European Review for Medical and Pharmacological Sciences 2022; 26: 5978-5982

The complexity of immunology: a rare adverse event following a Pfizer-BioNTech vaccine booster shot

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Abstract. – OBJECTIVE: Several mRNA vaccines have been developed to tackle the global pandemic. Despite their remarkable clinical efficacy, they are not devoid of severe short- and long-term adverse events.

CASE PRESENTATION: In this paper, we describe a rare delayed adverse event (arterial and venous renal thrombosis with myocardial injury) in an otherwise healthy adult female, which occurred three months after she received a booster shot of Pfizer COVID-19 vaccine. The patient was successfully treated for subacute renal ischemia with intra-arterial urokinase, and her myocardial injury was diagnosed with imaging (contrast-enhanced thoracic CT and cardiac magnetic resonance) and percutaneous coronary intervention. Deferred post-vaccine myocarditis was diagnosed and resolved with steroid therapy.

CONCLUSIONS: In this paper, we report a useful clinical case for the pharmacovigilance database. Although scientific evidence confirms that the benefits of vaccination far outweigh the risk of adverse events, we would like to point out how important watchful observation is in the medium and long term, especially when the subject belongs to a specific risk category.

Key Words:
mRNA vaccine, Myocarditis, Delayed adverse events.

Introduction

The global pandemic has led to the development of several mRNA vaccines with remarkable clinical efficacy, including BNT162b2 (Pfizer COVID-19 vaccine) and mRNA-1273 (Moderna COVID-19 vaccine). However, the use of these vaccines on a wide-ranging population has noticeably increased the risk of unknown severe long- and short-term adverse events.

In this paper, we report a rare delayed adverse event in an otherwise healthy adult female, which occurred three months after she received a booster shot of BNT162b2 SARS-CoV-2 vaccine.

Case Presentation

A 72-year-old woman was admitted to our Emergency Department (ED) with a contrast-enhanced CT abdominal scan performed elsewhere for persistent lumbar pain which had developed over the previous two weeks. The scan revealed left renal artery and vein thrombosis complicated by renal hypoperfusion.

Her medical history included fibromyalgia, ophthalmic migraine, essential arterial hypertension, and heterozygosity for Factor V Leiden (FVL) without thromboembolic arterial events or adverse pregnancy outcomes. She had no history of smoking or obesity (normal body mass index – 21 kg/m^2) and had been fully vaccinated against COVID-19 (booster dose of BNT162b2 SARS-CoV-2 received 92 days earlier).

She was hemodynamically stable and complained persistent lumbar pain. Her blood test results were normal, except for an increase

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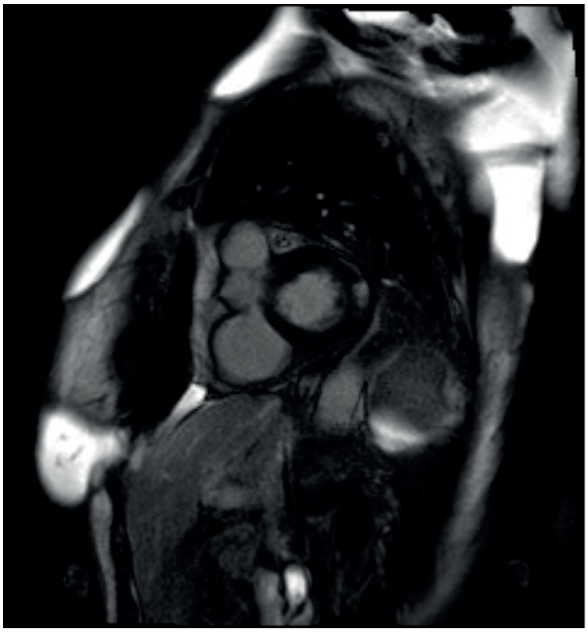

Figure 1. T2 weighted CMR: myocardial subepicardial edema in the lateral segment.

in NT-proBNP (2,572 pg/ml, range 0-125), high-sensitivity (HS) troponin (369 pg/ml, range 0-57), and pancreatic enzymes (amylase 246 U/L, range 11-54; lipase 248 U/L, range 0-50).

An electrocardiogram (ECG) gave normal results apart from non-specific repolarization abnormalities. The patient was treated for subacute renal ischemia with intra-arterial thrombolysis using urokinase, a recombinant tissue plasminogen activator (rTPA), which led to a positive outcome with complete recanalization of the left renal artery and no clinical or laboratory signs of bleeding (hemoglobin, hematocrit, platelets, partial thromboplastin time, and fibrinogen levels were monitored). Treatment for deep vein thrombosis was then continued with an anticoagulant (low molecular weight heparin – LMWH enoxaparin), and she was referred to our Emergency Medicine Ward for further diagnostic investigations.

The laboratory tests performed documented isolated non-specific neutrophilic leukocytosis (wbc 19.050/mm^3, N 12.450/mm^3), mild multifactorial anemia (Hb 10.9 g/dl, MCV 92 fl, with iron deficiency and signs of chronic inflammation), absence of anti-phospholipid antibodies (lupus anticoagulant, anticardiolipin, and anti-beta2 glycoprotein I), and a moderate non-specific rise in plasma homocysteine (19.5 micron/L, range 5-15), with a progressive, significant, fully asymptomatic, serum cardiac troponin increase (zenith 110.180 pg/ml, nadir 254 pg/ml).

The relevant myocardial injury was investigated through a contrast-enhanced thoracic CT scan, which excluded pulmonary embolism, and through transthoracic echocardiography, which revealed a normal sized left ventricle with basal and lateral hypokinesia associated with grade II diastolic dysfunction. On the assumption that the patient had a coronary artery disease, she underwent radial artery catheterization for a coronary angiography which was negative for critical stenoses. A local procedural complication developed characterized by right radial erythromelalgia with a local superficial thrombosis, which receded over time.

A cardiovascular magnetic resonance (CMR) scan was then carried out for a suspected deferred post-vaccine myocarditis, which revealed a diagnostically significant high native T2 value (a quantitative marker of edema) in the parenchyma (Figure 1). Steroid therapy was therefore initiated, which gave rise to clinical and laboratory improvement. In the end, the patient was discharged with anticoagulant therapy for her thrombotic history and continued a ta-

pering oral steroid therapy for her myocardial inflammation. The outcome was positive both objectively and radiologically: the second CMR scan was normal (Figure 2).

Discussion

The introduction of vaccines has led to greater protection against the severe forms of COVID-19 and resulted in a sharp reduction in severe cases[1,2]. The effectiveness of the first two shots of vaccine wanes over time, especially against infection with the Omicron variant. Therefore, a booster shot (a third shot given five months after the first two) can further reduce the risk of symptomatic infection in eligible patients[3].

Vaccine recipients are always informed of the immediate side effects (local and systemic reactions including pain at the injection site, headache, fever, and fatigue), but they are not always told about the possibility of medium to long term events, since these are not always predictable[4].

Scientific evidence has shown that mRNA COVID-19 vaccines may increase the risk of myocarditis and thrombotic events [the latter appears to be less severe than the effects associated with the adenoviral vector vaccine (Ad26.COV2.S Janssen COVID-19 vaccine)][5].

Arterial thrombotic and venous events have been specifically described. The first category (primarily stroke and acute myocardial infarction) is more frequent than the latter (mainly pulmonary embolism and deep vein thrombosis), with coexistence being rare[6]. The clinical outbreak mostly occurs within 20 days from the first dose and 10 days after the second[7]. Raw data concerning adverse events following the booster shot are being collected and there is evidence of idiopathic thrombocytopenic purpura[8].

The risk of post-vaccine myocarditis appears to be directly proportional to the number of shots (the risk after the second dose is greater than after the first) and occurs within the first month[9].

Similarly, myocardial inflammation following the booster dose has been predominantly correlated to Pfizer COVID-19 vaccine in men under 40 years of age[10].

In this paper, we report a useful clinical case for the pharmacovigilance database, especially concerning the adverse side effects caused by booster doses (not yet completely available). In particular, not only did the symptoms emerge in our patient with a three-month delay (a rare

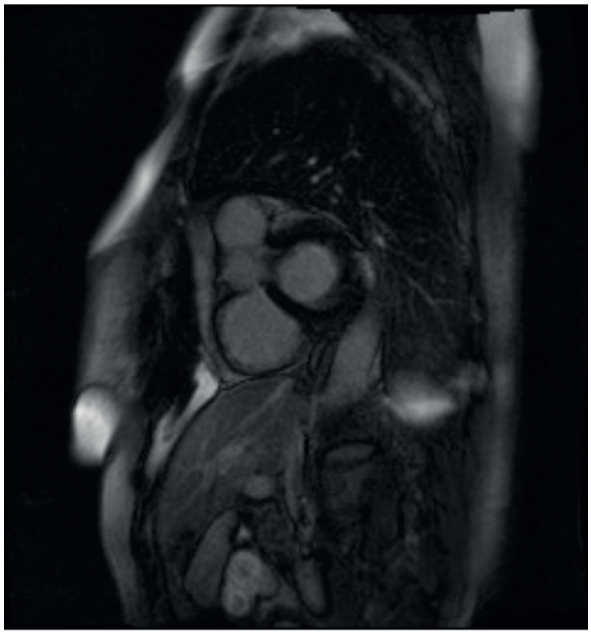

Figure 2. T2 weighted CMR: resolution of the Myocardial subepicardial edema.

occurrence considering that most thromboembolic events from mRNA vaccines arise in the first week) but a concomitant left renal artery and venous thrombosis was also detected. This association has not yet been mentioned in the current literature. Since our patient has a heterozygosity for FVL, she could certainly be regarded as being susceptible when compared with the normal population.

Conclusions

Although scientific evidence confirms that the benefit of vaccination far outweighs the risk of adverse events, we would like to point out, throughout our clinical case, how important watchful observation is in the medium and long term, especially when the subject belongs to a specific risk category. This is fundamental since the prevention and/or prompt recognition of a possible harmful inflammatory reaction is crucial when seeking the most effective possible treatment.

Funding
This research received no financial support.

Conflict of Interest
There are no conflicts of interest.

Consent for Publication
This manuscript is original, has not been published before, and is not being considered for publication elsewhere.

Informed Consent
The patient signed a written informed consent before publishing the study.

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