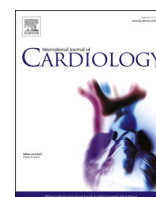




Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Short communication

Fulminant myocarditis and systemic hyperinflammation temporally associated with BNT162b2 mRNA COVID-19 vaccination in two patients

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ARTICLE INFO

Keywords:

Vaccine
Myocarditis
Coronavirus
Covid-19

ABSTRACT

Immune-mediated myocardial injury following Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV2) infection has been described in adults and children. Cases of myocarditis following immunization for SARS-CoV2 have recently been documented, mostly associated with mild severity and spontaneous recovery. We herein report two cases of fulminant myocarditis following BNT162b2 mRNA Covid-19 vaccination associated with systemic hyperinflammatory syndrome and refractory shock requiring support with veno-arterial extracorporeal membrane oxygenation.

Immune-mediated myocardial injury following Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV2) infection has been described in adults and children [1,2]. Cases of myocarditis following immunization for SARS-CoV2 have recently been documented [3–8]. We herein report two cases of fulminant myocarditis following BNT162b2 mRNA Covid-19 vaccination the show unique features of systemic hyperinflammation, already described in young males affected by Covid-19 [9]. The cases were reported to the Vaccine Adverse Event Reporting System of the Food & Drug Administration of the United States of America. Informed consent was provided by the next of kin.

A 27-year-old male with trisomy 21 complicated by speech impairment without history of cardiovascular disease presented in cardiogenic shock 2 days after his second vaccine dose. He had received the first dose without adverse effects. Approximately 36 h after the second dose, he developed nausea and vomiting. He presented to another hospital in shock (blood pressure 77/54 mmHg and heart rate 133/min) and found to have diffuse ST segment elevation in electrocardiogram (Fig. 1). Cardiac catheterization showed no coronary obstructions. Initially, creatine kinase myocardial band level (CK-MB) was 252 ng/mL (normal value [NV] < 5). Transthoracic echocardiogram showed severe left ventricular systolic dysfunction (LVEF 20%) and a small circumferential

pericardial effusion without tamponade. A diagnosis of presumed fulminant pericarditis was made and methylprednisolone 1000 mg and human immunoglobulin (IVIG) 60 g were given. The course was complicated by hemodynamically unstable ventricular tachycardia refractory to electrical cardioversion followed by pulseless electrical activity. He was resuscitated with veno-arterial extracorporeal mechanical oxygenation (VA-ECMO). After return of circulation, he was supported by multiple vasopressors, mechanical ventilation, and renal replacement therapy (RRT). Despite these interventions, multiorgan failure and refractory shock persisted. Lactic acid increased from 6 to 28 mmol/L (NV < 2), D-dimer increased from 4.21 to >20 µg/mL (critically high >5.0), INR increased from 2.0 to 10.0, and fibrinogen dropped to 100 mg/dL. C-reactive protein (CRP) and ferritin were highly elevated on admission at 13.1 mg/dL (NV < 0.5) and 23,000 ng/mL, respectively, leading to a decision to administer anakinra (Kineret®). Interleukin-6 level eventually came back highly elevated at 333 pg/mL (NV < 13). Thrombocytopenia developed progressively from $223 \times 10^9/L$ to $21 \times 10^9/L$, while hemoglobin decreased from 11.5 to 8.7 g/dL. The patient demonstrated acute liver injury (ALI) with alanine transferase (ALT) and aspartate transferase (AST) at 7995 and 9003 u/L. Polymerase chain reaction (PCR) for SARS-CoV2 and other common respiratory viruses more

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<https://doi.org/10.1016/j.ijcard.2021.08.018>

Received 17 June 2021; Received in revised form 10 August 2021; Accepted 12 August 2021

Available online 18 August 2021

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