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CASE REPORT

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Progression of hemolysis in a patient with hereditary spherocytosis after the second dose of COVID-19 mRNA vaccine

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ABSTRACT

Herein, we report the case of a 22-year-old woman with hereditary spherocytosis (HS) whose condition worsened after administration of the coronavirus disease 2019 (COVID-19), mRNA vaccine 'BNT162b2 Pfizer-BioNTech.' The woman had been diagnosed with HS in 2005, and her condition remained stable until February 2021. In March 2021, she received the first dose of the above vaccine and experienced pain at the injection site. After the second dose in April 2021, she developed fever and general malaise. Investigations revealed progression of hemolysis, which improved after a few days. To the best of our knowledge, this is the first report of progression of hemolysis in a patient with HS after administration of the mRNA vaccine COVID-19, BNT162b2 'Pfizer-BioNTech.'

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Introduction

Recently, vaccine-induced exacerbation of hematological diseases, especially idiopathic thrombocytopenic purpura, has been reported.[1–3] Such adverse effects of vaccination may occur secondary to a pathophysiology termed autoimmune/inflammatory syndrome induced by adjuvants contained in vaccines. Moreover, B-cell hyperfunction and increased activation of immune cells can cause adverse reactions to vaccines. Several vaccines have recently been introduced to control the spread of coronavirus disease 2019 (COVID-19). However, adverse effects of these vaccines have also been reported.

The pharmacokinetics of the vaccine after muscle injection can be summarized as follows.[4] Upon administration of the vaccine, dendritic cells (DCs) invade the lymph nodes, where they take up the mRNA and produce high levels of S protein of SARS-CoV-2 and present it to the T cells. Consequently, naïve T cells are stimulated, and finally B cells are activated to promote antibody production. During this process, the DCs also release inflammatory cytokines, such as type I interferons; it is suggested that this process induces fever. Two inoculations of the vaccine are typically administered with the aim of boosting immunity against the virus. However, many known adverse effects can occur after the second dose.[4]

Hereditary spherocytosis (HS) is a familial non-autoimmune hemolytic disorder. There are few reports on worsening of HS after SARS-CoV-2 infection.[5] Here, we report a case of a woman with HS who experienced progression of hemolysis after vaccination with the BNT162b2 'Pfizer-BioNTech' mRNA vaccine.

Patient presentation

A 22-year-old woman came to us with a chief complaint of general malaise. She was diagnosed with HS after parvovirus B19 infection in 2005 in the pediatric department of another hospital (not described). Blood transfusions had also been performed during that time. Her family history indicated that her father, older brother, and younger sister had also been diagnosed with HS. On March 26, 2021, she received the first dose of mRNA vaccine BNT162b2 'Pfizer-BioNTech,' after which the only adverse effect noted was pain at the injection site. Three weeks later, on April 16, she received the second dose of the vaccine at 11:30 a.m. The following day, she took acetaminophen at 1:30 a.m. because she had developed fever (37.6°C), generalized pain, headache, and general malaise. The fever increased to 38.6°C because the acetaminophen had no antipyretic effect; thus, she took the same antipyretic again that night. On April 18 (day 3 after vaccination), her temperature dropped to 37°C, and she took the same antipyretic again because it had no antipyretic effect. On April 19 (day 4), the general malaise was still present. On April 20, 2021 (first visit), the patient was taken to the hospital emergency department because of the malaise. By this time, the severity of her headache had decreased and her body temperature was normal. Blood work revealed a high bilirubin level and anemia.

Until hospitalization after vaccination, there was no progression of anemia outside the Hb 8.0 range.

Since the patient had already been diagnosed with HS, we rechecked her spherocyte count in peripheral blood specimens (Figure 1). Therefore, the patient was admitted to the hospital

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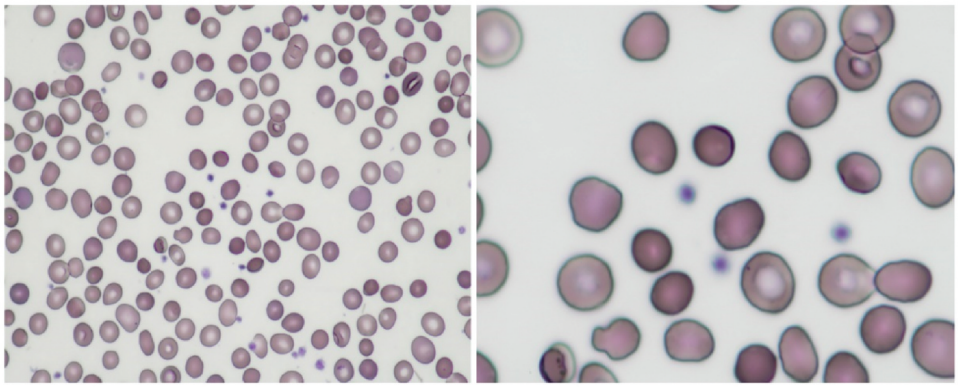

Figure 1. Hospitalization examination findings (2021). Confirmation of peripheral blood specimen; spherocytes.

for treatment on the same day (Figure 2) after informed consent was obtained.

The patient's laboratory values on admission were as follows: White blood cell count, 11,000/μL; red blood cell count, 188×10^4/μL; hemoglobin, 6.7 g/dL; hematocrit, 19.4%; platelet count, 26.6×10^4/μL; C-reactive protein, 0.29 mg/dL; total bilirubin, 5.60 mg/dL; direct bilirubin, 2.07 mg/dL; aspartate aminotransferase, 18 U/L; alanine aminotransferase, 8 U/L; lactate dehydrogenase, 384 U/L; alkaline phosphatase, 48 U/L; gamma-glutamyl transpeptidase, 9 U/L; creatinine, 0.53 g/dL; haptoglobin, <10 mg/dL; and presence of hemolysis. Because her hemoglobin level was 8.0 g/dL in February 2021, we diagnosed advanced hemolysis. The main infectious findings were as follows: Influenza virus, negative; COVID-19 (polymerase chain reaction), negative; IgG positive for parvovirus B19, IgG positive and IgM false positive; and parvovirus DNA, negative.

The final diagnosis was hemolysis progression following the mRNA vaccine BNT162b2 'Pfizer-BioNTech.' We diagnosed the progression of anemia because the test performed in February of the same year showed an Hb value of 8.3 g/dL. The requirement for approval was waived by the Ethics Committee.

Discussion

Influenza vaccines have been reported to exacerbate idiopathic thrombocytopenic purpura, a hematological disorder. A recent report described an exacerbation of paroxysmal nocturnal hemoglobinemia caused by the mRNA BNT162b2 'Pfizer-BioNTech'vaccine.[6] In patients with paroxysmal nocturnal hemoglobinemia, activation of the complement system as part of the inflammatory reaction may lead to deterioration of the patient's condition.[6] The same vaccines have also been known to exacerbate aplastic anemia.[7] Both of these studies suggest the involvement of immune mechanisms such as autoimmunity following vaccine adjuvants and hyperactivity of B cells.[6,7] Additionally, one case report described

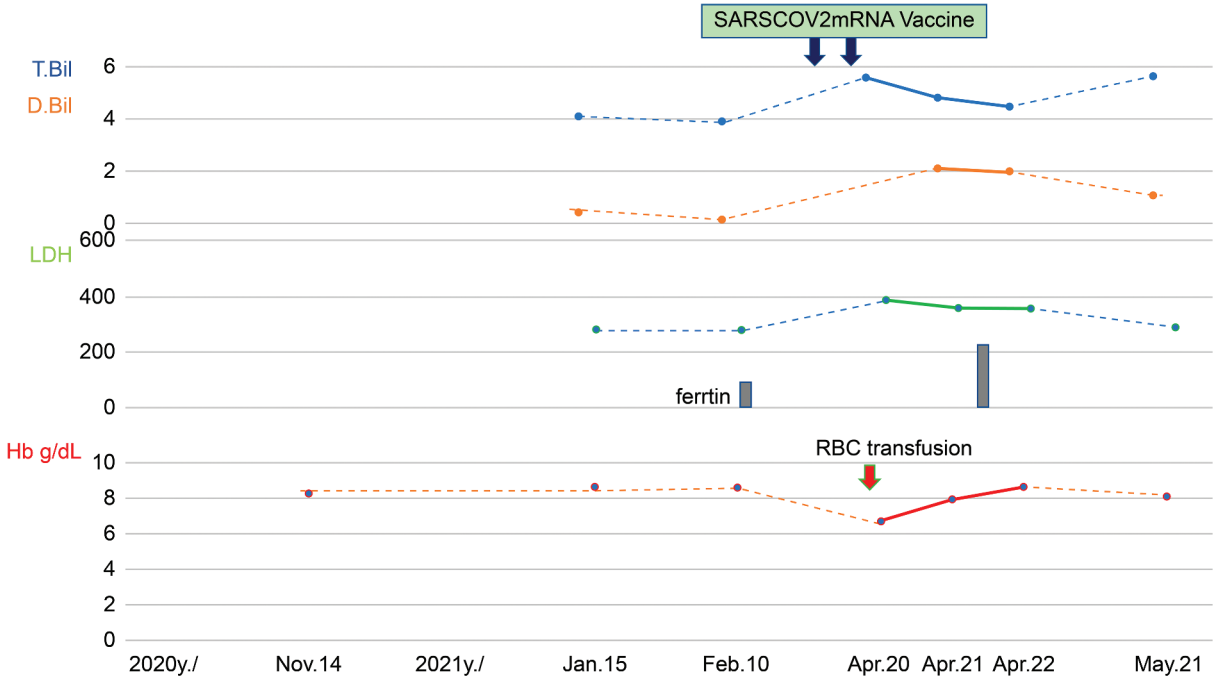

Figure 2. After COVID-19 vaccination.

a hemolytic crisis in a patient with HS that was due to infection with SARS-CoV-2.[5] Stressors such as fever and hypoxia were thought to trigger the hemolytic crisis. The mRNA BNT162b2 'Pfizer-BioNTech' vaccine administered to our patient did not contain adjuvants, and HS is a non-autoimmune disease.

Here, we suspected that the progression of hemolysis was related to inflammatory cytokines rather than to the pharmacokinetics of the vaccine. Inflammatory cytokines released by DCs in the body after vaccine injection create an environment similar to that of infection.[4,5,7] Therefore, we speculate that in our patient, HS cells vulnerable to osmosis were destroyed by hemolysis due to fever-induced changes in osmotic pressure.

At HS, hemolytic crisis due to SARS-CoV-2 infection has been reported, but not hemolysis after vaccination.

Moreover, we speculate that acetaminophen ingestion may have contributed to the initiation of hemolysis, although we found no literature supporting this hypothesis.

We also considered the possibility of drug-induced hemolysis, particularly hemolysis induced by acetaminophen. We conducted a literature search and found one case report of acetaminophen-induced hemolysis in an individual with glucose - 6 - phosphate dehydrogenase deficiency;[8] no study has reported the association between acetaminophen and hemolysis in individuals with HS. Therefore, the hemolysis in this case may have been caused by the vaccine.

Conclusion

We encountered a case of HS in which hemolysis progressed after administration of the second COVID-19 mRNA vaccine 'BNT162b2 Pfizer-BioNTech.' This is the first report of progression from HS after vaccination.

In conclusion, our report suggests that careful observation is necessary during the mRNA vaccine BNT162b2 'Pfizer-BioNTech' administration in patients with HS, especially after the second vaccination.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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