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BRIEF REPORT

Transmission of SARS-CoV-2 Alpha Variant (B.1.1.7) From a BNT162b2-Vaccinated Individual

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Cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) acquisition after vaccination with BNT162b2 have been described, but the risk of secondary transmission from fully vaccinated individuals remains ill defined. Herein we report a confirmed transmission of SARS-CoV-2 alpha variant (B.1.1.7) from a symptomatic immunocompetent woman 4 weeks after her second dose of BNT162b2, despite antispike seroconversion.

Keywords. BNT162b2; SARS-CoV-2; transmission; vaccination.

BNT162b2, an mRNA vaccine encoding the spike protein, was the first licensed vaccine against coronavirus disease 2019 (COVID-19). In macaques, BNT162b2 induced strong antispike-specific immune responses associated with potent protection of the upper respiratory tract against challenge with infectious severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. Vaccine effectiveness of BNT162b2 against symptomatic COVID-19 was estimated around 95% 7 days after the second dose, both in the phase 3 randomized pivotal trial [2] and in the nationwide mass vaccination campaign in Israël [3].

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Despite high effectiveness for preventing both symptomatic and asymptomatic SARS-CoV-2 infection [3–6], recent observations point to the remaining risk for SARS-CoV-2 acquisition in a minority of individuals fully vaccinated with BNT162b2. In 36 659 health care workers (HCWs) undergoing weekly testing by polymerase chain reaction (PCR) assay of nasal swabs, the absolute risk of testing positive for SARS-CoV-2 was estimated at 0.05% in those who had received the second vaccine dose ≥2 weeks earlier [5].

Although uncommon, acquisition and transient nasal carriage of SARS-CoV-2 in vaccinated individuals raise the question of their ability to subsequently transmit the virus, thereby contributing to residual transmissions in the community.

We herein report a documented case of SARS-CoV-2 (B.1.1.7; alpha variant) transmission from a BNT162b2-vaccinated adult to 1 contact case >30 days after a full vaccination scheme.

CASE REPORT

The index case (#P1) was a 42-year-old female HCW with no remarkable medical history. She had a negative serological assessment on June 2020 and received 2 doses of BNT162b2 on January 14 (batch number EJ6795) and February 10, 2021 (batch number EJ6789), respectively. Both vaccine doses were administered <6 hours after reconstitution.

On March 18, 2021 (36 days after the second dose), #P1 had a face-to-face contact at a 1.2-meter (4 feet) distance without a mask with 3 other individuals. All 4 participants spent around 3 hours in the same room, ventilated by opening 2 windows. They had no direct physical contact and did not share glasses or cutlery. #P1 was asymptomatic at the time of contact. Twenty-four hours later, she reported mild rhinorrhea and moderate asthenia, with no other symptoms. Anosmia appeared in the following 24 hours. Nasopharyngeal rapid antigen testing (Panbio COVID-19 Ag Rapid Test Device, Abbott) performed on March 21 (48 hours after symptom onset) was positive and confirmed the same day by reverse transcription PCR (RT-PCR; cycle threshold [Ct], 28; 106 000 copies of N gene RNA copies in the entire sample as measured by droplet digital PCR). She declared no contact with COVID-19 cases in the past 14 days. The source of acquisition remains unknown.

At the time of contact, #P2 and #P3 were fully vaccinated with BNT162b2. #P2 had received the second dose 28 days earlier and #P3, who had laboratory-confirmed COVID-19 on October 2020, received 1 dose 32 days before contact. Both #P2 and #P3 remained asymptomatic in the following weeks. #P2 had a negative antigen test on day 3 after contact. Both #P2 and #P3 had a negative RT-PCR test on day 8.

In contrast, #P4 declared headaches and fatigue 4 days after contact (the nasopharyngeal antigen test was negative on the same day) and tested positive by RT-PCR on day 8 (Ct, 21). #P4 received a single dose of ChAOx1 vaccine 8 days before the contact. Both the index case #P1 and the contact case #P4 fully recovered 2–3 days after symptom onset. The timeline of vaccination, exposure, and testing is summarized in Figure 1A. In-depth questioning did not identify any common contact shared by P1 and P4 within 1–2 weeks preceding D0: They live and work in different cities and do not work in the same professional sector as their respective household members.

Infectivity of #P1's Nasopharyngeal Sample

#P1's nasopharyngeal swab sampled on March 21 (3 days after contact and 2 days after symptom onset) was tested by S-Fuse assay as described [7]. This rapid culture test is based on U2OS-ACE2-TMPRSS2 GFP1-10 or GFP 11 cells, also termed S-Fuse-T cells, which become GFP+ when they are infected by SARS-CoV-2. The nasopharyngeal swab was added to the S-fuse cells at serial dilutions from 1:10 to 1:1 000 000. Eighteen hours later, cells were fixed with 2% PFA and stained with Hoechst (dilution 1:1000, Invitrogen). Images were acquired with an Opera Phenix high-content confocal microscope (PerkinElmer). The GFP area and the number of nuclei were quantified using Harmony (PerkinElmer). The viral titer (infectious units/mL) was calculated from the last positive dilution, with 1 infectious unit (IU) being 3 times the background (GFP area in noninfected controls). The viral titer was of 98 IU/mL (1.99 log IU/mL), confirming the infectiousness of the nasopharyngeal swab collected 2 days after symptom onset.

SARS-CoV-2 Whole-Genome Sequencing Evidencing Transmission Between #P1 and #P4

Full-length viral genomes were obtained by Illumina sequencing [8]. Multiple sequence alignment of DNA sequences was performed with Clustal Omega (version 1.2.2). Phylogenetic tree inference was based on the Neighbor-Joining method, and genetic distances were computed using the Tamura-Nei model [9]. SARS-CoV-2 MN908947.3 was used as the reference strain, and genomes were classified into lineages using Pangolin. The phylogenetic tree includes all the sequences (286 sequences including 198 B.1.1.7

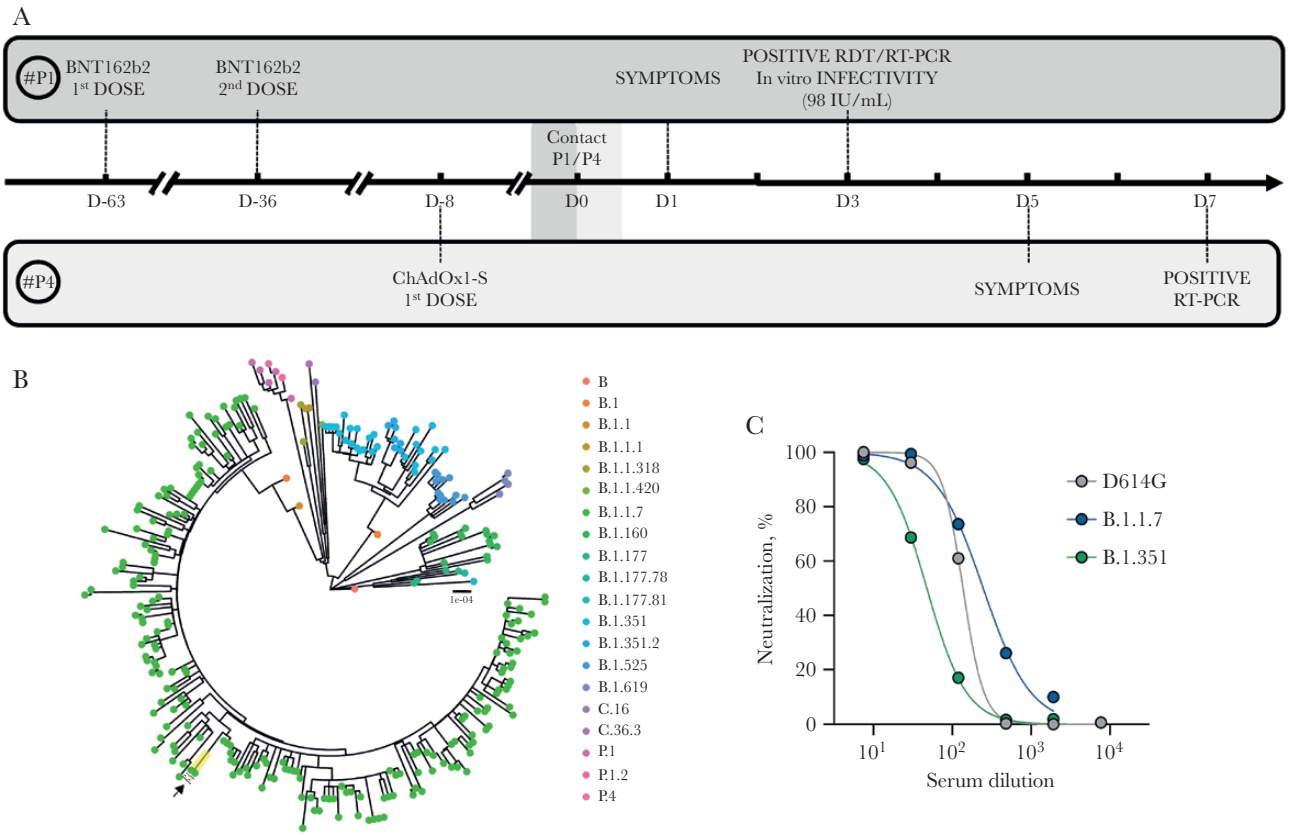

Figure 1. Evidence of transmission of B.1.1.7 (alpha variant) from BNT162b2-vaccinated #P1 to #P4. A, Timeline of vaccine injections, contact, and testing in #P1 and #P4. B, Phylogenetic tree including #P1 and #P4 B.1.1.7 identical sequences (black arrow) in a representative group of other circulating SARS-CoV-2 strains from the same geographical area (286 sequences including 198 B.1.1.7 sequences) at the time of #P1 and #P4 sampling. Genomes were classified into lineages using Pangolin. C, Neutralization curves with serum from #P1 at day 4 postcontact against the D614G (B.1), B.1.1.7 (alpha variant), and B.1.351 (beta variant) infectious viral variants. Abbreviations: RDT, rapid diagnostic test; RT-PCR, reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

sequences) generated by our laboratory between March 11 and April 22 that are available on GISAID (Supplementary Data). Sequences of the #P1 and #P4 strains showed 100% identity (Figure 1B).

#P1 Serum- and Nasopharyngeal-Specific Antibody Detection

#P1 serum was collected the day after the positive RT-PCR test (40 days after the second dose of vaccine and 4 days after the contact). #P1 was confirmed to be HIV negative, and the plasmatic protein electrophoresis was normal. Antinucleoprotein serology assessed using Abbott SARS-CoV-2 immunoglobulin (Ig) G assays (Des Plaines, IL, USA) was negative, while antispike serology assessed using Beckman Coulter Access SARS-CoV-2 IgG assays (Brea, CA, USA) was positive (index value, 7.9; positivity threshold, 1). SARS-CoV-2 antispike antibody detection in serum and in the nasopharyngeal sample was also performed using the S-Flow assay as recently described [10]. Serum was positive for both specific IgG and IgA (83% and 55% of positive cells, respectively), while the nasopharyngeal sample was weakly positive for IgG and negative for IgA (28% and 3%, respectively). Live virus neutralization assay against the 3 main circulating variants D614G (B.1), B.1.1.7, and B.1.351 (beta variant) was performed as recently described [11] to evaluate the effective neutralizing activity of #P1 serum (Figure 1C). The dilutions required to inhibit 50% of the infection (ED_{50}) were 137.2, 247.3, and 47.73 for the D614G (B.1), B.1.1.7, and B.1.351 variants, respectively. These results are in the range of data obtained from BNT162b2-vaccinated people with the same technique [11].

DISCUSSION

We herein reported the case of a healthy adult woman with laboratory-confirmed SARS-CoV-2 infection 36 days after receiving the second dose of the BNT162b2 vaccine, who transmitted the virus to another individual during a 3-hour face-to-face contact. This case is the first to describe a documented transmission of SARS-CoV-2 after a full vaccination scheme with BNT162b2.

The clinical context and virological findings strongly suggest transmission of the #P1 strain to #P4. Both patients had only 1 contact on March 18, and the timeline of symptom onset was consistent with known incubation times. Genome sequencing showed 100% identity between both strains, and #P1's nasopharyngeal sample was still infectious in vitro 3 days after contact. No other common source of infection of #P1 and #P4 could be found. Moreover, the phylogenetic tree shows that in our local area, on a large period of time surrounding the sampling of #P1 and #P4, we could not find any other sequence identical to the #P1 and #P4 sequences. This reinforces the idea that identity between the #P1 and #P4 sequences was not due to randomness.

In Israel, the SARS-CoV-2 RNA load in oro-nasopharyngeal swabs was substantially reduced for infections occurring 12–37 days after the first dose of BNT162b2 messenger RNA vaccine [12]. In Chicago, Illinois, 22 skilled nursing facility residents and staff members presented SARS-CoV-2 breakthrough infections despite being fully vaccinated. The median interval from last dose to positive test (interquartile range) was 29 (23–42) days [13]. Our observation confirms that SARS-CoV-2 infection can occur despite the presence of circulating neutralizing antibodies induced by vaccination. #P1 serum could not be tested for neutralizing activity before infection, but 2 days after symptoms onset. Anti-N antibodies were negative at that time point. Therefore, the neutralizing activity observed here could only be due to BNT162b2 vaccination, although a rapid anamnestic anti-S response soon after the infection cannot be formally excluded. Despite the absence of correlates of protection, Khoury et al. recently estimated the neutralization level for 50% protection against detectable SARS-CoV-2 infection to be 20.2% of the mean convalescent level [14]. #P1's neutralization titer was around 13% of the mean convalescent titer of our convalescent cohort [15]. This low titer was not sufficient to prevent infection or transmission. This case further suggests that, at least in some individuals, vaccination does not provide sufficient immunity to prevent nasopharyngeal shedding of SARS-CoV-2, allowing consequently for viral transmission. Illustration of significant upper respiratory tract infectivity despite vaccination in some immunocompetent individuals, although rare, mitigates the putative effect of BNT162b2 vaccine on transmission. The transmission described here occurred with the B.1.1.7 SARS-CoV-2 variant, against which neutralizing antibody response after vaccination was shown to be comparable to the vaccine strain [11]. Whether other variants, such as B.1.351 (beta variant), against which vaccine-induced antibody neutralization is weaker, would be more transmitted from vaccinated individuals will deserve investigation.

Overall, this case confirms that in the event of SARS-CoV-2 infection in a fully vaccinated individual, the risk of virus transmission to nonimmunized persons persists. Nevertheless, the reduction in transmission from vaccination will be the product of the reduction in infections seen after vaccination and any reduction in relative infectiousness in those who are vaccinated. Our work underscores the critical importance of continued public health mitigation measures (masking, physical distancing, daily symptom screening, and regular testing, even in vaccinated individuals with mild symptoms), in both vaccinated and unvaccinated individuals, until herd immunity is reached at large.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases online*. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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Patient consent. The patients' written consent was obtained. The design of the work was approved by the local ethical committee (institutional review board registration #00011928).

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