

A Challenging Diagnosis: A Case of Multisystem Inflammatory Syndrome Following COVID-19 Vaccination

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To the Editor

mRNA vaccine-linked rheumatic disease flares and/or unveiling autoimmune disorders have been increasingly published in the literature.¹⁻³ The multisystem inflammatory syndrome in adult (MIS-A) was firstly described in patients following the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection, typically characterized by persistent fever, edema due to increased vascular permeability, and systemic inflammation.⁴ Herein, we report a case presented with hyperinflammation symptoms similar to MIS-A after coronavirus disease-19 (COVID-19) vaccination. Informed consent to publish this paper was obtained from the patient.

A 50-year-old female was consulted due to persistent fever, widespread rash, proteinuria, and hyperferritinemia. One month prior, she was admitted to another hospital due to fever, myalgia, and shortness of breath, prompting administration of antibiotics. She was then hospitalized due to persistent fever and development of pulmonary edema, requiring non-invasive mechanical ventilation. During this time, she developed seizures in addition to her ongoing fever. Cerebrospinal fluid (CSF) analysis and magnetic resonance imaging of the brain were noncontributory, and no evidence of infectious foci were observed serologically and microbiologically. Her past medical record was significant for a childhood history of meningitis. She described no evidence of COVID-19 symptoms before presentation, and stated that the second dose of Biontech-Pfizer vaccine was administered 6 weeks before symptoms onset. Polymerase chain reaction tests for SARS-CoV-2 were negative on multiple occasions. Physical examination showed widespread salmon-colored rashes on her trunk and extremities. Her laboratory findings were as follows: C-reactive protein of 286 mg/L, erythrocyte sedimentation rate of 70 mm/h, ferritin of over 100,000 ng/ml (NV: 13-150), hemoglobin of 10.2 g/dl (NV: 11.9-14.6), aspartate aminotransferase of 594 U/L (NV: 0-33), alanine aminotransferase

of 141 U/L (NV: 0-35), lactate dehydrogenase of 3,494 U/L (NV: 135-214), serum albumin of 3.0 mg/dl (NV: 3.5-5), creatinine of 1.0 mg/dl (NV: 0.4-0.98), D-dimer of 9.28 mg/l (NV: 0-0.5), fibrinogen of 289 mg/dl (NV: 170-420), proteinuria of 1.8 g/day, and serum proBNP of 10,522 pg/ml (NV: 0-125) with normal cardiac enzymes. Furthermore, echocardiography showed left ventricle systolic dysfunction and mild pericardial effusion, ANA and RF were negative, bone marrow examination (BME) was unremarkable, and SARS-CoV-2 immunoglobulin (IgG) antibody levels were positive. Based on these findings, a diagnosis of multisystem inflammatory syndrome, possibly related to vaccination (MIS-V), was considered, and pulse methylprednisolone was initiated. Due to persistent fever and high ferritin levels (> 100,000 for three following occasions), anakinra, an interleukin (IL)-1 inhibitor, was added to the treatment. The patient was discharged at day 21 after clinical and laboratory improvement. She is currently in remission with a regimen of anakinra and low dose methylprednisolone.

Based on her clinical features, a diagnosis of MIS-A was initially considered. However, despite the presence of SARS-CoV-2 IgG antibodies, the lack of COVID-19 symptoms before presentation and her history of complete vaccination were nonsupporting. As vaccination-induced adult onset Still's disease (AOSD) has been reported previously, AOSD was also considered among differentials differential¹, however the presence of proteinuria and pulmonary edema due to cardiac failure were atypical. Moreover, macrophage activation syndrome was excluded based on normal BME findings. Given the growing number of vaccinated patients undergoing vaccination, similar clinical presentations have been identified among them which is termed as MIS-V in nomenclature.⁵ Based on limited experiences, the sole or combined administration of steroids, intravenous immunoglobulin, and IL-1 inhibitors might be beneficial in controlling systemic inflammation.⁵ In conclusion, all clinicians should be cognizant of this novel clinical entity and its importance, highlighting the need for an extensive investigation.

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