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Clinical Notes

Multisystem inflammatory syndrome in Children After BNT162b2 Messenger RNA SARS-CoV-2 Vaccination

Running Title: MIS and SARS-CoV2 Vaccination (29 characters including spaces)
Or MIS-children and SARS-CoV2 Vaccination (38 characters including spaces)

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We report a case of a 15-year-old male presenting with Multi-System Inflammatory Syndrome in Children (MIS-C) following vaccination with the BNT162b2 mRNA SARS-CoV-2 vaccine. Fifty days after receiving the second dose of the vaccine, he visited local institution complaining of fever and chest pain. Then, he was referred and admitted to our institution due to suspected acute myocarditis on an electrocardiogram (ECG). His father is a Japanese Brazilian. His body mass index was 29.6 kg/m^2. Physical examination revealed a body temperature of 39.8 °C, 96% oxygen saturation (room air), and blood pressure of 109/69 mmHg. His bilateral eyeball revealed conjunctival hyperemia. ECG

revealed II, III, aVf, V5, and V6 ST abnormalities changes (Figure 1, Panel A). Blood examination revealed white blood cell count as **11.2 × 10^3** /μL (neutrophil 73.9%, lymphocyte 17.1%), platelet 14.7 × 10^4 /μL, C-reactive protein 7.12 mg/dL, aspartate aminotransferase 70 IU/L, alanine aminotransferase 173 IU/L, total bilirubin 2.2 mg/dL, sodium 136 mEq/L, albumin 4.4 g/dL, D-dimer 0.5 μg/dL, brain natriuretic peptide 5.8 pg/mL, and troponin I was less than 0.007 ng/mL. SARS-COV-2 from a nasopharyngeal swab was negative for the nucleocapsid protein antibody and positive for the SARS-CoV-2 spike protein antibody. In addition, the Enterovirus (including Echovirus), Adenovirus, and Parvovirus B19, which could be the causative of myocarditis, were not detected by PCR in the initial blood samples. There was no significant increase in the viral antibody titers**. Unfortunately, the possibility of *Yersinia* infection could not be eliminated.** Echocardiography revealed no findings of pericardial effusion and no coronary artery dilation was observed. Cardiac MRI findings showed that the left ventricular ejection fraction (LVEF) was 49%. No images were observed in early T1 enhanced images early gadolinium enhancement (EGE), or delayed contrast and late gadolinium enhancement (LGE). After admission, the patient complained of abdominal pain and diarrhea. The day after admission, the fever tended to disappear; however, chest pain persisted and troponin I increased by 1.664 ng/mL. Echocardiography revealed a global longitudinal strain (GLS) of −13% and abnormal wall motion in the anteroseptal at the base (Figure 1, Panel C). However, ECG was not changed at admission, so when carefully managed by the intensive care unit, the chest pain was improved by the administration of acetaminophen **without intravenous gamma globulin** administration. Troponin I peaked on the day after admission and gradually decreased, and chest pain was improved simultaneously. On the 8th day of admission, a cardiac MRI revealed EGE in the anteroseptal at the base (Figure 1, Panel D), in a similar region as echocardiography. Thereafter, the symptoms improved, and the patient was discharged. One month after discharge, the chest pain did not recur, and the ST change on ECG was improved (Figure 1, Panel B).

At admission, this case was suspected of acute myocarditis due to SARS-CoV-2 vaccination or other viral infections; however, the patient suffered from multi-organ symptoms, such as chest and abdominal pain, and bilateral ocular conjunctival congestion with myocardial abnormality after 50 days of vaccination. MIS-C is a new disease concept that causes strong inflammation across multiple organ systems after the onset of COVID-19[1]. Salzman et al reported the first three MIS-C cases associated with SARS-CoV-2 vaccination[2]. Although MIS-C in the early stage after vaccination is associated with autoimmune/inflammatory syndrome induced by adjuvants[3], it is difficult to diagnose the disease because it lacks specific biomarkers. Immune response deficiency associated with SARS-CoV-2 infection as well as vaccines may cause MIS-C[4]. **Assuming a severe course of COVID-19 with a systemic cytokine storm and hyperinflammation that may cause fast clinical deterioration and progressive multi-organ failure, MIS-C symptoms are expected to typically manifest 4–6 weeks after SARS-CoV-2 infection or exposure. However, despite the limited current**

understanding of MIS-C and MIS-Adult, the expert's definition of MIS-C recommends the diagnostic criteria of onset up to 12 weeks after infection or exposure to keep a uniform case definition for patients of all ages[4]. Though the incidences of MIS-C associated with SARS-CoV2 vaccination are significantly lower than SARS-CoV-2 infection[5], with this clinical note, we recommend that SARS-CoV-2 vaccines should be carefully promoted in children to avoid rare adverse events.

Author Contributions

List of authors: All authors have made substantial contributions to the conception and design of the article as follows: Satoru Iwashima and Kana Sakaida; performed echocardiography, interpreted the data, and wrote the paper, Junichiro Katuki interpreted the data. Keisuke Satou interpreted a cardiac MRI. Isao Miyairi interpreted it to estimate the PCR in the initial blood samples.

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Figure legend

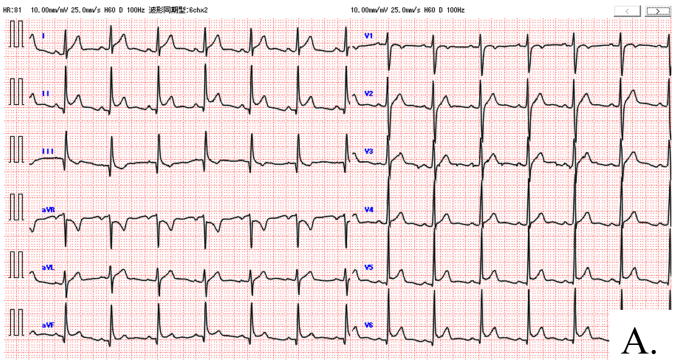
Figure 1:

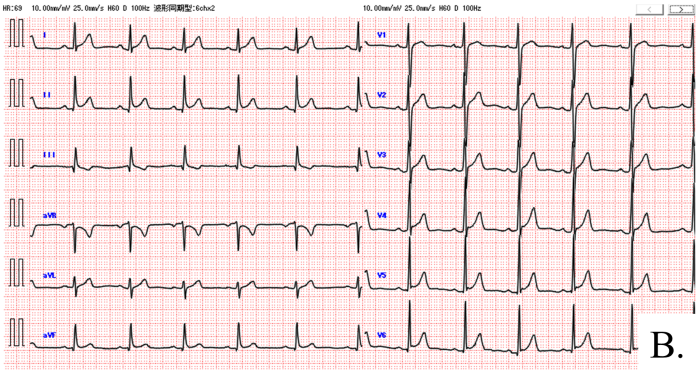
A; ECG findings on admission revealed II, III, aVf, V5, and V6 ST abnormalities.

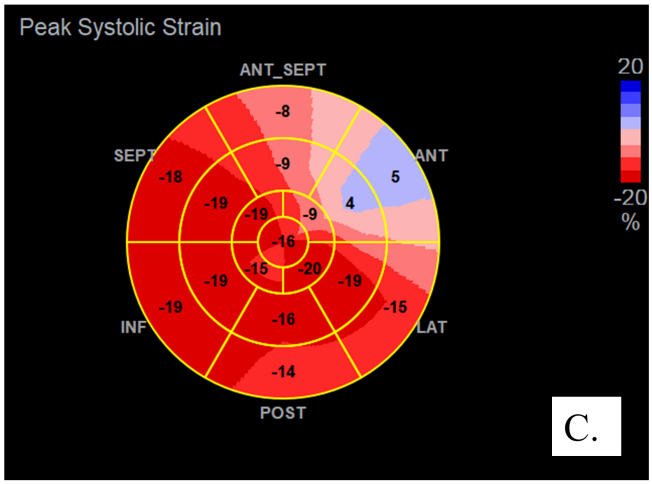
B; One month after discharge, the ST change on ECG was improved.

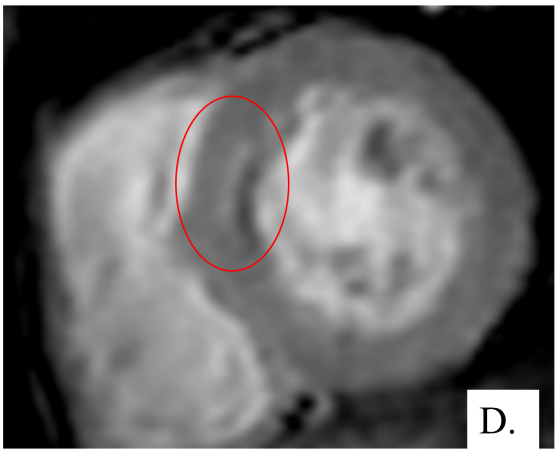
C; Two-dimensional speckle tracking findings by echocardiography revealed a global longitudinal strain as −13% and abnormal wall motion in the anteroseptal at the base.

D. Cardiac MRI revealed early gadolinium enhancement in the anteroseptal at the base (red circle).









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