A Case of Multisystem Inflammatory Syndrome in a 12-Year-old Male After COVID-19 mRNA Vaccine

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Abstract: The pathophysiology of multisystem inflammatory syndrome (MIS) in children (MIS-C) is unknown. It occurs several weeks after COVID-19 infection or exposure; however, MIS is rarely reported after COVID-19 vaccination, and cases are mostly in adults. Herein, we present a 12-year-old male who had no prior COVID-19 infection or exposure and developed MIS-C after his first dose of COVID-19 mRNA vaccine.

Key Words: COVID-19, mRNA vaccine, multisystem inflammatory syndrome, children

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Multisystem inflammatory syndrome (MIS) in children (MIS-C) mainly affects previously healthy children and manifests as a hyperinflammatory syndrome with multiorgan involvement. Although MIS is believed to be a postinfectious sequela of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, the pathophysiology of this syndrome remains poorly understood.[1,2] It occurs several weeks after SARS-CoV-2 infection or exposure[2]; however, MIS has rarely been reported after COVID-19 vaccination, and the cases are mostly in adults.[3–5] Herein, we describe the case of a 12-year-old male, the youngest case reported to date, who was diagnosed with MIS-C 27 days after receiving his first dose of COVID-19 messenger ribonucleic acid (mRNA) vaccine (Pfizer-BioNTech) and was successfully treated with intravenous immunoglobulin (IVIG) and methylprednisolone therapy.

CASE REPORT

A previously healthy 12-year-old male presented with a 4-day duration of fever, eye redness, diarrhea, neck pain and swelling. Before admission, the patient had been treated with intramuscular ceftriaxone for presumed bacterial lymphadenitis for 2 days, without clinical improvement. He had no history of recent COVID-19 infection or exposure. He had received his first dose of COVID-19 mRNA vaccine (Pfizer-BioNTech) 27 days before the onset of symptoms. On examination, he had a body temperature of 39 °C, heart rate of 127/min, respiratory rate of 24/min, blood pressure of 90/60 mm Hg, and oxygen saturation of 96% in ambient air. He had bilateral nonpurulent conjunctivitis and a 3×2 cm-sized lymphadenopathy that was firm and tender in the right anterior cervical area (Fig. 1). His neck movements were extremely limited due to pain. Empirical intravenous therapy with ceftriaxone and clindamycin was initiated after obtaining blood, urine and stool cultures.

Laboratory tests showed lymphocytopenia (940/mm^3), elevated levels of C-reactive protein (171 mg/L), erythrocyte sedimentation rate (60 mm/h), procalcitonin (5 ng/ml), ferritin (331 ng/mL), fibrinogen (818 mg/dL), interleukin-6 (95 pg/mL), pro-brain natriuretic peptide (578 pg/mL) and D-dimer (3,564 ng/mL). The SARS-CoV-2 real-time polymerase chain reaction from the nasopharyngeal swab was negative but anti-SARS-CoV-2 total antibody level was positive. Blood, urine and stool cultures were negative. Troponin level and echocardiographic examination were found to be normal. Chest radiography was unremarkable. Abdominal ultrasonography revealed periportal and mesenteric multiple lymphadenopathies, increased echogenicity in mesenteric fat planes and pelvic free fluid (15 mm). Contrast-enhanced neck computed tomography which was performed due to the clinical findings of limited neck movements, neck pain and swelling suggestive of deep neck infection, showed thickening and edema of the prevertebral soft tissue, hypodense appearance in the right parapharyngeal area and changes of parapharyngeal fat planes due to inflammation (Fig. 1). Ophthalmologic examination was performed due to persistent redness of the eyes and revealed bilateral anterior uveitis.

The patient met the diagnostic criteria of MIS-C with documented fever lasting ≥24 h, laboratory evidence of inflammation, multisystem (≥2) organ involvement (gastrointestinal and mucocutaneous symptoms), and positive SARS-CoV-2 serology.[1] Because he had no history of COVID-19 infection or exposure apart from vaccination, we ordered specific measurements for SARS-CoV-2 anti-nucleocapsid and anti-spike antibody levels. He had a negative anti-SARS-CoV-2 nucleocapsid total antibody level, but a high level of anti-SARS-CoV-2 spike IgG (257 BAU/mL; >0.8 BAU/mL: positive result), indicating a vaccine-induced antibody response rather than a SARS-CoV-2 infection-induced antibody response. He was treated with IVIG (2 g/kg) and methylprednisolone (2 mg/kg). The patient became afebrile within 24 h and his lymphadenopathy, conjunctivitis, neck pain and swelling gradually resolved over the following 2 days. Acute phase reactants returned to normal values in 4 days. He was discharged 5 days after admission with no sequela or complication.

DISCUSSION

Although current data show that COVID-19 vaccines are well tolerated and safe,[6] there are some concerns about possible adverse effects, even though the side effects of COVID-19 vaccines are generally mild, such as pain in the injection site, headache, fatigue, low-grade fever and general musculoskeletal pain. These side effects commonly occur within the first 3 days of vaccination and resolve within a few days of onset.[7] However, severe side effects of COVID-19 vaccines have recently been reported, such as myocarditis, especially in male adolescents.[8,9] To the best of our knowledge, MIS-C after vaccination is an extremely rare condition, especially in children.

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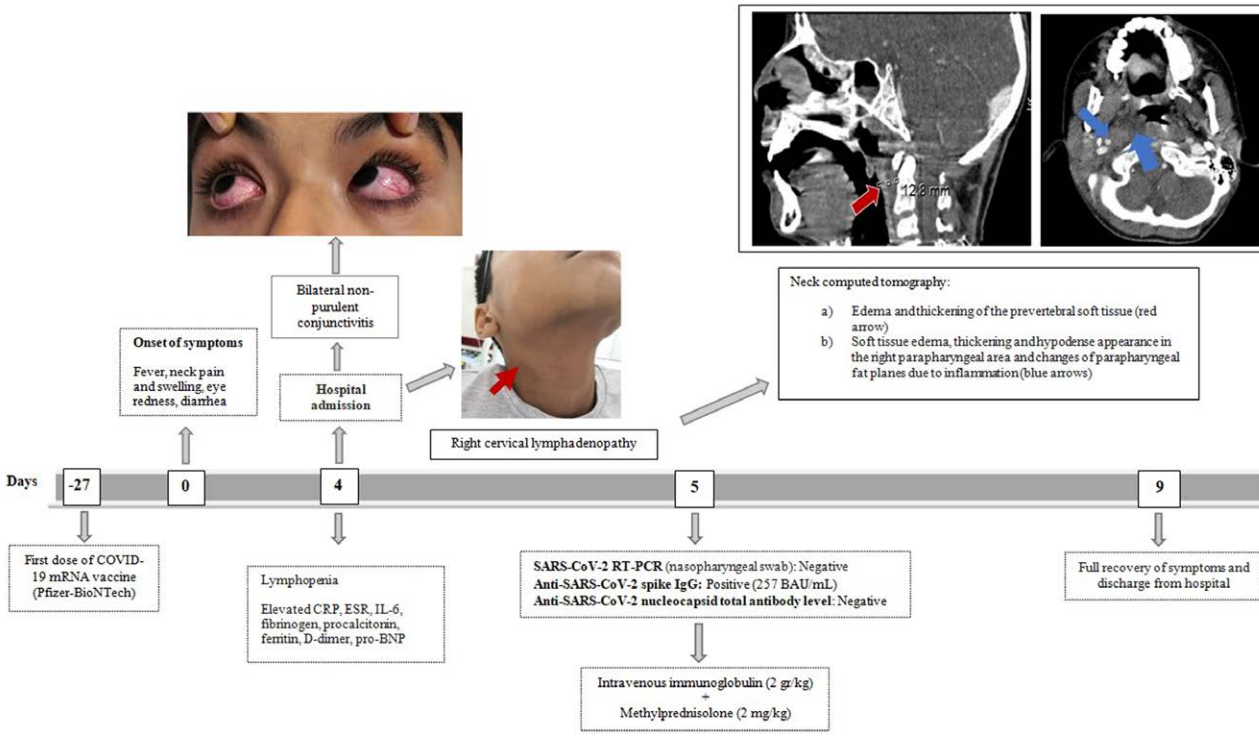

FIGURE 1. Timeline showing the clinical presentation and follow-up of the patient who had multisystem inflammatory syndrome after COVID-19 vaccination. BNP, brain natriuretic peptide; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IL-6, interleukin-6; RT-PCR, real-time polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

After recognition of MIS-C, a similar condition was also described in adults, referred to as MIS in adults (MIS-A). Although MIS pathogenesis is yet to be clarified, both MIS-C and MIS-A appear to be post-infectious manifestations of COVID-19, and the Brighton Collaboration Network has listed both conditions as postvaccination adverse events of special interest with respect to COVID-19 vaccines.[2] Although it is currently unknown whether MIS-C/A might follow vaccination against COVID-19, there are some reports in adults describing the occurrence of MIS-A after COVID-19 vaccination.[3–5] Notably, some of these adult cases also had a history of recent COVID-19 infection before vaccination.[3] To our knowledge, there is only one reported pediatric case of MIS-C after COVID-19 vaccination, a 17-year-old male who developed MIS-C 5 days after his second dose of the Pfizer-BioNTech vaccine.[10] As in our case, the patient had no history of a previous SARS-CoV-2 infection. Currently, our patient is the youngest vaccine-related MIS-C case reported to date.

Following widespread use of COVID-19 vaccines, serologic discrimination between vaccine-induced and SARS-CoV-2 infection-induced antibody response has become an issue of relevance. Although it is known that vaccination leads to a reactive result on anti-SARS-CoV-2 spike antibodies, it may not be helpful to distinguish between prior infection and prior vaccination because these antibodies may also occur as a result of infection with SARS-CoV-2. However, vaccination does not lead to a reactive test result on anti-SARS-CoV-2 nucleocapsid antibody which is produced during and after the infection. Therefore, measurement of both anti-spike and anti-nucleocapsid-based serology has been recommended for discrimination of responses after spike-protein-based vaccination and natural infection.[11]

In our case, the diagnosis of vaccine-related MIS-C was strongly suspected due to various reasons, including the development of MIS-C 27 days after the first dose of COVID-19 mRNA vaccine, absence of previous SARS-CoV-2 infection or exposure and positive result for anti-spike IgG but negative result for anti-nucleocapsid antibodies. He met the Brighton Collaboration Level 1 of diagnostic certainty for a definitive case.[2] The case was reported to the vaccine adverse event reporting system of our Ministry of Health.

To conclude, our case raises suspicion that COVID-19 vaccination might trigger MIS-C. Future epidemiologic studies are needed to determine whether an association exists between COVID-19 vaccination and MIS-C development.

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