

**742 Myocarditis after SARS-CoV-2 vaccine: is that so simple?**

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SARS-CoV-2 vaccination is associated with potential side effects, particularly following second vaccine dose. Recent case series have reported a potential association between SARS-CoV-2 vaccination and acute myocarditis, predominantly in young males. We hereby describe a previously healthy 17-year-old man, with no past cardiac history, who presented to the emergency department with persistent chest pain and fever (up to 38°C). The patient had received the first dose of Cominarty (BioNTech/Pfizer) vaccine 10 days before symptom onset and reported flu-like symptoms and conjunctivitis involving both eyes one week before administration of the first vaccine dose. On that occasion, no COVID test was performed and the patient was treated with anti-inflammatory drugs and antibiotic eye drops. On admission, laboratory tests were performed (Troponin-I  $\Delta$  19 500-23 270 ng/l, CRP 23 mg/dl, ESR 43 s, WBC 17 570 cell/mm<sup>3</sup>) as well as COVID-19 PCR, Serological tests and Autoimmune disorders panel all resulting negative. CT coronary angiogram did not reveal any spontaneous coronary artery dissection or anomalous origin of coronary arteries and Calcium Score was 0. Transthoracic echocardiography showed a depressed LVEF (36%) with concomitant posterior and inferior wall as well as posterior and anterior basal interventricular septum hypokinesia. Endomyocardial biopsy revealed multifocal lymphocytic myocarditis with sub-endomyocardial and interstitial fibrosis. CMR was also performed (1-week after presentation) demonstrating mildly depressed systolic function (LVEF 47%), with hypokinesia of the posterior and

inferior wall, increased signal intensity on T2 maps (58 ms, n.v. <55 ms), prolonged native T1 values (1083 ms, n.v. <1030 ms) as well as subepicardial and intramyocardial LGE enhancement of infero-lateral segments reflecting intercellular fibrosis. Thereafter, the patient was discharged with medical therapy including ACE-inhibitor, colchicine, and ibuprofen. Given the close proximity between SARS-CoV-2 vaccine administration and the absence of other predisposing conditions, the aetiology of myocarditis was attributed to the vaccine. In addition, as the patient suffered from flu-like symptoms and conjunctivitis 1 week before the vaccine, a previous paucisymptomatic SARS-CoV-2 infection was suspected and anti-SARS-Coronavirus Nucleocapsid Protein antibody test revealed high antibody levels with low IgG avidity. Given that myocarditic symptoms evolved after complete Sars-Cov2 symptom resolution, our first hypothesis is that the infection is unlikely to be the cause of acute myocarditis in this patient. Indeed, current literature on COVID-related myocarditis reports close temporal association between respiratory symptoms and myocarditis onset. In support to our hypothesis, recent trials have reported that myocarditis more frequently occurs following administration of mRNA vaccines especially in male adolescents and young adults like our patient. However, cardiac side effects typically occur after full vaccination and symptoms appear within three days following the second dose, which does not fully apply to this case. Notwithstanding this, more recent studies have reported myocarditis even after first vaccination dose in patients with previous COVID-19 infection, analogously to the case described. This case suggests a complex interaction between immunological factors and covid infection/vaccination with potential significant implications on the cardiovascular system. From current literature, much uncertainty remains regarding time interval criteria for reliable post-vaccination myocarditis diagnosis, hence large-scale clinical trials are needed to address this issue.