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Prolonged Diarrhea Following COVID-19 Vaccination: A Case Report and Literature Review

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Vaccination against coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is currently underway across countries worldwide. However, the prevalence and characteristics of prolonged adverse events lasting for several months after receiving the vaccine remain largely unknown. We herein report a 46-year-old woman with prolonged diarrhea and vomiting after receiving the BNT162b2 mRNA vaccine for COVID-19. She had no notable medical history, including that of gastrointestinal diseases. She developed vomiting several hours after receiving the first vaccine dose and further developed severe diarrhea after 7 days. Several days after the second vaccine dose, her condition deteriorated, unrelieved by symptomatic therapies, including anti-diarrheal drugs. Abdominal computed tomography (CT) revealed inflammatory changes in the entire segment of the small intestine with wall thickening. The upper and lower gastrointestinal and capsule endoscopies were unremarkable. The patient's symptoms persisted for more than 6 months after the second vaccine dose. A Vaccine Adverse Event Reporting System (VAERS) database search suggested that diarrhea is observed in approximately 3% of all vaccine recipients, but a literature review indicated that prolonged gastrointestinal symptoms lasting for several months is very rare. In summary, a case of prolonged unexplained gastrointestinal symptoms, possibly based on inflammatory changes in the small intestine, is described. A literature search revealed that this type of manifestation is very rare, and further evidence is needed to determine the causality between vaccination and gastrointestinal symptoms.

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Introduction

Vaccinations against coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), are currently ongoing worldwide. As of April 2022, more than 10 billion vaccine doses have been administered globally (World Health Organization 2022). Messenger RNA (mRNA) vaccines against COVID-19, including Pfizer/BioNTech mRNA BNT162b2 vaccine encoding receptor-binding domain of the spike protein or Moderna mRNA-1273 vaccine encoding SARS-CoV-2 full-length spike glycoprotein trimer antigen (S-2P), are the major type of vaccines being used in Japan since 2021 (Anderson et al. 2020), and more than 80% of Japanese citizens have received at least two doses of COVID-19 vaccines by the end of April 2022 (Prime Minister's Office of Japan 2022). Until now, COVID-19 vaccines have been found to be > 50% effective for all emerging SARS-CoV-2 variants, such as B.1.1.7 Alpha, B.1.617.2 Delta, and B.1.1.529 Omicron (Chemaitelly et al. 2021; Lopez Bernal et al. 2021; Akaishi et al. 2022; Andrews et al. 2022). Accumulated data indicate that common systemic adverse events of COVID-19 vaccines, such as fever, chills and fatigability, are self-remitting and usually resolve spontaneously within several days (Polack et al. 2020); however, a small number of COVID-19 vaccine

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recipients suffer from prolonged physical symptoms (Centers for Disease Control and Prevention, USA 2022). Because the causal relationship between vaccines and prolonged physical symptoms is difficult to objectively prove and is usually backed by circumstantial evidence, such as temporal consistency between the two phenomena (World Health Organization 2018), the rates and characteristics of vaccinees with prolonged physical symptoms remain uncertain. Here, we report a female patient with persistent vomiting and diarrhea for > 6 months, without any other symptoms, after receiving the first two doses of the BNT162b2 mRNA vaccine. Through literature review, we further highlight the common and different characteristics of the present case compared to previously reported cases with prolonged physical symptoms after vaccination.

Case Presentation

A 46-year-old woman with no notable medical history developed repeated vomiting approximately four hours after receiving the first BNT162b2 mRNA COVID-19 vaccine. After 2 days, she felt pain at the injection site, which resolved within several days. Seven days after the first vaccination, she further developed 3-5 loose-to-liquid stools per day, which corresponded to type 6 on the Bristol Stool Form (BSF) Scale (Lewis and Heaton 1997). Before vaccination, she had no significant gastrointestinal (GI) problems and had a normal bowel pattern and stool formation. Two weeks after the first vaccine dose, intermittent paraumbilical pain developed with associated loss of appetite. Although the patient was anxious about receiving the second vaccine dose, she decided to receive the second dose 21 days after the first dose. After 7 days, vomiting and diarrhea progressed, with 7-10 watery stools per day (BSF type 7). The symptoms did not alleviate with time, and she gradually felt difficulty in oral intake. Two weeks after the second vaccine dose, she visited a nearby hospital because of frequent watery diarrhea and fecal incontinence, and was prescribed 5-mg oxethazaine (Strocain) tablets to take thrice daily, 1.0-g natural aluminum silicate (Adosorbin) tablets to take thrice daily, and 20-mg *Clostridium butyricum* 588 strain (CBM 588) MIYA-BM tablets to take thrice daily. However, these medications were ineffective in alleviating the symptoms. Blood tests performed in another hospital 4 weeks after the second dose revealed normal levels of total and differential white blood cell (WBC) counts and serum C-reactive protein (CRP), slightly elevated D-dimer serum level (1.1 μg/mL), and slightly elevated serum C1 esterase inactivator activity. SARS-CoV-2 rapid antigen test was negative. Eight weeks after the second dose, the patient visited our hospital with prolonged abdominal pain, vomiting, and diarrhea. Throughout her clinical course, she did not have fever or extreme fatigue. She did not drink alcohol but had smoked 5-10 cigarettes per day from the age of 20 years. She had no relevant medical history, including allergic or digestive diseases. Regarding family history, her father had died in his 30s because of bone and soft-tissue sarcoma. Her mother had rheumatoid arthritis but was still alive and well.

The patient's vital signs during her first visit to our hospital were as follows: body temperature, 36.7°C; blood pressure, 110/64 mmHg; and heart rate, 76 bpm. Her body mass index was 20.3 kg/m^2. Her abdomen was soft and flat, and bowel sounds were normal or slightly increased. The blood test results were as follows: total WBC count, 7,400/μL; hemoglobin, 14.0 g/dL; CRP level, 0.01 mg/dL; total protein level, 7.6 g/dL; albumin level, 4.7 g/dL; sodium level, 138 mmol/L; potassium level, 4.2 mmol/L; chloride level, 98 mmol/L; and calcium level, 9.3 mg/dL. The serum iron and zinc levels were 168 μg/dL and 82 μg/dL, respectively. Thyroid stimulating hormone (TSH) and free T3/T4 levels were within the normal range. The differential WBC profile was as follows: neutrophils, 50.1%; lymphocytes, 43.1%; monocytes, 4.5%; eosinophils, 1.2%; and basophils, 1.1%. The multiple allergen simultaneous test revealed class 0 for all evaluated 36 specific antigens (SRI Corporation 2022), and the serum total IgE level was 35 IU/mL. The D-dimer level was normal. Serum anti-nucleic acid antibodies (ANA), anti-SSA/SSB antibodies, and anti-neutrophil cytoplasmic antibodies (ANCA) were all within normal limits. Spirometry results were normal. Non-contrast abdominal computed tomography (CT) revealed inflammatory changes in the entire segment of the small intestine, with thickening of the small bowel wall, fluid retention, and increased density of mesenteric fat around the small intestine (Fig. 1a, b). Upper GI endoscopy was performed 11 weeks after the second vaccine dose, which revealed only slight gastric erosion. Lower GI endoscopy performed 12 weeks after the second vaccine dose revealed diverticulosis and no signs of chronic inflammatory bowel disease (IBD). Stool culture of fecal samples obtained during endoscopy revealed the growth of normal microbial flora in the oral cavity. Pathologic evaluation of colonic mucosal biopsy stained with hematoxylin and eosin (H&E) revealed only a slight level of plasma cell infiltration and mucosal edema in the lamina propria mucosae, accompanied by a slightly decreased density of crypts without disarrayed crypt arrangement (Fig. 2). No abnormal eosinophil filtration was observed in any of the tissue samples. The findings suggested a diagnosis of post-vaccine non-specific intestinal inflammation, and any kind of specific GI disease or malignancy was considered unlikely. To further investigate the condition of the small intestine mucosae, capsule endoscopy with PillCam SB3 (Medtronic, Minneapolis, MN, USA) was performed 13 weeks after the second vaccine dose, which revealed no abnormal findings, such as mucosal erosion, reddening, or edema (Fig. 1c). The small bowel transit time was 99 min. At 28 weeks after the second vaccine dose the patient developed a fever of 39.8°C along with diarrhea and bloody stools and visited the emergency department of another hospital. Abdominal CT was performed again with almost normal findings, and the patient was diagnosed with gastroenteritis and hemorrhoids.

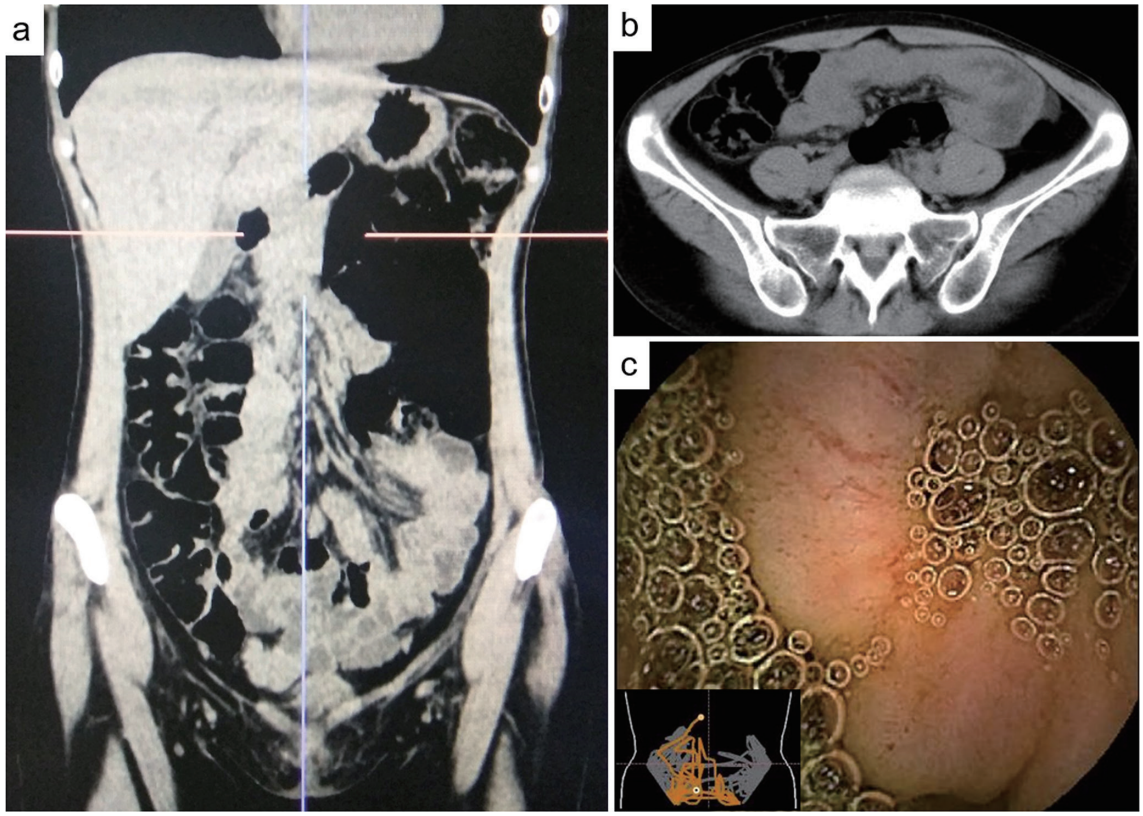

Fig. 1. Findings on non-contrast abdominal CT and small intestinal mucosa on capsule endoscopy.
(a, b) Non-contrast abdominal CT, taken at 8 weeks after the second vaccine dose, with coronal (a) and axial (b) slices showing inflammatory change in the whole segment of small intestine, with thickening of the small bowel wall in whole segments of the small intestine and retention of fluids inside. (c) Capsule endoscopy with PillCam SB3 (Medtronic, Minneapolis, MN, USA), performed at 13 weeks after the second vaccine dose, revealed an almost normal appearance of the small intestinal mucosa, without bleeding, erosions, or ulcerations that are suggestive of inflammatory bowel diseases.

Thirty-two weeks after the second vaccine dose, the patient's symptoms have not fully resolved yet, and she is being followed-up without medication. An overview of the patient's clinical course is shown in Fig. 3.

Methods and Results

Literature review

An electronic literature search of the PubMed database was performed to understand the clinical characteristics of prolonged diarrhea after COVID-19 vaccination. A combination of keywords "(COVID-19 OR SARS-CoV-2) AND vaccin* AND diarrhea*" identified 226 citations. Another combination of keywords "(SARS-CoV-2 OR COVID-19) AND vaccin* AND (prolonged OR persistent OR protracted) AND (diarrhea* OR enteritis)" identified 15 citations. All identified citations were screened by title and abstract, and for those that were ambiguous, the full text was reviewed. After excluding duplicate or irrelevant citations, nine citations that reported cases with unexplained symptoms, including diarrhea, after receiving the first or second dose of COVID-19 vaccines were identified (Fanni et al. 2021; Haji et al. 2021; Khan et al. 2021; Khogali and Abdelrahman 2021; Park et al. 2021; Poussaint et al. 2021; Shah et al. 2021; Chey et al. 2022; Taieb et al. 2022). These reports are summarized in Table 1. Eight of the nine patients survived, and one of them was described as having isolated symptoms of prolonged diarrhea that persisted for > 3 months (Chey et al. 2022). Our case appeared to be most similar to this previous case, which was diagnosed as transient microscopic lymphocytic colitis based on pathologic mucosal evaluation.

VAERS database search

To estimate the prevalence of diarrhea after COVID-19 vaccination among all vaccine recipients, we further searched for data from the Vaccine Adverse Event Reporting System (VAERS) through the Centers for Disease Control and Prevention's WONDER Online Database in May 2022 (Centers for Disease Control and Prevention, USA 2022). Among the 1,298,417 adverse events after COVID-19 vaccination that were reported to VAERS, 39,934 cases (3.1%) included symptoms of diarrhea. Among these 39,934 reported cases, 5,946 (14.9%) were hospitalized, 1,751 (4.4%) had prolonged symptoms, and 759 (1.9%) were deceased probably because of the adverse events. The most frequent time interval between

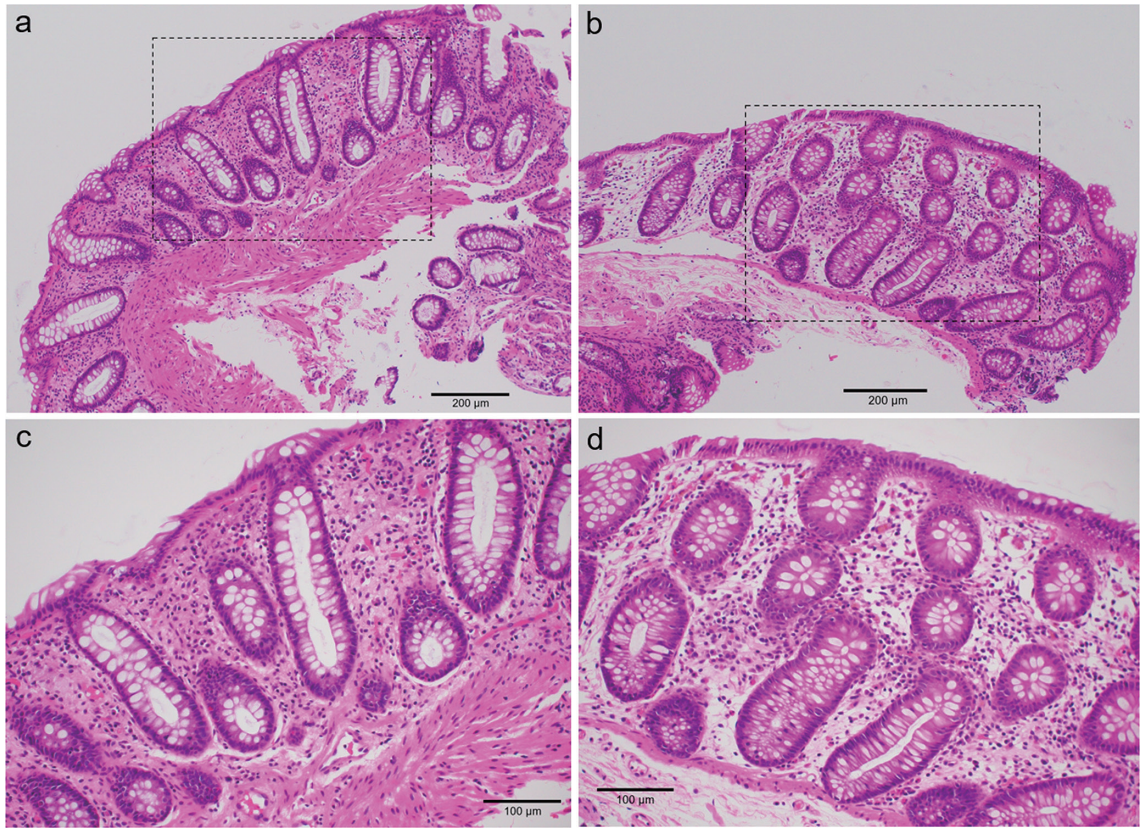

Fig. 2. Pathologic findings of hematoxylin and eosin stained colonic mucosa.
Colonic mucosal biopsies stained with hematoxylin and eosin (H&E) at a low magnification (a, b; scale bars represent 200 μm) and high magnification (c, d; scale bars represent 100 μm) are shown. A slight level of plasma cell infiltration, mucosal edema in the lamina propria mucosae, and a slightly decreased density of crypts without disordered crypt arrangement were observed. Lymphocytic infiltration of crypt epithelium was unremarkable. Based on these findings, non-specific inflammatory reactions in the intestinal mucosa were diagnosed.

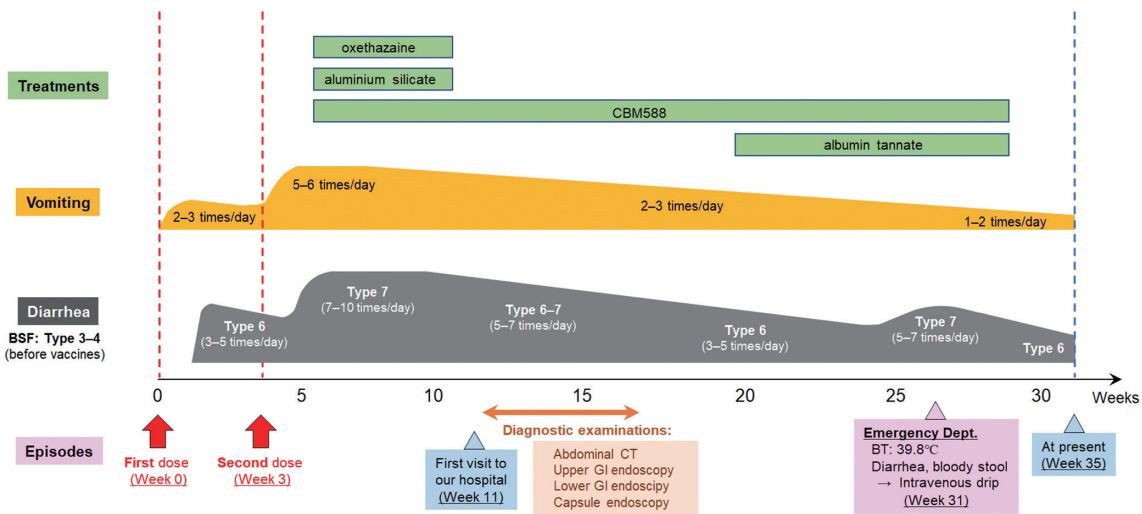

Fig. 3. Time course of the presented patient.
The time course of the symptoms and treatments in the presented case are shown. The patient never experienced chronic gastrointestinal symptoms before receiving mRNA vaccines for COVID-19. At 32 weeks after the second vaccine dose, her symptoms spontaneously resolved, but she still experienced vomiting 1-2 times per day and diarrhea 3-5 times per day. The patient was trying to avoid spicy or fatty foods to prevent diarrhea. In addition, she was trying to refrain from eating seaweed to avoid vomiting.
BSF, Bristol Stool Form; CBM588, *Clostridium butyricum* 588 strain tablet; GI, gastrointestinal.

Table 1. Summary of the literature review of cases with diarrhea after COVID-19 vaccination.

Author (Year)	Age, sex, PMH	Vaccine*	Days between vaccination and GI onset	Symptoms	Diagnostic studies on admission/Diagnosis	Treatments	Time to GI resolution after onset
Taieb et al. (2022)	43 F	BNT162b2 (Pfizer-BioNTech)	3 days after the first dose	Diarrhea, palpitation, muscle weakness, heat intolerance	(Lab data) normal WBC, elevated free T4 (Diagnosis) Graves disease, adjuvant-induced autoimmune/inflammatory syndrome	Thiamazol and propranolol	Before 3 months
Poussaint et al. (2021)	12 M	BNT162b2 (Pfizer-BioNTech)	2 days after the second dose	Neurological symptoms, headache, vomiting, diarrhea	(Lab data) CRP was elevated (Diagnosis) acute encephalopathy, CLOCC, MIS	Follow-up observation with symptomatic therapies	Before 24 days
Park et al. (2021)	67 M, HTN, DM	ChAdOx1 nCoV-19 (Covishield)	6 days after the first dose	Fever, maculopapular rash, diarrhea, headache, chills, dizziness	(Lab data) WBC and CRP were elevated (Diagnosis) MIS	mPSL (1 mg/kg) and diuretics	2 weeks
Haji et al. (2021)	63 M, daily marijuana use	Ad26.COV2.S (Johnson & Johnson)	1 day after the first dose	Nausea, vomiting, dyspnea, watery diarrhea, chills, sweats, heavy chest pain, fever, dyspnea, hypotension	(Lab data) elevated serum and urine catecholamines, elevated WBC and creatinine (Diagnosis) multisystem crisis based on undiagnosed pheochromocytoma (size: 7 cm), cardiomyopathy	Intensive care, mechanical ventilation, open adrenalectomy	Not specified, but recovered
Khan et al. (2021)	48 M	ChAdOx1 nCoV-19 (Covishield)	< 1 day after the first dose	(Day 0) fever, headache, nausea, vomiting, diarrhea; (day 21) ocular symptoms	(Lab data) WBC and CRP were normal (Diagnosis) bilateral keratolysis and bilateral massive choroidal detachment	Antibiotics, acyclovir, keratoplasty	14 days
Khogali and Abdelrahman (2021)	29 F, CKD	mRNA-1273 (Moderna)	12 days from the second dose	(Day 0) Fever, fatigue, myalgia, headache; (Day 12) nausea, vomiting, diarrhea, hypotension	(Lab data) WBC and CRP were normal† (Diagnosis) perimyocarditis	Intensive care, inotropes, steroids, hemodialysis	9 days
Fanni et al. (2021)	58 M	ChAdOx1 nCoV-19 (AstraZeneca)	13 days from the first dose	Abdominal pain, diarrhea, vomitus	(Lab data) thrombocytopenia, low fibrinogen level, increased D-dimer level (Diagnosis) multiple organ failure, VITT	Intensive care	Deceased 3 days after the onset
Shah et al. (2021)	59 F, SLE, ITP	Ad26.COV2.S (Johnson & Johnson)	2 days after the first dose	Abdominal cramps and diarrhea	(Abdominal CT) mild distal colitis (Lab data) thrombocytopenia (Diagnosis) vaccine-induced severe ITP	Dexamethasone (40 mg/day per os, 4 days)	Not specified, but recovered
Chey et al. (2022)	69 F, GERD, HL, HTN	BNT162b2 (Pfizer-BioNTech)	< 1 day after the second dose	Liquid stools, abdominal pain, and nausea	(Endoscopy) patchy erythema in the descending colon and rectosigmoid (Mucosal evaluation) lymphocytic colitis (Lab data) WBC and CRP were normal (Diagnosis) microscopic lymphocytic colitis	Follow-up observation with symptomatic therapies	113 days

CKD, chronic kidney disease; CLOCC, cytotoxic splenial lesion of the corpus callosum; CRP, C-reactive protein; DM, diabetes mellitus; GERD, gastro esophageal reflux disease; GI, gastrointestinal; HL, hyperlipidemia; HTN, hypertension; ITP, idiopathic thrombocytopenic purpura; lab, laboratory; MIS, multisystem inflammatory syndrome; mPSL, methylprednisolone; PMH, past medical history; SLE, systemic lupus erythematosus; VITT, vaccine-induced immune thrombotic thrombocytopenia; WBC, total white blood cell count.

*BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna) are mRNA vaccines, and ChAdOx1 nCoV-19 (Oxford-AstraZeneca) and Ad26.COV2.S (Johnson and Johnson) are viral vector-based vaccines.

†This patient with perimyocarditis had normal WBC and CRP levels on admission, which were abnormally elevated after hospitalization.

the last vaccination and the onset of diarrhea was 0 day (35.5%), followed by 1 day (23.9%), and 2 days (5.6%).

The prevalence of diarrhea after COVID-19 vaccination was further compared between that after receiving vaccines from different manufacturers. The incidence of diarrhea, regardless of any associated symptoms, was 2.9% (n = 2,536/87,247) with the Janssen Pharmaceuticals Ad26.COV2.S vaccine (adenovirus 26 vector vaccine; Johnson and Johnson), 3.0% (n = 13,726/454,549) with Moderna mRNA-1273, and 3.1% (n = 23,543/752,315) with Pfizer-BioNTech mRNA BNT162b2. Because of the large sample sizes, the incidence rate was significantly different among the three manufacturers ($p = 0.0004$, chi-square test), but the effect size with Cramer's V-value was as low as 0.0020, suggesting that the incidence of diarrhea did not remarkably differ according to COVID-19 vaccine type and manufacturer.

Discussion

The present case report describes a patient with prolonged isolated GI symptoms, without any other physical complaints, after receiving the first dose of the mRNA vaccine for COVID-19, which further exacerbated after the second vaccine dose. GI symptoms, sometimes with mild hepatic involvement, are common in COVID-19 patients (Ozkurt and Çınar Tanrıverdi 2022). Previous clinical studies across countries worldwide imply that GI symptoms after COVID-19 infection occur in 10-40% of the cases (Díaz et al. 2020; Jin et al. 2020; Lin et al. 2020; Wang et al. 2022), and these studies further suggest that the incidence of diarrhea is approximately 10%. GI symptoms after COVID-19 infection are common in both children and adults (Calitri et al. 2021). However, the exact incidence of GI symptoms after COVID-19 vaccination remains unknown. Furthermore, the types and incidence of prolonged symptoms lasting for months after receiving vaccines remain unknown. A report from Jordan indicated that the incidence of diarrhea among 1,086 vaccine recipients after the first dose of mRNA vaccines for COVID-19 is 6.4%, and the incidence could be slightly higher in women than in men (Omeish et al. 2022). Another report from Saudi Arabia, which enrolled 3,639 adult recipients of the BNT162b2 mRNA vaccine, reported a similar incidence of diarrhea after vaccination (approximately 6%), with almost similar rates after the first and second vaccine doses (Almohaya et al. 2021). A social media analysis from United Kingdom, which analyzed a total of 121,406 social media posts regarding adverse events after COVID-19 vaccination, revealed that the incidence of diarrhea would be approximately 3% of the overall vaccine recipients (Hussain et al. 2022). These reported incidences are similar to those suggested by the VAERS database search of the present study. The incidence of diarrhea after receiving the mRNA-1273 Moderna vaccine could be further increased by a history of COVID-19 infection (Kadali et al. 2022). However, these studies did not focus on the duration and treatability of GI symptoms among the evaluated vaccine recipients. A previous study based on the VAERS database search demonstrated that most cases of diarrhea after mRNA vaccination spontaneously resolved within 7 days of the last vaccination (Chey et al. 2022). Although the exact rate of prolonged symptoms after mRNA vaccination remains uncertain, patients with prolonged adverse events may have chronic inflammation based on perturbed cytokine networks (Kempuraj et al. 2020), as the mRNA vaccines instruct the production of SARS-CoV-2 spike protein and the subunits trigger proinflammatory pathways and enhance cytokine production (Shirato and Kizaki 2021). Meanwhile, if we consider that our patient had a cytokine storm, it is difficult to explain the fact that she had no other symptoms such as fever, throughout the clinical course, and her laboratory profiles including the total and differential WBC counts and CRP levels were all normal.

Based on our literature review, a case report was identified that described a patient with prolonged newly developed diarrhea, which persisted for nearly 4 months after receiving the COVID-19 vaccine (Chey et al. 2022). In the previous case, endoscopy revealed a largely normal appearance of the upper and lower GI walls, with the exception of patchy erythema in the descending and rectosigmoid colon. Based on the pathologic findings, the patient was diagnosed with transient microscopic lymphocytic colitis. The endoscopic appearance of GI mucosa in patients with microscopic enteritis can be normal, although closer inspection may reveal focal hypervascularity or exudative bleeding (Park et al. 2015a). Therefore, even when endoscopic examination reveals an almost normal appearance of the GI mucosa, pathologic examination is required to exclude the diagnosis. Elevated CRP and erythrocyte sedimentation rate levels, mild anemia, ANA, perinuclear ANCA, and rheumatoid factors can be observed in some patients with microscopic enteritis; however, none of these were observed in our case (Giardiello et al. 1987; Bohr et al. 1996). Nonsurgical treatments for microscopic enteritis include symptomatic therapies (antidiarrheals), 5-amino salicylic acid, corticosteroids, and other immunomodulators (Olesen et al. 2004; Park et al. 2015b). Although immunomodulators or anti-allergic agents could be effective in our case, these medications were not administered because the diagnostic findings did not offer sufficient evidence to suggest autoimmune-related or allergic mechanisms.

The most probable explanation for the GI symptoms observed in the present case could be the occurrence of gut dysbiosis after COVID-19 vaccination. The importance of gut microbiota in the immune response against the invasion of external pathogens through both the respiratory and GI tracts is widely known (Wu and Wu 2012). In patients with COVID-19, the microbiota of the respiratory and GI tracts have been shown to be dramatically altered after infection (Wang et al. 2022). The fecal microbiomes of patients with COVID-19 are deficient in beneficial anti-inflammatory symbionts, such as *Eubacterium*, *Lachnospiraceae*, and

Faecalibacterium, and are abundant in opportunistic microbes, such as *Clostridium* spp., *Enterobacteriaceae*, *Enterococcus*, and *Bacteroides* spp. (Zuo et al. 2020). Gut dysbiosis often persists even after recovery from COVID-19 and clearance of the virus (Yeoh et al. 2021). This fact strongly supports the theory that gut dysbiosis and the subsequent immunological disequilibrium triggered by COVID-19 infection or vaccines may contribute to persistent GI symptoms that last for more than several months. In addition to patients with COVID-19, vaccinees also have altered gut microbiota (Ng et al. 2022). Such post-vaccine gut dysbiosis may play a crucial role in the development of persistent GI symptoms in some vaccinees. Butyrate-producing bacteria are believed to be important mediators of allergic reactions by activating regulatory T cells and reducing IgE production in the GI tract (Chen et al. 2021). However, in the present case, oral CBM588 strain tablets were ineffective.

Another possible explanation for the unexplained GI symptoms in the present case may be the immunogenicity of the applied adjuvants or carrier molecules used for vaccine delivery in the COVID-19 vaccines. Vaccine adjuvants are used in protein subunit vaccines such as NVX-CoV2373 (Novavax), but other types of vaccines, including mRNA vaccines and adenovirus vector vaccines, also use excipients to stabilize the vaccine antigens and facilitate vaccine delivery. For example, BNT162b2 uses lipid-based nanoparticles (LNPs) as nonviral vectors for enhancing the mRNA to penetrate cell membranes, cholesterol for stabilizing the lipid bilayer of the LNPs, and polyethylene glycol (PEG)-conjugated lipids for further stabilization and solubility (Castells and Phillips 2021; Klimek et al. 2021). An immediate hypersensitivity to PEG is recently considered to be more common than was recognized before (Stone et al. 2019). There are several other additives in the mRNA vaccine, such as disodium hydrogen phosphate dihydrate and sucrose (Polack et al. 2020). As a possible theory, some COVID-19 vaccinees may be at a higher risk of complement-mediated immune system overactivity and allergic reactions that can cause prolonged adverse events after vaccination.

The limitations of the present report include the absence of evidence that confirms the causal relationship between COVID-19 vaccines and the observed chronic diarrhea in our patient. The causal relationship between these two phenomena was inferred by the temporal proximity between them, and this limitation may be applicable to most of the other case reports in the same field and reported data in the VAERS database. Future studies are needed to establish an objective and reliable criterion for judging the causal relationship between vaccines and developed symptoms. Furthermore, even if a causal relationship exists between the vaccine and adverse reactions, the vaccine may not be the only cause. The development of adverse events after vaccination is multifactorial, and additional factors may be needed for the development of pathology (Bellavite 2020). Another limitation was that although the electronic search and literature review of the present study implied that 3-5% of COVID-19 vaccine recipients would later develop diarrhea, the expected rate of diarrhea in the same population without receiving COVID-19 vaccination is unknown. In Greece, a cohort study of 1,007 patients with IBD who were recently vaccinated against COVID-19 revealed that less than 10% of the patients reported new-onset abdominal symptoms and diarrhea after the first and second vaccine doses (Orfanoudaki et al. 2022). Further studies are needed to determine whether COVID-19 vaccines would certainly increase the incidence of abdominal symptoms and diarrhea in vaccinees compared to those who did not receive the vaccines. Finally, although the suspected main lesions in the present case were in the small intestine, pathologic assessment was performed for the colonic mucosa. Therefore, it remains uncertain whether the diagnosis of lymphocytic enteritis or some allergic conditions localized to the GI tract can be excluded.

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Conflict of Interest

The authors declare no conflict of interest.

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