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# Case report: COVID-19 mRNA vaccine association with acute myocarditis

Reporte de caso: asociación de vacuna COVID-19 mRNA con cuadro de miocarditis aguda

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# **Keywords:**

Acute myocarditis, COVID-19, mRNA vaccine, ESAVI.

## Palabras clave:

Miocarditis aguda, COVID-19, vacunas mRNA, ESAVI.

# **ABSTRACT**

A 50-year-old woman presented to the Emergency Department with chest pain, the elevation of cardiac enzymes, and no electrocardiographic alterations. Coronary angiography was performed in which no obstructive lesions were found. A cardiac magnetic resonance study reported an image consistent with acute myocarditis without evidence of myocardial ischemia. The patient received the first dose of Pfizer-BioNTech vaccine two days before the onset of symptoms. In most cases of myocarditis, its clinical manifestations lie in a wide spectrum, and the etiological diagnosis is indeterminate. In recent months, the probable association between cases of myocarditis with COVID-19 mRNA vaccines has been established. The use of the COVID-19 mRNA vaccine has demonstrated significant benefits in reducing morbidity and mortality related to SARS-CoV-2 virus infection. This event may be a transitory process that does not represent a contraindication for the application of the vaccine.

# RESUMEN

Se presenta el caso de una mujer de 50 años atendida en el Servicio de Urgencias por dolor torácico y elevación de enzimas cardiacas; no tuvo alteraciones electrocardiográficas. Se realizó coronariografía en la que no se encontraron lesiones obstructivas. Un estudio de resonancia magnética cardiaca reportó imagen compatible con miocarditis aguda sin evidencia de isquemia miocárdica. La paciente había recibido una primera dosis de vacuna Pfizer-BioNTech dos días antes de la aparición de los síntomas. En la mayoría de los casos de miocarditis, el diagnóstico etiológico se encuentra indeterminado y sus manifestaciones clínicas tienen un amplio espectro. En los últimos meses, se ha establecido la asociación probable entre casos de miocarditis con vacunas COVID-19 mRNA. El uso de vacunas COVID-19 mRNA ha demostrado el beneficio significativo en la reducción de morbilidad y mortalidad relacionadas a la infección por el virus SARS-COV-2. Este puede ser un proceso transitorio que no representa una contraindicación para la aplicación de la vacuna.

# **INTRODUCTION**

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Received: 24/09/2021 Accepted: 22/02/2022 Myocarditis is an inflammatory disease of the myocardium, defined according to the World Health Organization (WHO) by histological, immunological, and histopathological criteria. Although the etiological diagnosis of a myocarditis picture is mostly indeterminate, a wide variety of infectious agents (especially viral infections), systemic diseases, drugs and toxins can cause the disease with a broad spectrum of

manifestations. The clinical manifestations range from subclinical disease to chest pain similar to the one caused by acute coronary syndrome or pericarditis. Myocarditis can even be complicated by the development of cardiogenic shock or sudden death from lethal arrhythmias.<sup>2</sup> In recent months, the probable association between cases of myocarditis with COVID-19 mRNA vaccines has been established. The use of the COVID-19 mRNA vaccine has demonstrated significant benefit in reducing morbidity and mortality related

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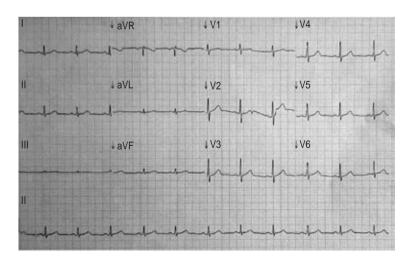
to SARS-CoV-2 virus infection. Multiple manifestations of side reactions to the vaccine have been described, such as the development of myocardial inflammation seen in this case.

# **CASE PRESENTATION**

A 50-year-old female patient with a history of systemic high blood pressure and smoking was treated in the Emergency Department. She presented oppressive chest pain of sudden onset unrelated to physical exertion, with irradiation to the lower jaw and left arm (intensity 10/10 visual analogue scale) accompanied by nausea and vomiting of gastric content.

In the initial evaluation, hours after the onset of symptoms, the patient was unchanged on physical examination, and the 12-lead electrocardiogram was normal (Figure 1). Initial laboratory tests highlighted elevation of troponins (high-sensitivity troponin 281 pg/mL) with a significant marker increase at two hours (hsTropT 441 pg/mL). With the clinical picture of angina and the increase in cardiac enzymes, the initial diagnosis was established of non-ST-segment elevation myocardial infarction (NSTEMI). The patient had received the first dose of COVID-19 Pfizer-BioNTech vaccine two days before the onset of symptoms.

The antithrombotic treatment was initiated (aspirin, clopidogrel and anticoagulation with enoxaparin), atorvastatin, metoprolol and



**Figure 1:** Initial electrocariogram (ECG). Normal ECG, without signs of myocardial ischemia.

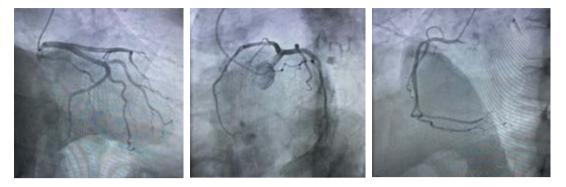
enalapril as part of the protocol established by NSTEMI management guidelines. Diagnostic coronary angiography (Figure 2) was performed, in which no significant angiographic lesions were found in epicardial arteries. Once the existence of obstructive coronary lesions as the cause of the myocardial injury had been ruled out, cardiac magnetic resonance imaging was performed (Figure 3). The process of acute myocarditis was observed, and a preserved biventricular function; myocardial ischemia was discarded.

With this information, the diagnosis of acute myocarditis was integrated; a treatment previously indicated for the management of NSTEMI was discontinued. The subsequent evolution was towards clinical improvement; the patient not develops heart failure and was discharged home with a diagnosis of acute myocarditis.

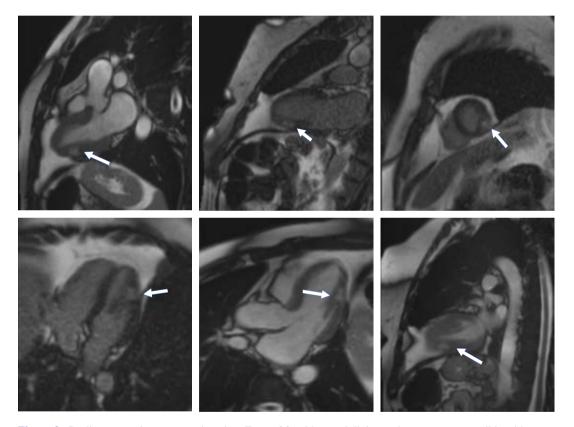
# **DISCUSSION**

Myocarditis affects individuals of all ages with a predominance of young people.3 In all cases of this inflammation, it is necessary to exclude coronary artery disease or other cardiovascular diseases that could explain the clinical manifestations. Electrocardiographic manifestations are nonspecific and may include concave elevation of the ST segment, atrioventricular block, increased duration of the QRS complex, alterations (if any) of repolarization. The elevation of troponins is also frequent because it causes acute myocardial damage.<sup>2</sup> Based on the clinical picture, electrocardiographic alterations, and the elevation of troponins, it is not uncommon for myocarditis to be initially classified as an acute coronary syndrome.

Although the gold standard for the diagnosis and definition of myocarditis requires an endomyocardial biopsy for histopathological study, it is only recommended in some cases. A significant percentage of patients with myocarditis are diagnosed with non-invasive imaging studies in conjunction with the clinical picture and laboratory studies. Cardiac magnetic resonance imaging is a valuable tool in the diagnosis of this pathology because it detects of inflammation, edema, necrosis, and fibrosis in myocardial tissue.<sup>4</sup>



**Figure 2:** Coronary angiography. Coronary arteries without significant stenosis, thrombolysis in myocardial infarction (TIMI) 3 flow.



**Figure 3:** Cardiac magnetic resonance imaging. Zone of focal late gadolinium enhancement compatible with acute myocarditis (arrows).

Because of the absence of a clear etiology, the antecedent of having received the Pfizer-BioNTech vaccine two days before the onset of symptoms was considered the causative agent of the myocarditis in this case. Although a significant percentage of the acute myocarditis cases do not demonstrate a definite etiology,

it is important to emphasize that, recently, an association has been suggested between cases of myocarditis and COVID-19 mRNA vaccines, including the Pfizer-BioNTech vaccine.<sup>5</sup>

Case events reported in the literature have usually appeared after the application of the second dose of COVID-19 mRNA vaccine;

the clinical manifestations include chest pain two to three days after the vaccine is applied. Most patients described in these publications were young men who required hospitalization for myocarditis; none of them had a history of other illnesses or a COVID-19 infection. All the patients presented an elevation of cardiac enzymes. The cardiac magnetic resonance study results were compatible with myocarditis. It is important to emphasize in the very low incidence of myocarditis associated with mRNA vaccines. In the larger series, after approximately 300 million COVID-19 mRNA vaccine doses were administered, there were 1,226 reports of probable myocarditis/ pericarditis, 67% of which followed the second dose, making it a rare adverse event.<sup>6</sup>

The Institutional Center for Pharmacovigilance was informed of the case, which was evaluated as an event allegedly attributable to vaccination or immunization. The case was considered as serious and with a causality association consistent with the a vaccine-related event, according to the Manual of Standardized Procedures for epidemiological Surveillance of Events Allegedly Attributable to Vaccination or Immunization (ESAVI), version 2021.<sup>7</sup> The case was reported to the corresponding health authority in the national ESAVIs reporting system.

# **CONCLUSIONS**

The case of a diagnosed patient with acute myocarditis and a history of COVID-19 vaccination close to the onset of symptoms is reported. A causal relationship between vaccination and myocarditis can be attributed here because there is a temporal relationship between vaccine administration and the appearance of ESAVI with no other underlying cause. Of note, there is consistency with similar reports in the literature. It is important to

continue monitoring future cases closely and reporting similar ESAVIs in a timely manner to establish whether a pharmacovigilance signal exists.

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