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CASE REPORT

INTERMEDIATE

CLINICAL CASE

Acute Myocarditis

A New Manifestation of Monkeypox Infection?

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ABSTRACT

A 31-year-old male patient with confirmed monkeypox infection developed acute myocarditis days after the eruption of skin lesions. Cardiac magnetic resonance study confirmed myocardial inflammation. The patient was treated with supportive care and had full clinical recovery. This case highlights cardiac involvement as a potential complication associated with monkeypox. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2022;4:1424-1428) © 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 31-year-old man presented to the clinic with a 5-day history of malaise, myalgias, and fever followed by the eruption of multiple swollen and umbilicated cutaneous lesions on his face, hands, and genitalia. He denied any other symptoms. Monkeypox infection was confirmed by a positive polymerase chain reaction assay of a swab sample from a skin lesion.

Three days later, the patient returned to the emergency department with chest tightness radiating to the left upper extremity that awoke him during the night.

On physical examination, he displayed several skin vesicles and pustules on his face, wrists, thighs (Figure 1), and genitalia, with one ulcerated lesion on his penis accompanied by painful swelling of the foreskin and glans and lymphadenopathy in the left inguinal area. The patient was afebrile and hemodynamically stable. Cardiopulmonary auscultation and the remaining physical examination were unremarkable.

LEARNING OBJECTIVES

- To recognize cardiovascular complications among patients with Monkeypox infection.
- To understand the role of cardiac magnetic resonance in the diagnosis of myocarditis and potential avoidance of invasive procedures.

PAST MEDICAL HISTORY

The patient was routinely followed in an infectious disease outpatient clinic and his only medication included preexposure prophylaxis against HIV because of sexual risk exposure (men who have sex with men).

His past medical history included a paucisymptomatic SARS-CoV-2 infection 2 months before this

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event, tobacco and, rarely, cannabis use, and he denied consumption of other illicit drugs, medication, or alcohol. There was no history of drug reactions or allergies.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included causes of thoracic pain, such as acute myocarditis and acute coronary syndrome.

INVESTIGATIONS

The initial electrocardiogram revealed sinus rhythm with nonspecific ventricular repolarization abnormalities (Figure 2). Chest x-ray showed a normal cardiothoracic index, and no interstitial infiltrates, pleural effusion, or masses (Figure 3). Transthoracic echocardiography displayed preserved biventricular systolic function and no pericardial effusion. Routine laboratory tests revealed elevated C-reactive protein (70 mg/L; normal level <3 mg/L), a creatine phosphokinase of 291 U/L (normal range: 10-172 U/L), a high-sensitivity troponin I of 6,000 ng/L (normal level <34 ng/L), and a brain natriuretic peptide of 155 pg/mL (normal level <100 pg/mL). Urine and blood toxicology tests were both negative.

The patient was admitted to an intensive care unit under airway isolation, with the clinical suspicion of acute myocarditis.

Because of the clinical stability of the patient, a cardiac magnetic resonance (CMR) (3-T Magnetom Vida Siemens) was performed 24 hours after admission. Cine acquisitions with b-steady state free precession sequences showed normal left ventricle (LV) wall thickness and volume (LV tele-diastolic index 80 mL/m^2; normal values [N]: 68-103 mL/m^2) without regional or global wall motion abnormalities and a LV ejection fraction of 56%. In T2-weighted images, areas of increased signal intensity in the basal inferior and lateral segments were found, corresponding to myocardial edema. Late gadolinium enhancement sequences revealed subepicardial enhancement in the mid inferolateral segment and midwall enhancement in the remaining inferior and lateral segments of the LV, findings compatible with necrosis. In addition, parametric mapping demonstrated regional increase of T2 (52 ms; N: 41 ± 2.8 ms) and T1 native (1,563 ms; N: 1,217 ± 36.5 ms) values and the calculated extracellular volume (44%; N: 26% ± 4%) indicated an abnormally expanded myocardial extracellular volume in the lateral wall. Postcontrast T1 mapping confirmed myocardial gadolinium accumulation (217 ms; N: 1,217 ± 36.5 ms) with a non-ischemic pattern in the lateral wall (Figure 4). There was no pericardial effusion nor abnormal uptake of the contrast by the pericardium. Overall, the CMR study was consistent with myocardial inflammation and the diagnosis of acute myocarditis was assumed by the presence of both major updated Lake Louise criteria.[1-4]

HIV, herpes simplex virus, syphilis, and hepatitis B and C serologies were negative. Serologies and polymerase chain reaction serum assays for the most common cardiotropic viruses were performed, the results being all negative. Thyroid function was

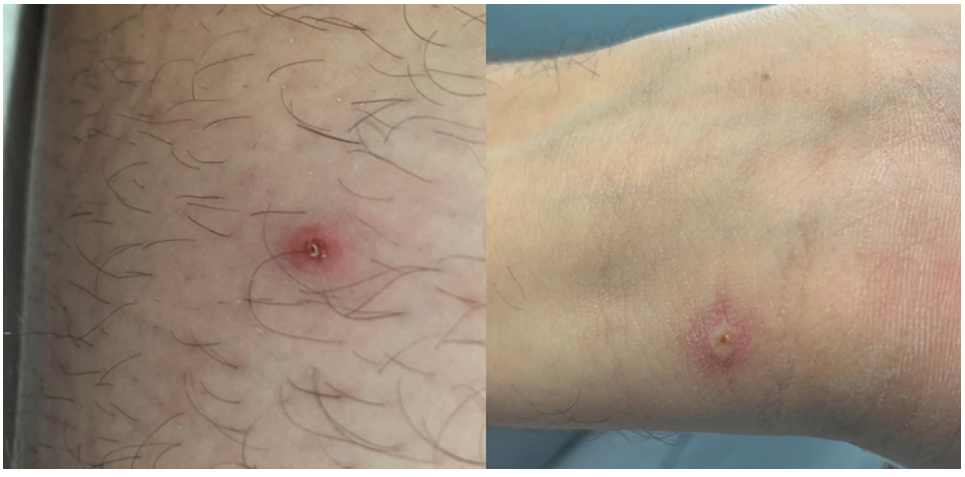
ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance

EMB = endomyocardial biopsy

LV = left ventricle

FIGURE 1 Monkeypox Skin Lesions



Vesiculopustular lesions on the patient's left thigh and left wrist.

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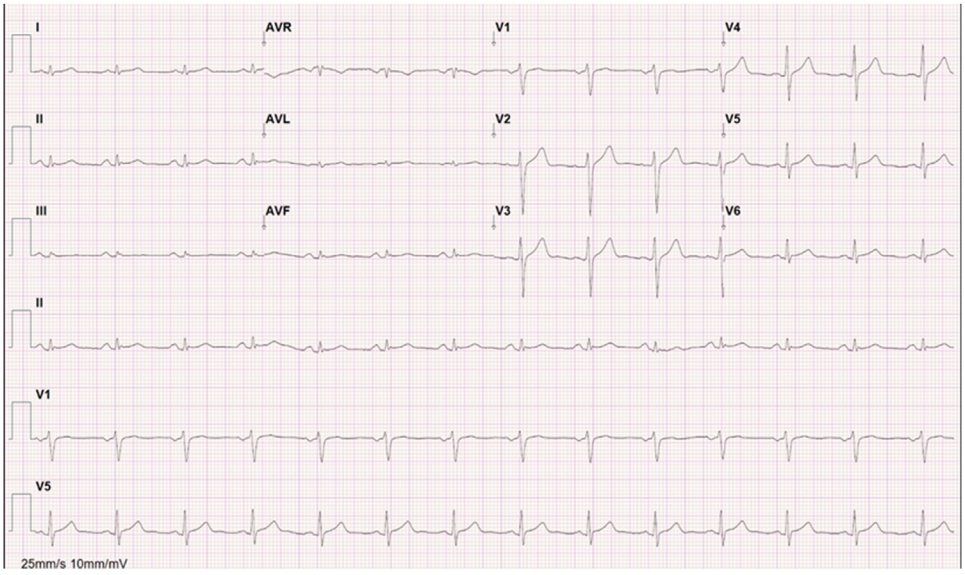
FIGURE 2 Admission Electrocardiogram



Electrocardiogram showed sinus rhythm with nonspecific ventricular repolarization abnormalities.

normal. Screening of antinuclear antibodies and rheumatoid factor was negative. Maximum high-sensitivity troponin I levels were 12,000 ng/L.

According to recent recommendations, given the clinical and hemodynamic stability of the patient and preserved biventricular systolic function, there was a low likelihood that endomyocardial biopsy (EMB) results would change medical decisions in this case. A clinical diagnosis of acute myocarditis was assumed without histological analysis.

MANAGEMENT

The patient was treated with supportive care and exercise restriction. Nonsteroidal anti-inflammatory drugs, in particular acetylsalicylic acid, were withdrawn.

DISCUSSION

Monkeypox virus is a zoonotic Orthopoxvirus, a genus that includes the now eradicated variola virus (smallpox), which caused 300 million deaths globally, and vaccinia, the virus used in smallpox vaccine.[5,6] Following the recent outbreak of monkeypox virus infection in nonendemic regions, the world's attention has been directed to the clinical manifestations of this disease.

Monkeypox typically causes a systemic illness that includes fever, lymphadenopathy, and myalgias, with a characteristic rash whose distinctive lesions often present first as macular, then papular, vesiculopustular, and, sometimes, ulcerative. Most infections are mild, and the clinical course is usually self-limited, with symptoms lasting from 2 to 4 weeks, even though disseminated infections with a high rate of complications and mortality, mostly in immunocompromised persons, have already been described in endemic areas.[5,6] The cases reported in the current outbreak in nonendemic countries since May 2022 are mainly clustered in men who have sex with men, many of whom presented with atypical anogenital and oropharyngeal lesions and favorable outcomes.[7]

In the past, infections with smallpox, a genetically related but more aggressive virus, were associated with myocarditis. Furthermore, cardiac complications of smallpox vaccination have been reported since the initiation of vaccination in the 1950s in Europe, including post-vaccinial myocarditis and myopericarditis.[8] By extrapolation, the related Monkeypox virus can have tropism for myocardium tissue or cause immune-mediated injury to the heart.

Myocarditis, an inflammatory disease of the myocardium, is a challenging diagnosis because of its heterogeneous clinical presentation and histological forms. Prognosis depends largely on etiology and disease stage, ranging from acute myocarditis that either resolves in weeks or progresses to persistent cardiac dysfunction, with the development of chronic

inflammatory cardiomyopathy, to fulminant myocarditis with hemodynamic compromise and need for cardiovascular support techniques. Viral myocarditis is often presumed when accompanied by a clinical picture of febrile illness, myalgias, and malaise, followed by rapid onset of cardiac symptoms.

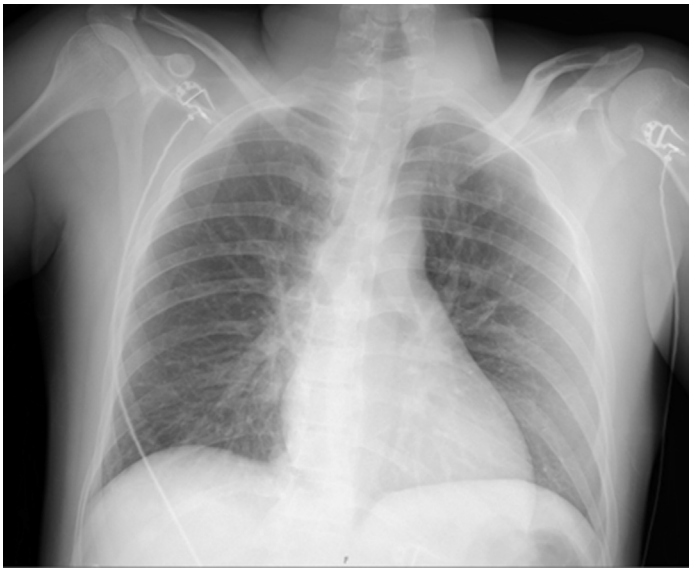
A combination of clinical presentation and noninvasive diagnostic findings including typical CMR abnormalities may be used to make a diagnosis of clinically suspected myocarditis.[9,10] EMB remains the gold standard for the definitive diagnosis of myocarditis; however, it is an invasive procedure that portends some risks with a relatively low sensitivity and etiological diagnostic yield, mainly due to the focal nature of inflammation in most cases. EMB is fundamental to identify the mechanisms and define the need for prompt therapy in specific clinical scenarios, such as acute myocarditis presenting as severe heart failure or cardiogenic shock, or complicated by severe myocardial dysfunction, ventricular arrhythmias, or high-degree atrioventricular block; acute myocarditis or chronic inflammatory cardiomyopathy with persistent or relapsing symptoms and biomarkers of myocardial necrosis; myocarditis associated with suspected or known autoimmune disorders or suspected specific subsets with individualized treatment, such as giant cell myocarditis; every time that appropriate diagnosis has implications for patient management, treatment, and prognosis.[9,10] In patients without indication for EMB, CMR is the noninvasive gold standard for the diagnosis.[1,3,4,9]

CMR has informed clinical decision making in our and many other patients and can avoid invasive procedures. CMR findings consistent with myocarditis should be based on the updated Lake Louise criteria.[1-4]

In patients with clinical suspected and confirmed myocarditis, the history and clinical presentation may suggest a specific etiology, but a definitive cause in often difficult to identify. Frequently the diagnosis is presumptive considering temporal related exposures and epidemiologic context.

Our patient presented with acute myocarditis temporally related to the current monkeypox infection, a virus closely related to others that already have an established direct or indirect association with cardiac tissue injury. Because of the rapid clinical recovery of the patient, EMB was not performed and the presence of the monkeypox virus or, alternatively, of a cellular immune infiltrate, in the myocardium was not demonstrated. In parallel with the recent global pandemic of COVID-19, many case reports have described findings consistent with a diagnosis of clinically suspected myocarditis, but there have been few cases of histologically confirmed myocarditis, and viral myocarditis caused directly by SARS-CoV-2 has not been definitively confirmed but assumed because of epidemiologic context.

FIGURE 3 Admission Chest X-Ray



Chest x-ray showed a normal cardiothoracic index, and no interstitial infiltrates, pleural effusion, or masses.

The clinical suspicion is based primarily on the temporal relationship. Further research is needed to identify the pathological mechanism underlying monkeypox-associated heart injury.

FOLLOW-UP

The patient had a full clinical recovery, being discharged after 1 week, with cardiac enzymes within the normal range, sustained electric and hemodynamic stability, and re-epithelialization of the skin lesions.

CONCLUSIONS

This case highlights cardiac involvement as a potential complication associated with monkeypox infection.

We believe that reporting this potential causal relationship can raise more awareness of the scientific community and health professionals for acute myocarditis as a possible complication associated with monkeypox and might be helpful for close monitoring of affected patients for further recognition of other complications in the future.

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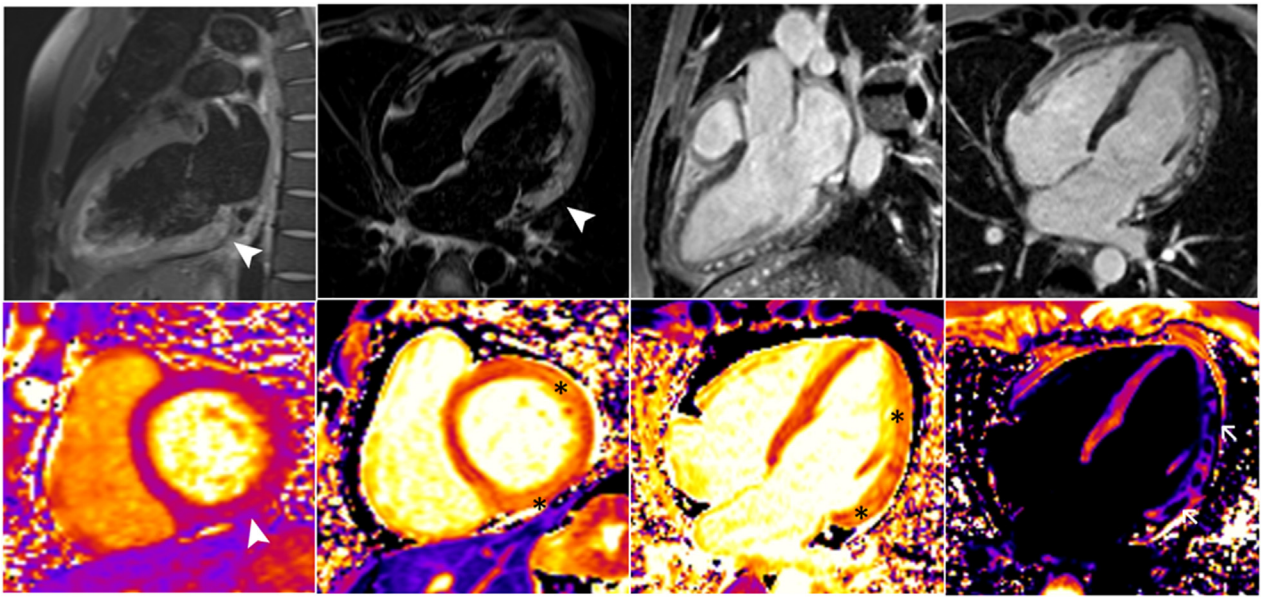
FIGURE 4 Cardiac Magnetic Resonance Findings Suggestive of Acute Myocarditis



Signs of myocardial edema (increased signal intensity on T2-weighted short-Tau inversion recovery images and short-axis T2 map [52 ms; normal value (N): 41 ± 2.8 ms], underpinned by **arrowheads** in the basal inferior and lateral segments) and of nonischemic myocardial injury (late gadolinium enhancement subepicardial/midwall in the inferior and lateral segments and increased native T1 values (1,563 ms; N: 1,217 ± 36.5 ms) in the same regions **(*)**. Postcontrast T1 map with marked reduction of T1 values (217 ms), underpinned by **arrows**, with extracellular expansion (44%; N: 26% ± 4%) in the lateral wall.

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