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Case report

Trajectory of SARS-CoV-2 anti-S IgG levels following transfusion and a third dose of BNT162b2 vaccine in a patient with massive postoperative bleeding: A case report

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ABSTRACT

Objective: Vaccination against SARS-CoV-2 has been shown to be effective in preventing infection and severe disease. Massive bleeding and transfusion after vaccination can lead to a decrease in the antibody level. The effect of an additional dose of vaccine after blood transfusion has not been described previously. In this case report, we report the SARS-CoV-2 anti-S IgG trajectory in a male patient who received a third dose of vaccine after a massive postoperative bleed and blood and plasma transfusion.

Case presentation: A 57-year-old male physician had a SARS-CoV-2 anti-S IgG level of 44 AU/mL, measured using the Lumipulse Presto chemiluminescence assay 3 months after receiving 2 doses of the BNT162b2 vaccine. The patient underwent a hemicolectomy for colon cancer, experienced massive postoperative bleeding, and required a transfusion. The patient's SARS-CoV-2 anti-S IgG level dropped to 9.2 AU/mL. A third dose of BNT162b2 vaccination was administered to reduce the risk of breakthrough infection. Fifteen days after receiving the third vaccine dose, the patient's SARS-CoV-2 anti-S IgG level increased to 421 AU/mL, likely to reflect protection.

Conclusion: This report suggests that administering an extra dose of vaccine is useful for restoring protective antibody levels in vaccinated patients who experience massive postoperative bleeding.

Introduction

Vaccination against SARS-CoV-2 with 2 doses of the BNT162b2 (Pfizer-BioNTech) messenger RNA (mRNA) vaccine has been reported to produce neutralizing antibodies and be highly effective in preventing the disease (Dagan et al., 2021; Walsh et al., 2020). However, neutralizing antibodies decrease within 6 months, which may make vaccinated patients and health care workers susceptible to nosocomial SARS-CoV-2 infection (Levin et al., 2021; Naaber et al., 2021; Tartof et al., 2021). A third dose has been shown to increase neutralizing antibodies to a protective level (Bar-On et al., 2021; Pfizer, 2021).

The neutralizing antibody level directly determines the functional capacity of the immune response. However, because of the complex procedure, it is not suitable for routine use. Measuring IgG antibody to spike surface protein has been investigated as an alternative method of assessing immune response to SARS-CoV-2 vaccination. Although it is unclear whether the IgG antibody level is correlated with protection against infection and reducing disease severity, the levels are significantly correlated with neutralizing antibody levels (Michos et al., 2021; Salvagno et al., 2021). To the best of our knowledge, there have been no previous reports of changes in antibody levels because of bleeding in patients after SARS-CoV-2 vaccination with BNT162b2 and other vaccinations.

In this report, we describe changes in serum SARS-CoV-2 anti-S IgG levels in a male patient who received 2 doses of BNT162b2 vaccine and was given a third dose after experiencing massive postoperative bleeding.

Case Report

A 57-year-old Japanese male physician was admitted for transverse colon cancer surgery. The patient was taking amlodipine, pemafibrate, and rosuvastatin for hypertension and dyslipidemia. Four months before admission, the patient had received a second dose of the BNT162b2 vaccine. One month before admission, a colonoscopy revealed an adenocarcinoma in the transverse colon. Five days before admission, the polymerase chain reaction test was negative for SARS-CoV-2. The patient had not reported any

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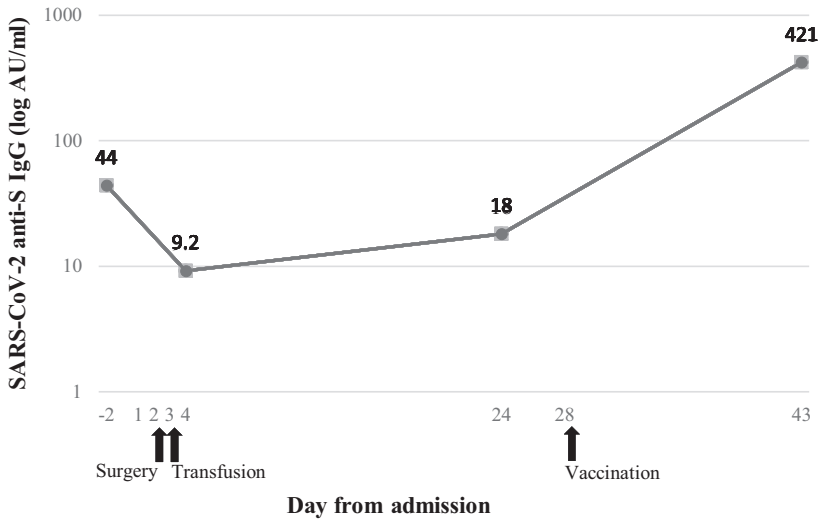

Figure 1. Trajectory of SARS-CoV-2 anti-S IgG levels in the case patient.
SARS-CoV-2 anti-S IgG levels were measured using the Lumipulse Presto chemiluminescence assay. The patient underwent surgery 2 days after admission and received 9 units of red blood cells and 10 units of fresh frozen plasma for massive postoperative bleeding 3 days after admission. The SARS-CoV-2 anti-S IgG levels decreased from 44 AU/mL before admission to 9.2 AU/mL after the transfusion. The patient received the third dose of BNT162b2 vaccine 28 days after admission, and the levels of SARS-CoV-2 anti-S IgG increased to 421 AU/mL 15 days later.
anti-S = anti-spike; AU = arbitrary unit; IgG = immunoglobin G; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

COVID-19 symptoms such as anosmia, dysgeusia/ageusia, anorexia, headache, fever, and fatigue.

On hospital day 2, the patient underwent laparoscopy-assisted left hemicolectomy and D2 lymph node dissection. The next day, the patient developed abdominal pain and vomiting and experienced a drop in hemoglobin level. Contrast-enhanced computed tomography showed active bleeding from the left gastroduodenal artery, and bloody ascites; emergency laparotomy was performed and the left gastroduodenal artery was ligated. The total blood loss was 4,185 mL. The patient required 9 units of red blood cells and 10 units of fresh frozen plasma transfusion. On hospital day 12, the patient was discharged without any further complications.

The patient's SARS-CoV-2 anti-S IgG levels were monitored using a commercial quantitative chemiluminescence immunoassay (Lumipulse Presto, Fujirebio, Japan). The cutoff level for a positive result was 1.0 AU/mL.

The patient's SARS-CoV-2 anti-S IgG level 2 days before admission was 44 AU/mL and decreased to 9.2 AU/mL 4 days after admission, after massive postoperative bleeding. The SARS-CoV-2 anti-S IgG level remained low (18 AU/mL) 24 days after admission (Figure 1). Being a health care worker, the patient was at high risk of exposure to SARS-CoV-2 infection. A third dose had not yet been approved in Japan at the time. The patient provided written informed consent and was administered the vaccine 16 days after discharge. The patient's SARS-CoV-2 anti-S IgG level 15 days later was 421 AU/mL.

Discussion

This case demonstrated a rapid, sharp decline in the SARS-CoV-2 anti-S IgG level after massive postoperative bleeding, which increased after the administration of a third dose of the BNT162b2 vaccine. The blood used for transfusion in this patient is thought to have been donated approximately 1 month before the transfusion. SARS-CoV-2 vaccination within the month before surgery is recommended for health care workers and individuals older than 65 years. At the time the patient received the blood transfusion, the 2-dose vaccination rate for those younger than 65 years and those aged 65 years and older was 6.5% and 39.5%, respectively (Ministry of Health, Labour and Welfare, 2021). The number of antibodies against SARS-CoV-2 in the fresh frozen plasma transfusion is thus likely to have been low.

The BNT162b2 vaccine has been reported to induce sustained germinal center B-cell response, with the generation of SARS-CoV-2 S-specific neutralizing antibodies and cellular immunity of both CD4+ and CD8+ T cells after 2 doses of vaccine (Turner et al., 2021: Sahin et al., 2021). Even if the antibody level decreases over time, antibodies are likely to rapidly generate upon re-exposure (Bar-On et al., 2021; Pfizer, 2021). This patient experienced a mild increase in antibody level in the natural course of recovery, but the titer had previously been low. It has been reported that a low serum antibody level may increase the risk of breakthrough infection (Bergwerk et al., 2021), and therefore, it is desirable to maintain a moderate serum antibody level in individuals at high risk of infection, such as health care workers.

A third dose of vaccination has been initiated in some countries to boost serum antibody levels. According to the Pfizer report (2021), a third dose elicits neutralizing titers against the Delta variant that are more than 5 times and 11 times higher among individuals aged 18 to 55 years and 65 to 85 years, respectively, than after 2 doses of vaccine.

The IgG (spike protein receptor-binding domain) titer, measured using the Abbott Architect SARS-CoV-2 IgG Quant II assay (Abbott, Sligo, Ireland), was determined to have a threshold of 4,160 AU/mL for protection (Ebinger et al., 2021). The Lumipulse Presto SARS-CoV-2-IgG-S assay used in this study has been compared with the Abbott Architect SARS-CoV-2 IgG Quant II assay in 100 Japanese health care workers (n = 100), and the correlation has been examined (Hibino et al., 2021). Blood samples were collected 3 times from all 100 participants after they had received both doses of the vaccine. The concordance results in all 300 samples before and after vaccination was 99.7% (299 of 300, 95% confidence interval [CI]: 98.1%-99.9%), and the kappa coefficient was 0.99 (95% CI: 0.98-1.00). The Pearson's correlation coefficient was 0.963 (95% CI: 0.954-0.970, $P < .001$). According to the manufacturer's report, the neutralizing capacity threshold of 4,160 AU/mL for the Abbott Architect SARS-CoV-2 IgG Quant II assay was estimated to be equivalent to 72 AU/mL measured by the Lumipulse Presto SARS-CoV-2-IgG-S assay. In this patient, the SARS-CoV-2-IgG-S level on the 16th day after the third vaccination was 422 AU/mL, which was

well above the threshold of 72 AU/mL, indicating an adequate antibody level. Because the recovery in the antibody titer after massive bleeding is only slight in the natural course, patients may be susceptible to SARS-CoV-2 infection after massive bleeding. Additional vaccination may be necessary for health care workers, such as this patient, and for older adults and immunocompromised individuals with weak immune responses.

This study evaluated only 1 case, and therefore, it is desirable to accumulate further reports of similar cases and to conduct further research on antibody titers in the natural course of recovery after a massive postoperative bleed.

Conclusion

A 57-year-old male physician who had received 2 doses of BNT162b2 experienced a sharp decrease in SARS-CoV-2 anti-S IgG level after massive postoperative bleeding. A third dose of BNT162b2 vaccine was administered because the low antibody level indicated that the patient was at risk of breakthrough infection. After receiving the third dose of BNT162b2 vaccine, the patient's SARS-CoV-2 anti-S IgG titer increased to a level likely to reflect protection.

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Authors' contributions

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Ethical approval statement

Ethical approval by the institutional review board of Saitama Medical Center, Jichi Medical University, was not required in the authors' institution for this case report. The patient provided written informed consent for publication.

Consent for publication

The patient provided written informed consent for publication.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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