





RESEARCH

Open Access



Can the current monkeypox affect the heart? A systematic review of case series and case report

Reem Sayad¹ , Abdelmonem Siddiq² , Ahmed Hashim³  and Ahmed Saad Elsaeidy^{4*} 

Abstract

Background Monkeypox is a zoonotic viral infection first reported in May 2022. Monkeypox cases present with prodromal symptoms, rash, and/or systemic complications. This study systematically reviews the monkeypox cases presented with any cardiac complications.

Methods A systematic literature search was done to locate papers that discuss any cardiac complications associated with monkeypox; then, data were analyzed qualitatively.

Results Nine articles, including the 13 cases that reported cardiac complications of the disease, were included in the review. Five cases previously had sex with men, and two cases had unprotected intercourse, which reveals the importance of the sexual route in disease transmission. All cases have a wide spectrum of cardiac complications, such as acute myocarditis, pericarditis, pericardial effusion, and myopericarditis.

Conclusion This study clarifies the potential for cardiac complications in monkeypox cases and provides avenues for future research to determine the underlying mechanism. Also, we found that the cases with pericarditis were treated with colchicine, and those with myocarditis were treated with supportive care or cardioprotective treatment (Bisoprolol and Ramipril). Furthermore, Tecovirimat is used as an antiviral drug for 14 days.

Keywords Monkeypox, Mpox, Cardiomyopathy, Myocarditis, Carditis, Pericarditis

Introduction

Monkeypox (Mpox) is a viral zoonotic disease caused by the Mpox virus, a member of the *Orthopoxviral* genus from the *Poxviridae* family of viruses [1]. The first human Mpox case was detected in 1970 [2]. Mpox was mainly endemic to central and western Africa, with a few sporadic cases outside Africa. Traveling to the endemic regions and importing animals such as Squirrels and

rodents from Ghana in 2003 led to the Mpox outbreak in the United States [3].

The first human case of Mpox-outbreak-2022 was reported to the WHO on May 07. In 2022 from a traveler who returned from Nigeria then, the cases started to increase, which prompted the WHO to declare the Mpox disease as a public health emergency of international concern to raise awareness about it and promote the countries' preparedness [4]. According to the Center for Disease Control and Prevention (CDC), the total number of Mpox cases is 87,078 in both the endemic and non-endemic sites of the disease [5].

The disease manifestation starts with a prodromal phase of fever, headache, myalgia, and lymphadenopathy, followed by the eruption of multiple swollen and

*Correspondence:

Ahmed Saad Elsaeidy
Ahmed.Saad.Elsaeidy@gmail.com

¹ Faculty of Medicine, Assiut University, Assiut, Egypt

² Faculty of Pharmacy, Mansoura University, Mansoura, Egypt

³ Faculty of Medicine, Ain Shams University, Cairo, Egypt

⁴ Faculty of Medicine, Benha University, Benha, Egypt



© The Author(s) 2023. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

umbilicated cutaneous lesions on the patient's face, hands, and genitalia. Anal pain and the other features last five days, a common period of *Orthopoxviruses*, followed by a rash. The rash proceeds over different phases, starting with macular, papular, vesicular, pustular, and finally, the crusting phase lasting from two to four weeks on common sites on the body such as the face, palm, and soles, and oral membranes. Certain complications may occur, such as cellulitis, encephalitis, corneal infection, and sepsis [6]. The above data points clearly to the diversity of the disease manifestations, but other manifestations are unknown till now, so we aim here to summarize the cardiac complications of the Mpox infection.

Methods

We followed the approaches for conducting the current study based on the Cochrane Handbook of systematic reviews on Interventions [7]. While drafting our manuscript, we strictly followed the recommended reporting items for the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines [8].

Search strategy

Firstly, the following electronic databases were systematically searched: PubMed, Cochrane, Medline, Scopus, and Web of Science until December 01, 2022. We used the following search strategy in the previously mentioned databases: ((Monkeypox) AND (cardi* OR Heart OR myocarditis or cardiomyopathy)). All the included studies' references were screened to avoid missing any studies and guarantee high-quality screening. Then, we updated the search process on April 29, 2023, during the revision round.

Eligibility criteria

We included any primary study (case reports, case series, cohort) with patients suffering from heart injuries after the onset of Mpox symptoms. On the other hand, we excluded non-human studies, conference abstracts, reviews, and non-English studies.

Screening and study selection

Using Endnote software (version X20.4.1), we collected the different records from the different databases and removed duplicates. The retrieved references were examined. The screening was done in two steps; title and abstract screening, followed by full-text screening for final eligibility. Two independent authors conducted the screening, and after comparing their findings, group discussions were used to settle any differences.

Data extraction

The following data were extracted from the included studies by two independent authors. Study ID, Country, Study design, Age, Male gender, Presenting symptoms (Systemic, Non-systemic, and Cardiac), History of vaccinations, History of other etiology of myocarditis or infections, Homosexual/bisexual/MSM, Route of transmission, Immunocompromised, Treatment (Mpox and Myocarditis), Duration of hospitalization, and Investigation (Mpox, Myocarditis, and Follow-up). Arguments were later resolved through group discussion.

Quality assessment

The quality of included studies was assessed using the National Institute of Health (NIH) quality assessment tool for case reports and case series. The tool assesses the quality of each study at the level of nine domains. Each domain, as well as the overall quality, is rated either good, fair, or poor [9]. Two independent authors assessed the quality of the included studies, and arguments were later resolved through group discussion.

Data synthesis

Qualitative analysis was done by collecting and summarizing non-numerical data to understand symptoms, criteria, and how to manage the cases of Mpox associated with cardiac complications.

Results

Search results

The search strategy over the different medical databases (PubMed, Scopus, Web of Science, Medline, Cochrane) yielded 144 studies. Four studies were retrieved by manual searching, so the total number of studies became 110 after removing duplication. Screening the title and the abstract yielded 24 studies after excluding eighty-six papers because of being animal studies, out of the study criteria, and/or not primary studies. Twenty-four articles were screened for their full-text testing for eligibility. Nine case reports/case series met the study criteria [3, 10–17] and were further included in the quality assessment, as shown in Fig. 1. A summary of the included papers can be found in Table 1.

Baseline characteristics and data analysis

The included studies represent 13 Mpox cases with cardiac complications. Eleven cases were male patients. Five male patients have a history of having sex with men [10, 11, 13, 14, 17]. The patients who developed pericarditis or myocarditis have evidence of systemic inflammatory response in the form of fever, myalgia,

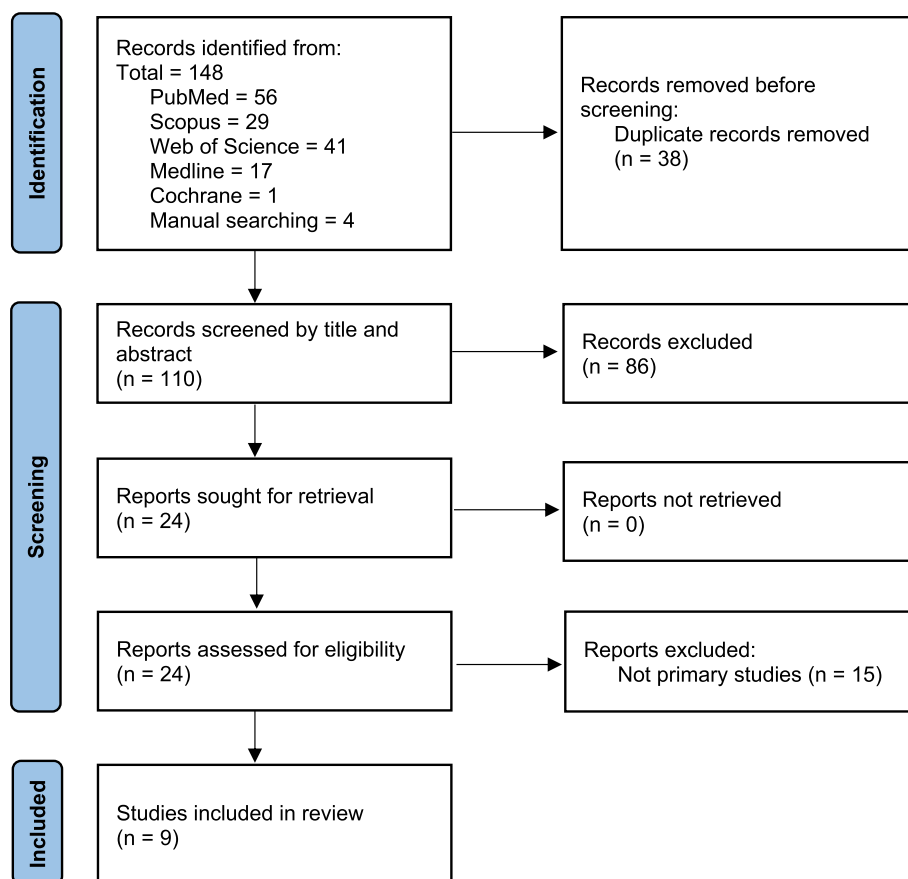


Fig. 1 PRISMA flowchart of the database search and searching process

and headache. Additionally, 11 patients developed a maculopapular eruption that is sometimes umbilicated [10–17]. The location of the rash was related to the site of sexual contact, including genital, anal, or oral regions. The presentation of myocarditis in the afflicted patients was usually manifested with chest pain that sometimes radiated to the left arm. The history of pox virus vaccination was either unavailable or negative in all selected patients. Despite the absence of clear vaccination history, three patients have a syphilis history [11, 16], with one patient having a history of well-controlled HIV [13]. Other sexually transmitted infections were routinely excluded from most of the patients. However, in one study, the analysis of other sexually transmitted infections was rejected due to safety considerations [13]. ECG was routinely utilized as an initial cardiac assessment tool. Different findings have been demonstrated, including sinus tachycardia, repolarization abnormality (e.g., T wave inversion), and widespread ST-segment elevation. The treatment was usually supportive because the patients presented with mild complications. However, one patient has

been prescribed doses of aspirin aiming to relieve the pericarditis [12].

Real-time Polymerase Chain Reaction (PCR) targeting the virus nucleic material from the skin lesion was surely the only method to diagnose the current infection with Mpox. Various methods are used to verify the pericarditis/myocarditis diagnosis. High-sensitivity serum troponin was used to diagnose associated myocarditis in most patients. In the included cases, we found elevated levels of High-sensitivity troponins (0.165–21.20 ng/ml) [11, 17], Creatine Kinase reached (291–740 U/L) [10, 13], and N-terminal prohormone B-type natriuretic peptide (155–1258 pg/ml) [10, 11]. In addition, a serial electrocardiogram was usually used to aid the diagnosis of pericarditis. Four patients have required cardiac magnetic resonance (CMR) imaging to confirm the myocarditis [10, 13, 15, 17]. Besides, eight patients have utilized echocardiography either (transthoracic (TTE) or transesophageal) to visualize the cardiac function and pericardial fluid collection properly [10–15, 17].

Magnetic resonance imaging occasionally demonstrated the inflammation location despite transesophageal

Table 1 A summary of included studies

Study ID	Country	Study design	Age (Years)	Male gender	Presenting symptoms		History of vaccinations	History of other etiology of myocarditis or infections	Homosexual/ bisexual/MSM
					Systemic	Non-systemic			
Santaliz-Ruiz et al. 2023 [17]	Puerto Rico	Case Report	21	Yes	Fever, Myalgia, Nausea, Vomiting, Headache, and Watery Diarrhea, Cervical Lymphadenopathy	Vesiculopustules on face, trunk, suprapubic area, and Extremities	NO	No	Yes
Brouillard et al. 2022 [15]	Canada	Case Report	34	Yes	Fever, Chills	A well-circumscribed, umbilicated papule on the pubis, and an ulcerated lesion on the glans penis	No	No, but later presented positive for Chlamydia and negative for Gonorrhea	NO, but stayed at a homosexual friend's house two weeks earlier
Dumont et al. 2022 [14]	France	Case series	21	Yes	Fever	Anal pustules	No	No	Yes
		Case 2	25	Yes	NA	Pustules on the face and penis	No	No	NA
		Case 3	32	Yes	Fever	Erosive cutaneous lesions on the penis	No	Slightly detectable Epstein-Barr virus DNA in blood < 500copies/mL	No
Miller et al. 2022 [16]	USA	Case-series	In his 302	Yes	NA	Rash on his face, head, back, and genitals then spread, coalesced, and developed central necrosis, Phimosi, urinary retention	NA	HIV, Syphilis	NA

Table 1 (continued)

Study ID	Route of transmission	Immunocompromised	Treatment		Duration of hospitalization		Investigation		Follow-up
			Mpox	Myocarditis	Mpox	Myocarditis	Mpox	Myocarditis	
Santaliz-Ruiz et al. 2023 [17]	Sexual transmission	No	NA	High-dose Aspirin, Oral Colchicine 0.6 mg daily	Five days	PCR assay of a swab sample from a skin lesion	CBC, CMP, ECG, Echo, Troponin, Cardiac MRI	Cardiac MRI after Eight weeks	
Brouillard et al. 2022 [15]	Contact with soiled linens of a homosexual friend	No	- Prophylactic Ceftriaxone and Azithromycin - Acyclovir in negative pressure room - Tecovirimat for 14 day after confirmed diagnosis	ACE inhibitors	Nine days	PCR assay of a swab sample from a skin lesion	ECG, Echo, Cardiac MRI, Troponin, Standard labs	The patient left the hospital before undergoing his control cardiac MRI	
Dumont et al. 2022 [14]	Case 1 Sexual transmission	No	NA	Bisoprolol and Ramipril	NA	PCR assay of a swab sample from a 14skin lesion	ECG, Troponin, CK, TTE, CRP, contrast CT chest	Cardiac MRI after four weeks	
	Case 2 Sexual transmission	No	NA	Bisoprolol and Ramipril	NA	PCR assay of a swab sample from a skin lesion	ECG, Troponin, CK, CRP, TTE	NA	
	Case 3 Sexual transmission	No	Oral Tecovirimat for 14 day after confirmed diagnosis	Bisoprolol, Ramipril and Anti-aggregation	NA	PCR assay of a swab sample from a skin lesion	ECG, Troponin, CK, TTE, CRP, Cardiac-CT Scan	Cardiac MRI after 11 days	
Miller et al. 2022 [16]	NA	Yes	- Oral Tecovirimat for 14 day after confirmed diagnosis, then IV in ICU - 2 doses of VIGIV - Antimicrobials	NA	- 4 weeks in the 1 st admission - 15-day in the 2nd admission	PCR assay of a swab sample from a skin lesion	NA	NA	

Table 1 (continued)

Study ID	Route of transmission	Immunocompromised	Treatment		Duration of hospitalization		Investigation		Follow-up
			Mpox	Myocarditis	Mpox	Myocarditis	Mpox	Myocarditis	
Pinho et al. 2022 [10]	NA	NA	NA	Supportive care and exercise restriction	One week	PCR assay of a swab sample from a skin lesion	ECG, Chest X-ray, TTE, CRP, CK, Troponin, Brain natriuretic peptide, urine and blood toxicology tests, Cardiac MRI	NO	
Rodriguez-Nava et al. 2022 [11]	Case 1 Sexual transmission	No	Oral Tecovirimat for 14 day after confirmed diagnosis	No specific treatment due to the rapid resolution	10 days	PCR assay of a swab sample from a skin lesion	ECG, Troponin, Chest X-ray, CRP, ESR, N-terminal prohormone B-type Natriuretic Peptide	Echo on hospital day2, Troponin in hospital day 6	
	Case 2 Sexual transmission	No	Supportive care	Supportive care	4 days	PCR assay of a swab sample from a skin lesion	ECG, Troponin, Echo, B-type natriuretic peptide	Cardiac enzymes testing	
Shaik et al. 2022 [12]	NA	No	Supportive care	Nitroglycerin at presentation, 1 g aspirin/h for 2 weeks	7 days	PCR assay of a swab sample from a skin lesion	ECG,TEE, Chest X-ray, Troponin, CBC, ALT, AST, BUN, Cr, CRP, ESR, HbA1c	High-dose aspirin, and a planned cardiac follow-up	
Tan et al. 2022 [13]	Sexual transmission	No	Valacyclovir for initial diagnosis consideration of HSV 1,or 2	Supportive care	NA	PCR assay of a swab sample from a skin lesion	ECG, CK, Echo, Cardiac Catheterization, Cardiac MRI, Troponin, Routine Chemistries, CBC	Full recovery after 25 days	
Thornhill et al. 2022 [3]	Case 1 NA Case 2 NA	NA NA	NA NA	self-limiting (<7 days)	NA NA	NA NA	NA NA	NA NA	

ALT Alanine transaminase, AST Aspartate transaminase, BUN Blood urea nitrogen, CBC Complete blood count, CK Creatine Kinase, CMP Comprehensive Metabolic Panel, Cr Creatinine level, CRP C-reactive protein, ECG Electrocardiography, Echo Echocardiogram, ESR Erythrocyte sedimentation rate, HbA1c Hemoglobin A1c, HIV Human immunodeficiency virus, HSV Herpes simplex virus, Mpox Monkeypox, MRI Magnetic resonance imaging, MSM Men Who Have Sex with Men, NA Not Available, PCR Polymerase chain reaction, TEE Transesophageal Echocardiography

echocardiography. In T2-weighted images, areas of increased signal intensity in the basal inferior and lateral segments were found, corresponding to myocardial edema [10]. Late gadolinium enhancement sequences revealed subepicardial enhancement in the mid inferolateral segment and mid-wall enhancement in the remaining inferior and lateral segments of the LV, findings compatible with necrosis [10]. In addition, parametric mapping demonstrated a regional increase of T1 and T1 native values, indicating an abnormally expanded myocardial extracellular volume in the lateral wall. Postcontrast T1 mapping confirmed myocardial gadolinium accumulation with a non-ischemic pattern in the lateral wall [10].

Quality assessment

We have used the NIH quality assessment tool for case series to assess the quality of the included studies as previously described [9]. Three of the included studies have a good quality (> 6) [3, 11, 16], Five studies have a fair quality (from 3 to 6 points) [12–15], and one study has a poor quality (< 3) [10] as shown in Table 2.

Discussion

The declaration of Mpox as a public health emergency by the WHO on July 23, 2022, has raised awareness and alertness about the disease's manifestations and complications [18]. We included nine studies that reported possible cardiac complications of Mpox in which a total of 13 patients were presented [3, 10–17]. Five male patients had sex with men [10, 11, 13, 14, 17] and three male

patients had unprotected sexual intercourses [11, 14] which reveal the importance of the sexual route in the disease transmission as it was reported by the CDC. Sexual contact with an infected Mpox patient is considered the main route of disease transmission during the current outbreak [19]. According to CDC, monkeypox infection is identified more in males [20].

In Mpox cases: The history began with typical Mpox symptoms such as fever, anal pain, and pustules on the face and penis a few days (four-seven days) after the last unprotected homosexual intercourse or with at-risk partners. Then, the Mpox diagnosis is confirmed by PCR. A few days later (two-seven days), patients presented with acute chest pain, elevated cardiac markers, and biological inflammatory syndrome. Typical electrocardiogram and TTE abnormalities associated with myocarditis were also identified [3, 10–17].

Few cases of cardiac involvement in Mpox infection have been reported. However, according to smallpox infection, genetically related to the Mpox virus but more aggressive, was associated with myocarditis. Furthermore, cardiac complications of smallpox vaccination have been reported since the initiation of vaccination in the 1950s in Europe, including post-vaccinal myocarditis and myopericarditis [21]. Both the live replicating smallpox vaccine ACAM2000 and the live non-replicating smallpox vaccine JYNNEOS, which are used to immunize people against the Mpox virus, have a high incidence of myocarditis but the exact mechanism remains unclear [22, 23]. On the other hand, some studies suggested

Table 2 The quality of included studies using the NIH tool for case series

Author (YOP)	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Overall rating
Santaliz-Ruiz et al. 2023 [17]	Y	Y	U	U	Y	Y	Y	U	Y	Fair
Brouillard et al. 2022 [15]	Y	Y	U	U	Y	Y	N	U	Y	Fair
Dumont et al. 2022 [14]	Y	Y	Y	Y	U	N	U	U	Y	Fair
Miller et al. 2022 [16]	Y	Y	Y	Y	Y	Y	Y	U	Y	Good
Pinho et al. 2022 [10]	N	N	U	U	N	N	U	U	N	Poor
Rodriguez-Nava et al. 2022 [11]	Y	Y	Y	Y	Y	Y	Y	U	Y	Good
Shaik et al. 2022 [12]	Y	Y	U	U	Y	U	Y	U	Y	Fair
Tan et al. 2022 [13]	Y	Y	U	U	Y	Y	Y	U	Y	Fair
Thornhill et al.2022 [3]	Y	Y	Y	U	Y	Y	Y	Y	Y	Good

Q1: Was the study question or objective clearly stated? Yes/No/Unclear

Q2: Was the study population clearly and fully described, including a case definition?

Q3: Were the cases consecutive?

Q4: Were the subjects comparable?

Q5: Was the intervention clearly described?

Q6: Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?

Q7: Was the length of follow-up adequate?

Q8: Were the statistical methods well-described?

Q9: Were the results well-described?

YOP Year of publication, Y Yes, N No, U Unclear, NIH National institute of health

two potential mechanisms of smallpox vaccine-related myopericarditis. The virus may affect the myocardium directly or by immune-mediated reaction, as evidenced by several studies that found a Th1-predominant cytokine profile associated with myocarditis after smallpox vaccination [24–26]. As *Orthopoxviruses* are closely related to the Vaccinia virus used in vaccination, it is reasonable that Mpox may also be associated with myocarditis. Extrapolating, the Mpox virus may have a tropism for myocardium tissue or cause immune-mediated injury to the heart [10].

Pericarditis is characterized by pericardial inflammation responding to various stimuli that cause an auto-immune or inflammatory response. It may result in pericardial effusion, impairing cardiac filling [27]. As most acute episodes of pericarditis are preceded by a flu-like or gastrointestinal syndrome, the etiological agents behind pericarditis are predominantly viruses [27, 28]. Myocarditis is an inflammatory myocardium disease diagnosed by established histological, immunological, and immune-histochemical criteria. It is considered a challenging diagnosis because of its heterogeneity in clinical presentation and histological forms [29].

A combination of clinical presentation and noninvasive diagnostic findings, including typical CMR abnormalities, may be used to diagnose clinically suspected myocarditis [30, 31]. The three diagnostic criteria of pericardial inflammation (chest pain, a friction rub, and diffuse ECG changes, including ST elevation) may be used to diagnose clinically suspected pericarditis [28]. The history and clinical presentation may suggest a specific etiology in patients with clinically suspected and confirmed myocarditis, but a definitive cause is often difficult to identify. As mentioned in Table 1, five cases presented without any history of potential etiology of myocarditis or pericarditis. So, Mpox infection may be the etiology of heart injuries in those patients [10, 13, 14, 17].

The management of viral myocarditis depends on the presenting symptoms, and the patient must be initially diagnosed appropriately by rolling out any other causes of the presenting symptoms [32]. Regarding our scope of cardiac complications, we will focus on managing pericarditis and myocarditis. Pericarditis can be managed by using Colchicine 1–2 mg as an initial dose that will be decreased gradually, acetylsalicylic acid, and a lower dose of nonsteroidal anti-inflammatory drugs (NSAIDs) can be used as symptomatic treatment [33, 34]. Patients who were given aspirin (1.2 g) twice daily for two weeks showed significant improvement. These patients displayed signs of recovery within eight days [12, 34]. Randomized controlled trials demonstrate colchicine's efficacy and rapid recovery in pericarditis patients [35] and significantly reduce the rate of subsequent

recurrences of pericarditis in patients with multiple recurrences [36]. Patients who do not respond to colchicine and NSAIDs receive low-dose steroids as a second line of treatment [34].

Our included myocarditis cases received supportive care, exercise restriction, and the initiation of ibuprofen and colchicine if the case was combined with pericarditis (myopericarditis). However, they did not receive any directed therapy for myocarditis. The patients had a full clinical recovery in one to two weeks. They were discharged with normal cardiac enzymes and sustained electric and hemodynamic stability [10, 11, 13, 15]. Three myocarditis cases received cardioprotective treatment (Bisoprolol and Ramipril) [10, 11, 13]. This treatment resulted in no recurrence of pain, and high-sensitivity troponin T decreased [14]. According to Miller et al. 2022 (newly included study), four cases received Tecovirimat as an antiviral drug for the 14-day duration with supportive treatment [11, 14–16], as recommended by the CDC guidelines [37]. Because those cases evolved rapidly, one of the cases left the hospital early before the assessment of the effect of Tecovirimat on myocardial inflammation without a follow-up CMR [15].

Early implementation of supportive care and pain control is recommended. The effectiveness of this measure is based on the patient's immune system. Usually, these treatments are sufficient for immunocompetent patients. Nevertheless, the illness outcome is determined by several factors, including the patient's initial health condition, existing diseases, immunization record, and co-morbidity. Thus, supportive care and pain control may not be enough for some people with weakened immune systems, and Tecovirimat should be considered [14, 16].

Tecovirimat is a drug that suppresses the activity of the VP37 envelope-wrapping protein of *Orthopoxviruses*, thus hindering the production of enveloped virions and diminishing the amount of viral DNA in the blood of a non-human primate organism [37]. While there is no data available on the effectiveness of Tecovirimat for treating people with Mpox, experiments conducted with a variety of animal species have yielded positive results regarding its ability to lessen the likelihood of death from *Orthopoxviruses* if it is taken early in the disease [38]. Furthermore, FDA declared that the indiscriminate usage of Tecovirimat might induce viral resistance making Tecovirimat ineffective for orthodox-infected patients [37]. Alternate treatment options have a less safety profile than Tecovirimat. So, when Tecovirimat is needed, it is important to be aware of the lack of evidence on its effectiveness for Mpox patients and the possibility of viral resistance. Tecovirimat is accessible from the Strategic National Stockpile of the United States and should be given out under the rigid guidelines of the CDC

Institutional Review Board. As per the CDC's advice, the medication should be considered for patients with intense illness, those in danger of developing a serious disease, and those whose body parts are at risk of being affected by the virus (such as the genitals) [37].

Strengths and limitations

The small number of the reported Mpox cases with cardiac complications limits the study. All the available studies are case reports or case series. Additionally, we had to include some studies despite missing data due to the lack of these cases. Some of the included cases have a history of HIV and syphilis which may impact the patients' immunity. These limitations reduce the evidence quality of this study.

The strong points of this study: this systematic review is novel to aggregate cardiac complications in monkeypox. Also, this study illustrates the importance to diagnose cardiac complications early which can improve patient outcomes.

Conclusion and recommendations

This study suggests the possibility of cardiac complications in Mpox patients. So, we advise doing cardiovascular investigations for the Mpox patients with suspected cardiovascular affection. No mortality was associated with the documented mild myocarditis and/or pericarditis sequelae. Further research is needed to identify the pathological mechanism underlying Mpox-associated heart injury. Also, we recommend conducting clinical trials to evaluate Tecovirimat's efficacy and safety in managing Mpox patients presented with cardiac complications.

Abbreviations

CMR	Cardiac magnetic resonance
CDC	Center for Disease Control and Prevention
ECG	Electrocardiography
MSM	Men Who Have Sex with Men
Mpox	Monkeypox
NSAIDs	Nonsteroidal anti-inflammatory drugs
PCR	Polymerase Chain Reaction
TTE	Transthoracic echocardiography
WHO	World Health Organization

Acknowledgements

None.

Authors' contributions

ASE and RS: Conceptualization, Methodology. RS, AS, and AH: Data curation, Writing- Original draft preparation. RS, AS, and AH: Visualization, Investigation. ASE: Supervision. ASE and RS: Software, Validation. ASE: Writing—Reviewing and Editing.

Funding

Open access funding provided by The Science, Technology & Innovation Funding Authority (STDF) in cooperation with The Egyptian Knowledge Bank

(EKB). This research received no specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of data and materials

Data will be provided upon request from Reem Sayad (reem.17289806@med.aun.edu.eg).

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests

Received: 8 March 2023 Accepted: 15 June 2023

Published online: 28 June 2023

References

1. McCollum AM, Damon IK. Human monkeypox. *Clin Infect Dis*. 2014;58(2):260–7.
2. Ladnyj ID, Ziegler P, Kima E. A human infection caused by monkeypox virus in Basankusu Territory, Democratic Republic of the Congo. *Bull World Health Organ*. 1972;46(5):593.
3. Thornhill JP, et al. Monkeypox virus infection in humans across 16 countries—April–June 2022. *N Engl J Med*. 2022;387(8):679–91.
4. WHO Director-General declares the ongoing monkeypox outbreak a Public Health Emergency of International Concern. <https://www.who.int/europe/news/item/23-07-2022-who-director-general-declares-the-ongoing-monkeypox-outbreak-a-public-health-event-of-international-concern> (Accessed 01 May 2023).
5. 2022 Mpox Outbreak Global Map | Mpox | Poxvirus | CDC. <https://www.cdc.gov/poxvirus/mpox/response/2022/world-map.html> (Accessed 01 May 2023).
6. Webb E, et al. Availability, scope and quality of monkeypox clinical management guidelines globally: a systematic review. *BMJ Glob Heal*. 2022;7(8):e009838.
7. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). *Cochrane Handbook for Systematic Reviews of Interventions version 6.3* (updated February 2022). Cochrane, 2022. Available from www.training.cochrane.org/handbook.
8. Page MJ, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. <https://doi.org/10.1136/bmj.n71>.
9. National Institutes of Health. National Heart Lung, and Blood Institute. Study Quality Assessment Tools. Bethesda: National Institutes of Health; 2018.
10. Pinho AI, et al. Acute myocarditis—a new manifestation of Monkeypox infection? *JACC Case Rep*. 2022;4:1424–8.
11. Rodriguez-Nava G, et al. Myocarditis attributable to Monkeypox virus infection in 2 patients, United States, 2022. *Emerg Infect Dis*. 2022;28(12):2508–12.
12. Shaik TA, et al. Monkeypox-associated pericarditis: a Maiden case. *Cureus*. 2022;14(9):e29638.
13. Tan DHS, et al. Atypical clinical presentation of monkeypox complicated by myopericarditis. *Open Forum Infect Dis*. 2022;9(8):ofac394.
14. Dumont M, Guilhou T, Gerin M, Frémont-Goudot G, Nivose PL, Koumbi A, Joly V, Bouadma L, Yazdanpanah Y, André MH, de La Porte des Vaux C. Myocarditis in monkeypox-infected patients: a case series. *Clin Microbiol Infect*. 2023;29(3):390.e5–390.e7. <https://doi.org/10.1016/j.cmi.2022.12.001>.
15. Brouillard P, et al. Monkeypox associated myocarditis: a case report. *IDCases*. 2022;30:e01628.
16. Miller MJ, et al. Severe Monkeypox in hospitalized patients — United States, August 10–October 10, 2022. *MMWR Morb Mortal Wkly Rep*.

- 2022;71(44):1412–7. <https://doi.org/10.15585/mmwr.mm7144e1>
10.15585/mmwr.mm7136a1|10.15585/mmwr.mm7132e3|10.1093/cid/ciaa143|10.1016/S1473-3099(19)30294-4|10.15585/mmwr.mm7142e1|10.15585/mmwr.mm7138e1|10.1056/NEJMoa2207323. Available: <https://stacks.cdc.gov/view/cdc/123141>.
17. IV Santaliz-Ruiz LE, Pabón-González F, Colón-Fontánez F. Monkeypox induced acute myocarditis in a young healthy adult. *JAAD Case Rep.* 2023;34:5–6. <https://doi.org/10.1016/j.jidcr.2023.01.018>.
 18. Sah R, et al. Public Health Emergency of International Concern declared by the World Health Organization for Monkeypox. *Glob Secur Heal Sci Policy.* 2022;7(1):51–6.
 19. Science brief: Detection and transmission of Mpox virus. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention. 2023. Available at: <https://www.cdc.gov/poxvirus/monkeypox/about/science-behind-transmission.html> (Accessed: F.
 20. Monkeypox Cases by Age and Gender, Race/Ethnicity, and Symptoms | Monkeypox | Poxvirus | CDC. Accessed 31 Oct 2022. <https://www.cdc.gov/poxvirus/monkeypox/response/2022/demographics.html>.
 21. Cassimatis DC, Atwood JE, Engler RM, Linz PE, Grabenstein JD, Vernalis MN. Smallpox vaccination and myopericarditis: a clinical review. *J Am Coll Cardiol.* 2004;43(9):1503–10.
 22. Keinath K, Church T, Kurth B, Hulten E. Myocarditis secondary to smallpox vaccination. *BMJ Case Rep.* 2018;2018:bcr-2017-223523, 2018.
 23. Halsell JS, et al. Department of Defense Smallpox Vaccination Clinical Evaluation Team Myopericarditis following smallpox vaccination among vaccinia-naïve US military personnel. *J Am Med Assoc.* 2003;289:3283–9.
 24. McNalley MC, Qamar Y. Cardiac complications of progressive generalized vaccinia: report of a case. *Dis Chest.* 1966;49(3):333–5.
 25. Bengtsson E, Lundström R. Postvaccinal myocarditis. *Cardiology.* 1957;30(1):1–8.
 26. Cohen JI, et al. Kinetics of serum cytokines after primary or repeat vaccination with the smallpox vaccine. *J Infect Dis.* 2010;201(8):1183–91.
 27. Chiabrando JG, et al. Management of acute and recurrent pericarditis: JACC state-of-the-art review. *J Am Coll Cardiol.* 2020;75(1):76–92.
 28. Adler Y, et al. 2015 ESC Guidelines for the diagnosis and management of pericardial diseases. *Kardiol Pol (Polish Hear Journal).* 2015;73(11):1028–91.
 29. Richardson P. Report of the 1995 World Health Organization/International Society and Federation of Cardiology Task Force on the Definition and Classification of cardiomyopathies. *Circulation.* 1996;93:841.
 30. Caforio ALP, et al. Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. *Eur Heart J.* 2013;34(33):2636–48.
 31. Rroku A, Kottwitz J, Heidecker B. Update on myocarditis—what we know so far and where we may be heading. *Eur Hear J Acute Cardiovasc Care.* 2021;10(4):455–67.
 32. Olejniczak M, Schwartz M, Webber E, Shaffer A, Perry TE. Viral myocarditis—incidence, diagnosis and management. *J Cardiothorac Vasc Anesth.* 2020;34(6):1591–601.
 33. Sarda L, et al. Myocarditis in patients with clinical presentation of myocardial infarction and normal coronary angiograms. *J Am Coll Cardiol.* 2001;37(3):786–92.
 34. Chetrit M, et al. Imaging-guided therapies for pericardial diseases. *Cardiovasc Imaging.* 2020;13(6):1422–37.
 35. Imazio M, et al. A randomized trial of colchicine for acute pericarditis. *N Engl J Med.* 2013;369(16):1522–8.
 36. Imazio M, et al. Efficacy and safety of colchicine for treatment of multiple recurrences of pericarditis (CORP-2): a multicentre, double-blind, placebo-controlled, randomised trial. *Lancet.* 2014;383(9936):2232–7.
 37. C. for D. Control and Prevention. Guidance for tecovirimat use under expanded access investigational new drug protocol during 2022 US monkeypox outbreak. 2022.
 38. Grosenbach DW, et al. Oral tecovirimat for the treatment of smallpox. *N Engl J Med.* 2018;379(1):44–53.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

