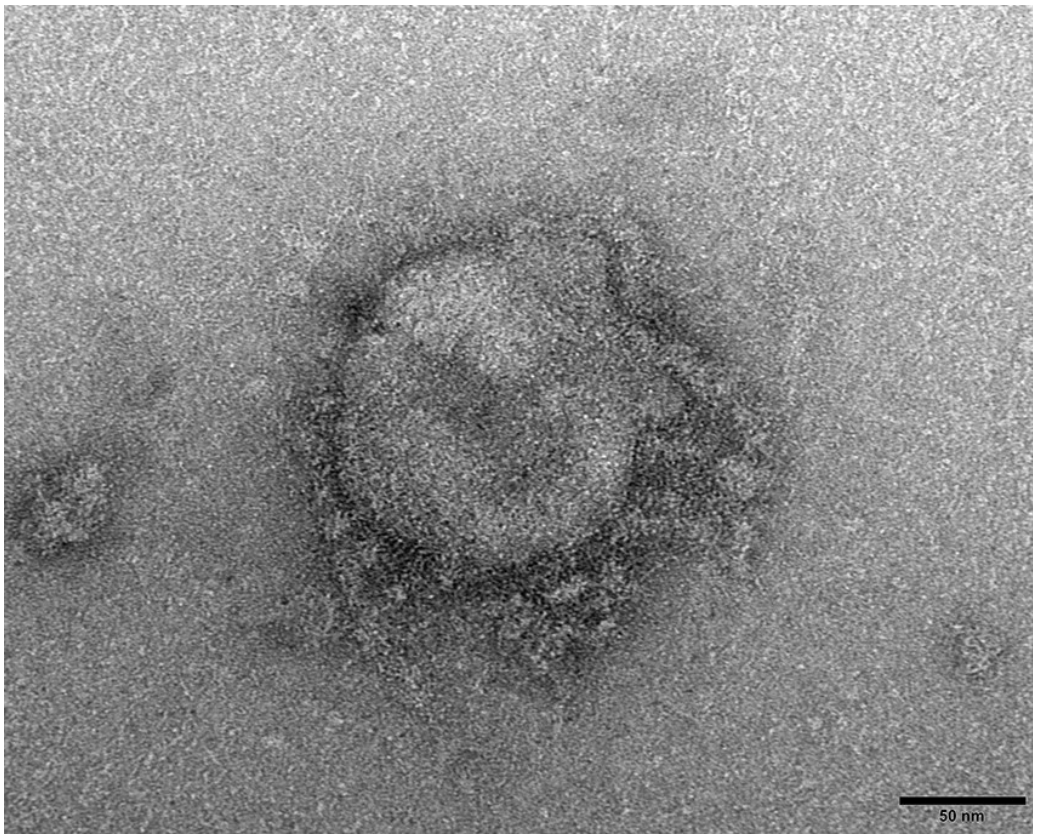

Figure 1 SARS-CoV-2 virus detected on transmission electron microscopy (180,000 × magnification) in specimen material from index case. Photo: Linh Hoang, Norwegian University of Science and Technology.

Discussion

The high levels of viral RNA detected on day 7 following the patient's arrival home indicate that she was infected before or just after arriving home. The incubation period for SARS-CoV-2 is 2–14 days, on average 5–6 days (4). Therefore, it is likely that she was shedding the virus for more than a day before the positive PCR test and that her unvaccinated children were exposed to a potentially highly infectious virus. PCR testing detects viral nucleic acids and not intact virions, and positive test results can be produced for several weeks

following a primary infection, even though the patient is no longer infectious (2, 3). Therefore, it was unexpected for the PCR test to revert to negative so quickly after such a high viral load.

An alternative to viral culture is detection of mRNA. This can be performed by PCR technique, and the test result becomes negative relatively rapidly once viral replication ceases because mRNA generally degrades rapidly (2, 3). However, opinions are divided about how rapidly the degradation takes place and how suitable this method is as a diagnostic assay (5). Transmission electron microscopy was performed directly on the specimen material in question to prove that intact virions were produced. The sensitivity of this technique is 10^5–10^6 virus particles/mL (6). This suggests that the sample contained at least 10^6 virus particles/mL, which is usually enough to propagate the virus in cell culture (2, 3). However, despite repeated attempts, viral cultures were negative.

As a quality control check on the culture, a SARS-CoV-2 positive specimen with the same virus variant and corresponding viral load from an unvaccinated patient was cultured in the same process along with other PCR-positive specimens, with a positive result. The serological results indicated a clear secondary antibody response to the spike protein, which may have contributed to more rapid neutralisation of the virus than with a primary infection. The anti-nucleocapsid antibodies were only detected on day 22, 15 days after the positive PCR test, which confirms that the patient had an asymptomatic primary infection that was cleared by the immune system.

Although secondary transmission from fully-vaccinated people does occur, this case report demonstrates that high levels of viral RNA detected on PCR testing do not necessarily reflect high transmissibility. Our findings are consistent with a major UK study that revealed that the majority (93 %) of cases of transmission from vaccinated people to household members were from people who had only received one dose of vaccine (7). However, the delta variant (B.1.617.2) is significantly more infectious and has been found to entail a 70 % higher risk of transmission to household members compared with the alpha variant (8). It is currently unknown how much more infectious the new omicron variant is compared with the other variants of the virus.

The patient and other people mentioned have given consent for the article to be published.

The article has been peer-reviewed.

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