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Brief reports

Acute Myocarditis after COVID-19 vaccination: A case report

Myocardite aiguë après vaccination au COVID-19 : à propos d'un cas



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ABSTRACT

Introduction. – The etiology of myocarditis often remains undetermined. A large variety of infectious agents, systemic diseases, drugs, and toxins can cause the disease. We report the case of a 19-year-old man who developed myocarditis three days after Pfizer-BioNTech COVID-19 booster vaccination.

Case report. – A 19-year-old man, presenting with troponin-positive acute chest pain, was referred to our department. He had received the Pfizer-BioNTech COVID-19 vaccine three days prior to his admission. The diagnosis of acute myocarditis was confirmed by cardiovascular magnetic resonance imaging. Patient hemodynamic status remained stable during hospitalization. The left ventricular ejection fraction was preserved during hospital stay and at one-month follow-up. We found no evidence for another infectious or autoimmune etiology.

Conclusion. – Although imputability of the vaccine cannot be formally established on the basis of this case report, the findings raise the possibility of an association between mRNA COVID-19 vaccination and acute myocarditis.

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R É S U M É

Introduction. – L'étiologie des myocardites reste souvent indéterminée. Une grande variété d'agents infectieux, de maladies systémiques, de médicaments et de toxines peuvent causer la maladie. Nous rapportons le cas d'un homme de 19 ans ayant développé une myocardite trois jours après une vaccination de rappel Pfizer-BioNTech COVID-19.

Observation. – Un homme de 19 ans, présentant une douleur thoracique aiguë avec élévation significative de la troponine, a été adressé à notre service. Il avait reçu le vaccin Pfizer-BioNTech COVID-19 trois jours avant son admission. Le diagnostic de myocardite aiguë a été confirmé par une imagerie par résonance magnétique cardiaque. L'état hémodynamique du patient est resté stable pendant l'hospitalisation. La fraction d'éjection du ventricule gauche a été préservée pendant l'hospitalisation et lors du suivi à un mois. Nous n'avons trouvé aucune preuve d'une autre étiologie infectieuse ou auto-immune.

Conclusion. – Bien que l'imputabilité du vaccin ne puisse être formellement établie sur la base d'un cas clinique, ces résultats soulèvent une possible association entre la vaccination par le mRNA COVID-19 et la myocardite aiguë.

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1. Introduction

On December 11, 2020, the U.S. Food and Drug Administration issued the first emergency use authorization (EUA) for a vaccine preventing from coronavirus disease 2019 (COVID-19) resulting in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). BNT162b2 mRNA Covid-19 Vaccine (Pfizer-BioNTech) was then the first to be distributed. The most commonly reported side effects were typically tiredness, headaches, muscle pain, fever, and other severe adverse events were also noted as paroxysmal ventricular arrhythmia, hypertensive crisis, and right leg paresthesia [1].

However, myocarditis, which has been previously reported with other virus strains vaccinations [2], was not recorded in this pivotal efficacy trial.

Since April 2021, there have been more than a thousand myocarditis and pericarditis reports to the Vaccine Adverse Event Reporting System (VAERS) happening after mRNA COVID-19 vaccination (Pfizer-BioNTech, Moderna) in the United States. These reports are rare, given the hundreds of millions of vaccine doses administered, and have been reported after the second dose particularly in adolescents and young adults [3].

We report the case of a 19-year-old man who developed myocarditis three days after Pfizer-BioNTech booster vaccination.

2. Case presentation

A 19-year-old Caucasian man with no prior medical history or cardiovascular risk factor, presented with an acute sharp chest pain, altered by breathing and posture, without dyspnea or palpitation. Three days earlier, he had received for professional purpose his second dose of Pfizer-BioNTech COVID 19 vaccine. The first day following vaccination, he presented influenza-like illness, with headache and asthenia.

There was no hemodynamic or respiratory failure upon admission. Heart rate was normal without heart murmur but with muffled heart sounds. The rest of physical examination did not show any anomaly. There was no fever.

Electrocardiography demonstrated a sinus rhythm without atrioventricular conduction defects. The electrocardiogram showed a persistent ST elevation without reciprocal depression (Fig. 1).

Transthoracic echocardiogram revealed a preserved left ventricular ejection fraction estimated at 72% by biplane Simpson method. Left ventricular global longitudinal strain was -19.5%. There was no pericardial effusion. No significant mitral or aortic regurgitation were noted, and the filling pressure of the left ventricle was normal (Fig. 2).

Upon arrival, Hs-troponin T was elevated at 600 ng/mL (reference level < 14 ng/mL) and creatinine phosphokinase at 399 UI/L (reference level < 300 UI/L). There was a mild elevation of C-Reactive protein at 59 mg/mL (reference level < 6 mg/L). The hemogram was normal. NT pro BNP was moderately elevated at 270 ng/mL (reference level < 125 pg/mL).

COVID-19 Polymerase Chain Reaction (PCR) testing and Influenza RT-PCR testing were negative. Nucleocapsid Covid-19 serology was negative. Viral serologies including, cytomegalovirus, adenovirus, HIV, Hepatitis C virus, Parvovirus B19 and P24 antigenemia were also negative. Epstein-Barr-Virus serology showed immune profile with negative EBNA-IgG and positive VCA-IgG. The patient was already efficiently vaccinated against Hepatitis B virus and seasonal flu. Blood cultures were sterile. Antiphospholipid autoantibodies, auto antinuclear antibodies, rheumatoid factor, and anti-neutrophil cytoplasmic antibodies detection test were negative.

Myocarditis was confirmed by cardiac magnetic resonance imaging (CMR) showing lateral subepicardial high signal intensity

(SI) in the LV myocardium on T2 short tau inversion recovery image, suggesting myocardial wall oedema. A subepicardial late gadolinium enhancement in the middle to apical lateral LV segments was also observed. These results satisfied two of the three Lake Louise tissue criteria for myocarditis diagnosis [4]. The left ventricle was nondilated (end-diastole volume is 45 mL/m² and the end-systole volume is 14 mL/m² with a 69% ejection fraction). No myocardial or wall thickening, or pericardial effusion was notified.

No ventricular rhythm disorders were reported during evolution, and chest pain resolved spontaneously the day after admission. Hemodynamic and respiratory status remained stable throughout the hospitalization. Cardiac enzymes returned to normal on the day of discharge. No further medication was prescribed.

Our case was reported to The National Agency for the Safety of Medicines and Health Products (*L'Agence nationale de sécurité du médicament et des produits de santé* or ANSM).

At one-month follow-up, the patient remained asymptomatic, with normal ECG and echocardiography.

3. Discussion

Acute myocarditis is frequently first diagnosed as nonischemic dilated cardiomyopathy in a patient with symptoms that have been present for a few weeks to several months [5]. However, manifestations range from subclinical disease to sudden death, with new-onset atrial or ventricular arrhythmias, complete heart block, or an acute myocardial infarction-like syndrome. Prodromes with fever, myalgia, and respiratory or gastrointestinal symptoms could be associated with myocarditis, but reported symptoms are highly variable.

Viral infection has been described as one of the most common causes of myocarditis, especially influenza and parvovirus B19 infection.

Although the etiology of myocarditis often remains undetermined, a large variety of infectious agents, systemic diseases, drugs, and toxins can cause the disease. Diagnosis may be supported by an electrocardiogram, increased troponin and occasionally an endomyocardial biopsy. Cardiovascular magnetic resonance (CMR) has become the primary tool for noninvasive assessment of myocardial inflammation in patients with suspected myocarditis.

It is essential to rule out other possible causes of the presentation, specifically acute coronary syndrome and other cardiovascular or extra-cardiac non-inflammatory diseases that could explain the clinical presentation. In this case, given the young age and absence of risk factors for coronary arterial disease, left heart catheterization was not performed.

Although clinical presentation, CMR findings, and temporal association suggest the possibility of vaccine-associated myocarditis, we cannot state formally about the imputability of COVID-19 vaccine, and we cannot exclude an undiagnosed infectious agent.

Similarly to our patient, most reported cases describe young male patients, with no past cardiac medical history, presenting with chest pain within a few days after their second vaccine dose of COVID-19 vaccine and finally diagnosed with myocarditis [6].

Vaccines against COVID-19 have been developed at unprecedented speed, with phase 3 clinical efficacy trials providing results less than a year after pandemic declaration [3]. This allowed some vaccines including Pfizer-BioNTech to be authorized by regulators since December 2020. The benefits of these vaccines in this pandemic context seem to outweigh the risks. As a result, large-scale vaccination programs are underway around the world, despite the possible link to rare diseases such as myocarditis or other potentially fatal side effects such as blood clots.

Several reports of myocarditis have already been associated with DTaP (diphtheria, tetanus, acellular pertussis) influenza

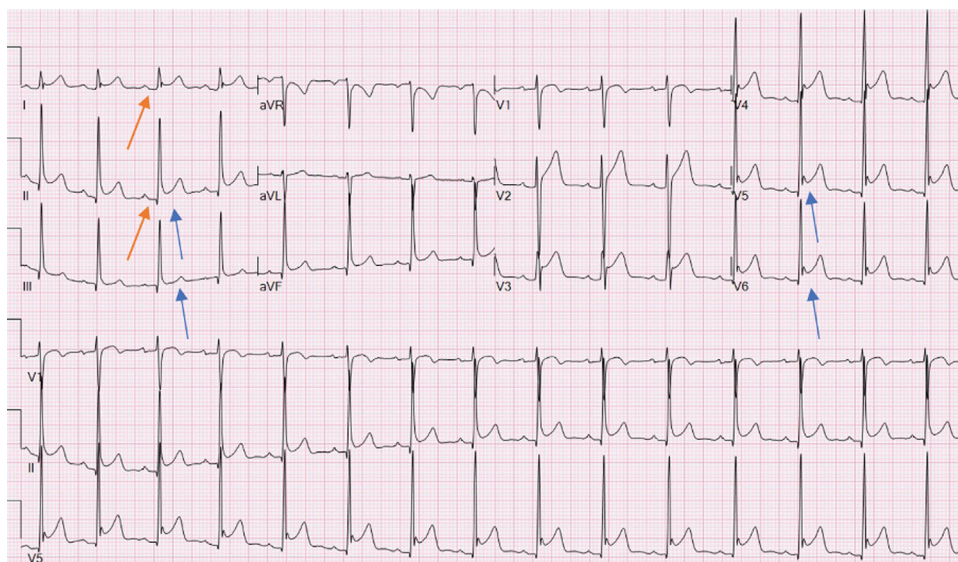


Fig. 1. Electrocardiogram in sinus rhythm showing a PR depression in inferior leads (orange arrows) and a persistent concave ST elevation (blue arrows) without reciprocal depression.

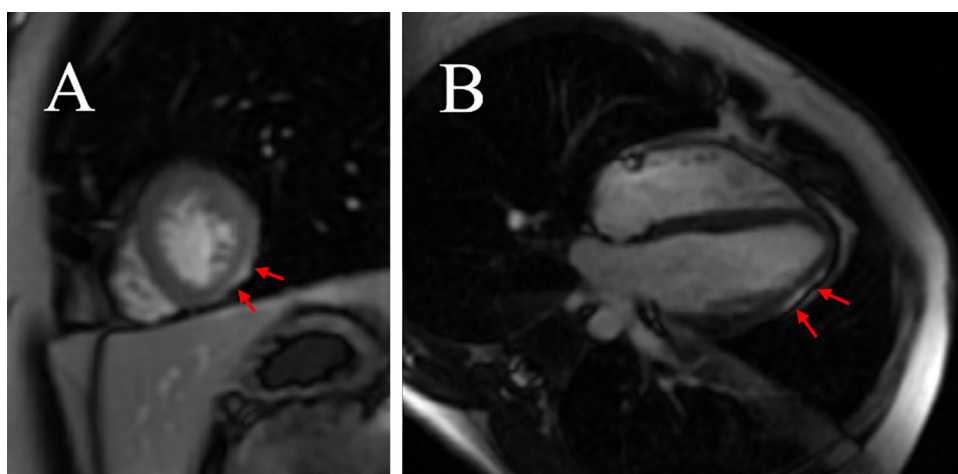


Fig. 2. Cardiac magnetic resonance imaging short axis (A) and four chamber (B) views with late gadolinium enhancement sequences identifying a lateral subepicardial enhancement.

or smallpox vaccines [2]. Although the mechanism remains unclear, it may potentially involve epitopic mimetism between a vaccinal antigen and myocardium proteins, in addition to immune-stimulatory effects of the vaccine adjuvant [7].

Messenger ribonucleic acid (mRNA) COVID-19 vaccine is a type of vaccine that uses a copy of a mRNA, encoding for the SARS-CoV-2 full-length spike, to induce humoral and cellular immunity. It then uses the host cell's translational machinery to produce the target antigen and initiate an adaptive immune response [8].

This response triggers the activation of several pro-inflammatory cascades, including the type I interferon (IFN-I) response and nuclear translocation of the nuclear factor kappa B (NF- κ B). [8].

The potential of vaccines to act as triggers for autoimmune reactions has been highlighted. That hypothetical mechanisms are not fully elucidated, but they could involve both an epitopic mimicry between vaccine antigen and self-antigen and a cascade of immunological events leading to aberrant activation of the innate and acquired immune system [9].

The first reports of myopericarditis cases after the Pfizer vaccine came from Israel at the end of April 2021 [10]. A total of 275 cases of

myocarditis were reported in Israel between December 2020 and May 2021 among more than five million vaccinated people. Most of the cases concerned men aged 16–19, usually after the second dose of vaccine.

The Vaccine Adverse Event Reporting System (VAERS) had received 1226 preliminary reports of myocarditis and pericarditis after about 300 million doses of the Pfizer and Moderna vaccines up to June 11th [11].

In May 2021, concerns about possible cases of myocarditis following COVID-19 vaccination were raised by the European Medicines Agency safety committee. As of 31 May 2021, 145 cases of myocarditis in the European Economic Area (EEA) have been identified among 177 million people who received Pfizer-BioNTech COVID-19 vaccine.

Recently, a French study analyzed 1251 reports of myocarditis involving a vaccine suspected of causing myocarditis in the international pharmacovigilance Vigibase [12]. Among these latter reports, 214 (17.1%) were related to the COVID-19 vaccines. Only messenger ribonucleic acid (mRNA) COVID-19 vaccines, including mRNA1273 (Moderna), and Tozinameran (Pfizer/BioNTech) were significantly associated with myocarditis.

Thus, we report a case of myocarditis with no identified infectious or autoimmune etiology, and with consistent temporal association to mRNA COVID-19 vaccine. The presentation pattern and clinical course suggest an association with an inflammatory response to vaccination, without formal evidence.

Although the actual incidence of myocarditis following mRNA COVID-19 vaccines still remains unclear, this calls for caution regarding the potential adverse cardiovascular effects including in young patient. However, we emphasize that this is a rare potential adverse event, which does not alter the highly favorable risk/benefit ratio of COVID-19 vaccination, and should not prevent vaccination, particularly in patients with underlying heart disease or cardiomyopathy.

Disclosure of interest

The authors declare that they have no competing interest.

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