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Case Report

A case report of breakthrough infection with the SARS-CoV-2 delta variant and household transmission: Role of vaccination, anti-spike IgG and neutralizing activity

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ABSTRACT

There have been several reports of breakthrough infections, which are defined as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections among individuals who had received at least two doses of vaccine at least 14 days before the onset of infection, but data on the antibody titers, including SARS-CoV-2 neutralizing antibody activity, and the clinical course of individuals with breakthrough infections are limited. We encountered a case of breakthrough infection with the SARS-CoV-2 delta variant in a 31-year-old female healthcare worker (the index case, Case 1) and a secondary case (Case 2) in her unvaccinated 33-year-old husband. We studied the role of the anti-spike immunoglobulin G (IgG) and neutralizing antibody activity in the two case patients. Case 1 had high anti-spike IgG detected on day 3 of the illness, with low neutralizing antibody activity. The neutralizing antibody activity started to increase on day 5 of the illness. In Case 2 both the anti-spike IgG and the neutralizing antibody activity remained low from days 4–11 of illness, and the anti-spike IgG gradually increased from day 9. In Case 1, the fever broke within 4 days of onset, coinciding with the rise in neutralizing antibodies, whereas the fever took 7 days to resolve in Case 2. SARS-CoV-2 infection can occur even in vaccinated individuals, but vaccination may contribute to milder clinical symptoms because neutralizing antibodies are induced earlier in vaccinated individuals than in unvaccinated individuals.

1. Introduction

Since the initial reports of coronavirus disease 2019 (COVID-19) from Wuhan, China in December 2019, COVID-19 has become pandemic. In Japan, between the first case of COVID-19 diagnosed in January 2020 and November 19, 2021, 1.7 million cases, including 1,800 deaths, were reported [1–3].

Several variants of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of COVID-19, have emerged, and as of November 2021, the delta variant has become the predominant variant in many countries, including Japan [2]. The delta variant is reported to be more transmissible and some reports suggest that the delta variant causes more severe disease than the wild-type and alpha variant [4,5]. Vaccination is expected to play an important role in controlling the COVID-19 pandemic, and the rollout began in February 2021 in Japan. Messenger RNA vaccines has been found to be highly effective at preventing asymptomatic SARS-CoV-2 infection, symptomatic infection, and severe COVID-19 [6]. Although breakthrough

Abbreviations: COVID-19, coronavirus disease 2019; IgG, immunoglobulin G; PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SpO2, peripheral oxygen saturation; TCID50, median tissue culture infectious dose.

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infections, which are defined as SARS-CoV-2 infections occurring at least 2 weeks after an individual has been fully vaccinated [7], have been reported [8], there are limited data on the antibody response, including the anti-SARS-CoV-2 neutralizing antibody activity, and the clinical course in individuals with breakthrough infections.

Here, we report a case of breakthrough infection with the SARS-CoV-2 delta variant, and a secondary case in a family member (in which the index case was fully vaccinated and the secondary case had not been vaccinated) with the clinical role of the anti-spike immunoglobulin G (IgG) and neutralizing antibody activity.

2. Case report

2.1. Case 1

A 31-year-old healthy female healthcare worker (physician, not involved in the treatment of COVID-19) presented to our hospital with a three-day history of fever, nasal discharge, and cough, complaining of malaise and breathing difficulty. She had received two doses of BNT162b2 mRNA COVID-19 vaccine (Pfizer-BioNTech), administered 109 days and 88 days before the onset of her symptoms. Her body temperature was 36.9°C, her respiratory rate was 18/minutes, and her peripheral oxygen saturation (SpO2) was 99% breathing room air. Blood tests revealed increased C-reactive protein (4.4 mg/dL), but no other abnormalities were found. She did not have any signs of pneumonia on chest radiography. A nucleic acid amplification test (ID Now SARS-CoV-2, Abbott, Chicago, IL, USA; ID now) revealed that she had breakthrough SARS-CoV-2 infection. She was admitted due to fatigue and fever but did not require supplemental oxygen. Her fever subsided on the fourth day of the illness, and she was discharged on the tenth day of the illness.

2.2. Case 2

Because Case 1 was diagnosed with COVID-19, her close contacts, including her husband, were tested for SARS-CoV-2. All 17 close contacts were asymptomatic, and had negative polymerase chain reaction (PCR) results on the initial test. However, on the fifth day after the onset of Case 1, her husband, a healthy 33-year-old male who had not been vaccinated, developed fever, and a PCR test performed the next day was positive. He was admitted to our hospital because of fever and fatigue. On the day of admission (day 2 after onset), his body temperature was 39.0°C, his respiratory rate was 20/minutes, and his SpO2 was 97% breathing room air. Blood tests revealed no abnormalities. Although he did not have pneumonia on lung computed tomography scan, his body temperature remained over 38.0°C, he had persistent cough, and his SpO2 decreased to 95% after admission. He was treated with remdesivir, starting 5 days after the onset. His fever subsided 7 days after the onset, he did not need any oxygen, and he was discharged from hospital 11 days after the onset.

2.3. Analysis of the virus genome and anti-spike IgG antibody and neutralizing antibody activity

Whole genome analysis of SARS-CoV-2 was conducted using nasopharyngeal swabs from both patients. Both patients were infected with a virus with an L452R spike mutation. Whole genome sequencing revealed that the virus belonged to the AV.29 sub-lineage of the Delta variant (EPI_ISL_3876359 and EPI_ISL_3881409). Both isolates had the identical sequence without any single nucleotide polymorphisms. Quantitative PCR performed on a nasopharyngeal swab collected from Case 1 on day 4 of her illness, showed a quantification cycle (Cq) value of 24.4 and live virus was isolated from the swab (median tissue culture infectious dose [TCID50], 316/mL).

The anti-spike IgG and neutralizing antibody activity against SARS-CoV-2 were evaluated using serum from both patients [9]. In Case 1, a high anti-spike IgG titer was detected on day 3 of the illness, but the neutralizing antibody activity was low. An increase in neutralizing antibody activity was detected on day 5 of the illness. In Case 2, both the anti-spike IgG and the neutralizing antibody activity remained low from days 4–11 of the illness, and the anti-spike IgG showed a slight increase from day 9 (Fig. 1).

3. Discussion

The two case patients were infected with the same SARS-CoV-2 delta variant. Case 1, the index case, was fully vaccinated and Case 2, a secondary case was unvaccinated.

This report has two important clinical findings. First, Case 1 experienced a rise in neutralizing antibodies sooner after the onset of illness than Case 2, although Case 1 did not have sufficient neutralizing antibodies to prevent symptoms in the early phase of infection. In Case 2, the level of both anti-spike IgG and neutralizing antibody activity remained low from days 4–11 of the illness. Although the BNT162b2 vaccine is highly effective at preventing SARS-CoV-2 infection, disease, and severe disease [6], it is thought to be less effective at preventing infection with the delta variant than at preventing infection with the wild-type and alpha variant of SARS-CoV-2 [10,11]. However, fully vaccinated individuals infected with the delta variant, have been reported to develop less severe disease than individuals who have not been vaccinated [12], while infections with the delta variant have been reported to be associated with more severe disease [5].

To our knowledge, there have been no previous reports comparing the changes in antibody titers, including neutralizing antibody activity and the clinical course, between vaccinated and unvaccinated individuals infected with the same virus. The novelty of this report is that we evaluated the antibody titers of the both vaccinated and unvaccinated infected individuals infected with the same virus. The results showed that, although Case 1 was fully vaccinated, she had almost no neutralizing antibodies by day 3 and began to produce neutralizing antibodies by day 5. The clinical course of Case 1 improved with the rise in the neutralizing antibody titer. It should be noted that although in Case 1, the fever broke within 4 days of onset, while it took 7 days for the fever to resolve in Case 2.

Second, Case 1 may have shed the delta variant of SARS-CoV-2 and transmitted it to Case 2. It has been reported that fully vaccinated individuals infected with the delta variant sometimes have low Ct values when infected, but are less likely to have a positive viral culture and are less likely to transmit the disease to others [13]. Although a previous report suggested that individuals with breakthrough infections were less likely than unvaccinated individuals to be a source of secondary infections [14], the results of whole genome analysis of SARS-CoV-2 revealed that both cases were infected with the same SARS-CoV-2 delta variant.

There are several limitations to our study. First, although we determined that the two cases were infected with the same virus, we cannot be sure that the virus was transmitted from Case 1 to Case 2. There is a possibility that both were infected at the same time from the same source. However, the fact that Case 2 developed the disease 5 days later than Case 1 suggests that the infection was transmitted from Case 1 to Case 2. The fact that live virus was detected in Case 1 also supports the possibility that the virus was transmitted from Case 1 to Case 2. Next, antibody titers were only observed for a short period, and long-term trends could not be evaluated. However, in Case 1, the increase in neutralizing antibody activity on day 5 coincided with an improvement in the patient’s clinical condition, and we assume that the neutralizing antibody activity continued to increase after the end of the monitoring period. Even after a short period of observation, the results are consistent with the hypothesis that vaccinated individuals may have a faster increase in antibody titer and neutralizing antibody activity than non-vaccinated individuals. However, due to the limited data in this case report, further large-scale studies are needed to confirm this hypothesis.

In conclusion, the index patient experienced a breakthrough
infection and the secondary case was infected with the SARS-CoV-2 delta variant. The index case was fully vaccinated and the secondary case had not been vaccinated. These two cases illustrate the role of the anti-spike IgG and neutralizing antibody activity. SARS-CoV-2 infection can occur even in vaccinated individuals, but vaccination may contribute to milder clinical symptoms because neutralizing antibodies are induced earlier in vaccinated individuals than in unvaccinated individuals.

Authorship statement

YM was in charge of the treatment of the cases as the clinical infectious disease physician, and wrote the manuscript. MI reviewed the manuscript. MU, AM, and YI performed the testing of antibody titers and serum SARS-CoV-2 neutralizing antibody activity and wrote the manuscript. TA, TK, and TS conducted the SARS-CoV-2 assays, analyzed the data, and wrote the manuscript. KK played a central role in writing the discussion section. All authors meet the ICMJE authorship criteria.

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Informed consent

Written informed consent for publication of the paper was obtained from both case patients.

Declaration of competing interest

The authors declare no conflicts of interest.

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