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# Multisystem Inflammatory Syndrome in Children Following COVID-19 Vaccine (Pfizer-BioNTech BNT162b2): A Case Report

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## Abstract

Although Coronavirus Disease 2019 (COVID-19) vaccines have been associated with a low incidence of Multisystem Inflammatory Syndrome in Children (MIS-C), several MIS-C cases following COVID-19 vaccination have been reported globally. Here, we report a case of persistent fever, mucocutaneous inflammation, and elevated inflammatory markers after COVID-19 vaccination. A previously healthy 13-year-old boy presented with fever and headache for two days. He had received a second dose of COVID-19 vaccine (Pfizer-BioNTech BNT162b2) approximately nine weeks prior. Laboratory tests revealed elevated levels of inflammatory markers and Echocardiography revealed normal ventricular function and a normal coronary artery. He had no history of diagnosis of COVID-19, and the severe acute respiratory syndrome coronavirus-2 reverse transcriptase polymerase chain reaction result was negative. After admission, the patient developed a skin rash, bilateral conjunctival injection, abdominal pain, and hypotension. Based on diagnostic criteria, MIS-C was strongly suspected. We initiated intravenous gamma globulin and methylprednisolone. Following treatment, the symptoms improved, and inflammatory markers decreased. We report the first Korean child who developed MIS-C following COVID-19 vaccination.

**Keywords: Coronavirus Disease 2019 (COVID-19); COVID-19 vaccination; Multisystem inflammatory syndrome; Children**

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## Introduction

Coronavirus Disease 2019 (COVID-19) vaccines have been found to be safe, immunogenic, and efficacious in children and adolescents [1-3], and have been associated with a lower incidence of Multisystem Inflammatory Syndrome in Children (MIS-C) [4,5]. A febrile hyper-inflammatory syndrome, MIS-C, develops in children with Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infection and is known to cause symptoms similar to those of Kawasaki disease [6]. The first case of MIS-C in Korea was reported in November 2020 [7]; with further cases being subsequently reported [8].

The incidence of MIS-C is known to decrease after COVID-19 vaccination; however, MIS-C cases following COVID-19 vaccination have been reported in other countries [9-12]. In addition, cases of Multisystem Inflammatory Syndrome in Adults (MIS-A) after COVID-19 vaccination have been reported in Korea [13]. To the best of our knowledge, no case of MIS-C after COVID-19 vaccination has been reported in children or adolescents. Here, we describe in detail a case of MIS-C induced by COVID-19 vaccine (Pfizer-BioNTech BNT162b2).

## Case Presentation

A previously healthy 13-year-old boy visited our Emergency Room (ER) on March 3rd, 2022 with a two-day history of fever and headache. He had received his first dose of COVID-19 vaccine (Pfizer-BioNTech BNT162b2) on November 27th, 2021 and had received a second dose of COVID-19 vaccine (Pfizer-BioNTech BNT162b2) on December 25th, 2021. He did not have any allergies, and had previously received National Immunization Program vaccines without any reaction. He had no history of COVID-19 infection, no close contact with known COVID-19 patients, and no family history of COVID-19.

At the time of the ER visit, his vital signs were a Blood Pressure (BP) of 130/80 mmHg, pulse rate of 100/min, respiratory rate of 20/min, body temperature of 38.3°C, and 100% O2 saturation.

**Table 1:** Results of laboratory examination.

| Variable | HD #1 | HD #2 | HD #4 | HD #8 | A week after discharge |
|---|---|---|---|---|---|
| WBC ($10^3$/μL) | 9.05 | 5.8 | 8.23 | 14.2 | 10.08 |
| ALC($10^3$/μL) | 0.45 | 0.4 | 0.88 | 3.8 | 5.48 |
| Hb (g/dL) | 13.6 | 11.8 | 11.5 | 12.9 | 13.4 |
| Platelet ($10^3$/μL) | 149 | 108 | 130 | 349 | 390 |
| AST (IU/L) | 38 | 32 | 18 | 31 | 23 |
| ALT (IU/L) | 55 | 54 | 30 | 33 | 34 |
| Total bilirubin (mg/dL) | 1.5 | 1.4 | 0.6 | 0.9 | 0.8 |
| Albumin (g/dL) | 4 | 3.5 | 3.1 | 3.3 | 3.8 |
| BUN (mg/dL) | 14.2 | 26.9 | 24.2 | 13.4 | 19.4 |
| Cr (mg/dL) | 0.74 | 0.94 | 0.57 | 0.43 | 0.66 |
| CRP (mg/dL) | 23.11 | 29.35 | 17.04 | 2.13 | 0.12 |
| CK (U/L) | 54 | 44 | | | 193 |
| CK-MB (μg/mL) | 3.4 | 4 | 2.7 | 1.1 | |
| Myoglobin (μg/mL) | 15.3 | 19.2 | 10.8 | | |
| hsTnI (pg/mL) | 153.37 | 162.65 | 135.81 | 24.59 | 11.83 |
| BNP (pg/mL) | 266 | 234 | 399 | 195 | 17 |
| Fibrinogen (mg/dL) | 707 | 673 | | | |
| D dimer (μg/mL) | 2.87 | 2.3 | | | |

HD: Hospital Day; WBC: White Blood Cells; ALC: Absolute Lymphocyte Count; Hb: Hemoglobin; AST: Aspartate Transaminase; ALT: Alanine Transaminase; BUN: Blood Urea Nitrogen; Cr: Creatinine; CRP: C-Reactive Protein; CK: Creatine Kinase; CK-MB: Creatine Kinase Mb Fraction; hsTnI: High Sensitive Troponin I; BNP: B-Type Natriuretic Peptide

Laboratory investigation revealed a white blood cell count of 9,050/μL (absolute neutrophil count 7,960/μL, absolute lymphocyte count 450/μL), hemoglobin of 13.6 g/dL, platelet count of 149,000/μL, ferritin of 311.8 ng/mL, C-Reactive Protein (CRP) of 23.11 mg/dL, procalcitonin of 4.861 μg/mL, interleukin-6 of 566.0 pg/mL, high sensitive troponin I of 153.37 pg/mL, and B-type natriuretic peptide of 266.0 pg/mg (Table 1). Blood, urine, and cerebrospinal fluid culture results were all negative, and other microbiological test results, including Epstein Barr virus viral capsid antigen Immunoglobulin M (IgM) antibody, cytomegalovirus IgM, herpes simplex virus Polymerase Chain Reaction (PCR), and tsutsugamushi and leptospira antibody tests, were negative. Abdominal computed tomography revealed no abnormalities other than multiple enlarged lymph nodes along the superior mesenteric and ileocecal vessels. Echocardiography revealed normal ventricular function, with a normal coronary artery and ejection fraction of 62.7%. Furthermore, SARS-CoV-2 Reverse Transcriptase PCR (RT-PCR) (Biosewoonic., Seoul, Republic of Korea) and nucleocapsid protein antibody (Seoul Clinical Laboratories, Gyeonggi-do, Republic of Korea) were negative, and the spike protein antibody (Seoul Clinical Laboratories, Gyeonggi-do, Republic of Korea) was positive (>75.00). These antibody tests included both immunoglobulin G and IgM.

On Hospital Day (HD) 2, he developed a skin rash, bilateral conjunctival injection, abdominal pain, dyspnea, and chest discomfort, and his BP fell below 90/60 mmHg (Figure 1). The diagnostic criteria for MIS-C are a fever of 38°C or higher for more than 24 h in patients under the age of 19 accompanied by multi-organ injury involving at least two organs and requiring hospitalization, elevation of inflammatory markers, and the absence of any other apparent microbial cause for inflammation [14]. As the patient was under 19 years of age, had persistent fever, multi-organ injury, and had no evidence of other microbial infections, MIS-C was strongly suspected. We initiated Intravenous Gammaglobulin (IVIG) 2 g/kg for one day and methylprednisolone 1 g for three days with concurrent supportive care, including inotropic agents (dopamine) and milrinone. On HD 4, his symptoms including rash, fever, bilateral conjunctival injection, abdominal pain, and respiratory difficulty improved, and his BP stabilized without inotropic agents. Follow-up echocardiography showed normal ventricular function with a normal coronary artery and decreased inflammatory markers. Consequently, low does aspirin (80 mg) and prednisolone (60 mg) were initiated. The patient was discharged on HD 9. Desquamation of the fingers and toes developed, and a week after discharge, echocardiography and inflammatory marker levels were normal.

## Discussion

The first case of MIS-C was reported in the UK as hyperinflammatory shock in April 2020 [15]. The clinical features of MIS-C are similar to those of Kawasaki disease and may occur in children and adolescents 3 to 6 weeks after SARS-CoV-2 infection. Patients with MIS-C typically present with persistent fever associated with gastrointestinal symptoms (pain, vomiting, and diarrhea), evidence of mucocutaneous inflammation (rash, conjunctivitis, and oromucosal changes), lymphopenia, and high levels of circulating inflammatory mediators. Some patients with MIS-C develop severe disease including hypotension/shock and evidence of cardiac involvement, including myocarditis, myocardial dysfunction, and coronary artery changes. Similar symptoms occur in adults after COVID-19, which is known as MIS-A [16].

We considered our case to be COVID-19 vaccine-induced MIS-C for the following reasons: 1) The patient had no history of COVID-19 infection and had no close contact with known COVID-19 patients; 2) the patient had received his second COVID-19 vaccine approximately 9 weeks before hospitalization; 3) persistent fever and hypotension occurred, and clinical symptoms of rash, fever, bilateral conjunctival injection, abdominal pain, and respiratory difficulty were accompanied by elevation of CRP, ferritin, and procalcitonin levels; and 4) other microbial causes of inflammation, such as bacterial sepsis and staphylococcal or streptococcal toxic shock syndrome, were excluded. The patient therefore met the criteria for MIS-C [14].

As MIS-C is similar Kawasaki disease, it is necessary to distinguish these clinical entities. Most patients with Kawasaki disease are younger than five years of age [17], but patients with MIS-C have a broader age range [6]. Gastrointestinal symptoms, thrombocytopenia, and shock are rare in Kawasaki disease, but are common in MIS-C [6,18]. In our case, the patient was 13 years old and MIS-C was considered more likely in the light of his abdominal pain, lymphopenia, thrombocytopenia, and hypotension.

A few cases of MIS-C after COVID-19 vaccination in children and adolescents have been reported [9-12]. Here patients were aged between 12 and 20 years. One patient had received Pfizer-BioNTech BNT162b2 and Moderna, while the others had received one or two doses of Pfizer-BioNTech BNT162b2. They had received the first dose of COVID-19 vaccine 5 to 21 days prior to the onset of symptoms, or the second dose of COVID-19 vaccine 2 to 84 days prior to the onset of symptoms. The patients mainly presented with fever and myocarditis, and in more than half of them, the symptoms improved after treatment with IVIG and steroids.

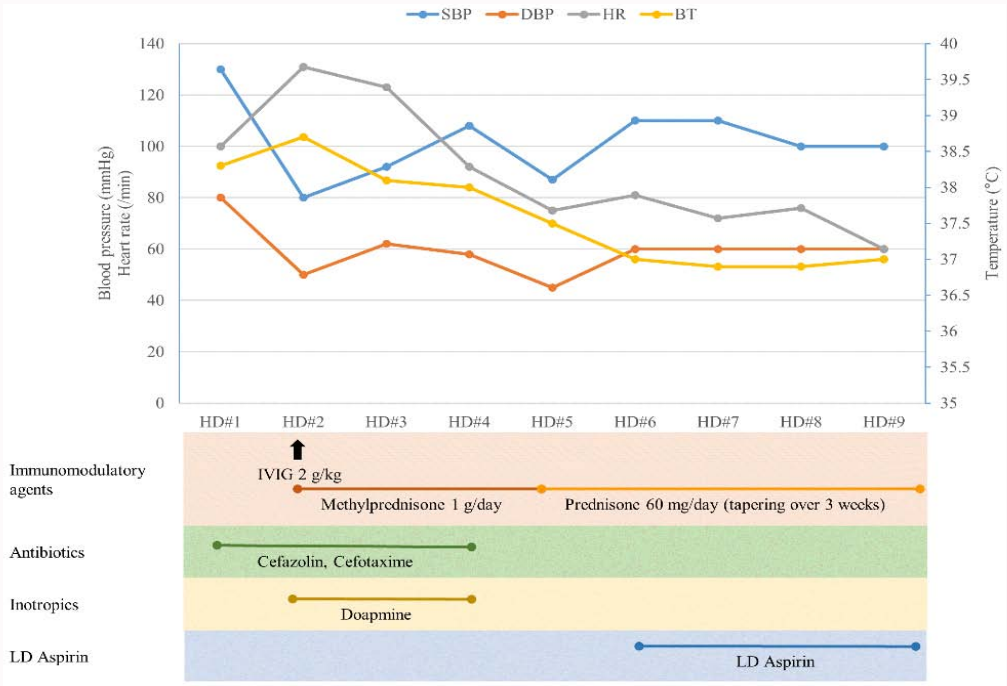


**Figure 1:** Patient's clinical course: Changes in vital signs and treatment with immunomodulatory agents, antibiotics, inotropics, and low dose aspirin. SBP: Systemic Blood Pressure; DBP: Diastolic Blood Pressure; HR: Heart Rate; BT: Body Temperature; HD: Hospital Day; IVIG: Intravenous Gammaglobulin; LD: Low Dose

The pathogenesis of MIS-C is unknown, and the clinical entity of COVID-19 vaccine-induced MIS-C has not been proven. One study suggested that MIS-C after COVID-19 vaccination is due to immune system dysregulation and cytokine storm, leading to multi-organ dysfunction [19]. Another study suspected that the SARS-CoV-2 spike protein is the target of the immune response [20]. In the face of a lack of evidence, further research is required.

To our knowledge, this is the first reported case of a Korean child who developed MIS-C following COVID-19 vaccination. In Korea, COVID-19 vaccination has been approved for use in children older than five years of age, and the proportion of children and adolescents vaccinated against COVID-19 is expected to increase. Therefore, recently vaccinated children and adolescents should be monitored closely for MIS-C.

## Ethics Statement

This study was approved by the Institutional Review Board of Pusan National University Yangsan Hospital (IRB No. 05-2022-071).

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