CASE REPORT

Reactive Arthritis After mpox Vaccination

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Abstract

Autoimmune inflammatory reaction after vaccination is a rare clinical entity. Reactive arthritis has been described after various vaccinations, but not after mpox vaccination. Here we present a case of recently diagnosed reactive arthritis after mpox vaccination that presented in the context of unrelenting fever and diarrhea complicated by migratory arthritis and anterior uveitis. We have reported this case to the Vaccine Adverse Event Reporting System (VAERS).

Keywords: Autoimmune reaction, Reactive arthritis, mpox vaccination, Monkeypox, Vaccine adverse event reporting system (VAERS)

1. Background

Two smallpox vaccines (ACAM 2000 and JYNNEOS) are approved by the U.S. Food and Drug Administration for prevention of mpox.[1] ACAM2000 is administered using a two-pronged (bifurcated) needle to prick the skin several times with a droplet of vaccine. It should not be injected by intradermal, subcutaneous, intramuscular, or intravenous route. JYNNEOS is administered in two doses of 0.5 cc each, spaced 4 weeks apart, and can be administered either subcutaneously or intradermally.[2] JYNNEOS is a live, attenuated, non-replicating orthopox viral vaccine with only rare reports of side effects, the most common being injection site discoloration and scarring.[2] There have been no reported cases of reactive arthritis after mpox vaccination.[3]

2. Case report

A 51-year-old man presented to an infectious disease clinic in the northeastern United States with continuous fever for 2 weeks and watery diarrhea for 1 week. Medical history was notable for asthma, right rotator cuff tear status post right arthroscopic rotator cuff repair 3 months ago and HIV with undetectable viral load for 5 years. His family history was remarkable for premature coronary artery disease in his father. His home medications included gabapentin, emtricitabine/tenofovir, dolutegravir, and albuterol inhaler. He stated that he had never missed his HIV medications since being diagnosed with HIV 10 years ago.

The patient received the mpox vaccine (JYNNEOS) 2 weeks before presentation, and 2 h after vaccination he developed continuous fever with associated rigors, despite taking acetaminophen every 4 h. Two days later, he developed severe watery diarrhea and mild discomfort during urination, which lasted for about a week. He was using bismuth subsalicylate for diarrhea and ibuprofen for fever. He denied nausea, vomiting, mucocutaneous rash, increased urinary frequency/urgency, recent travel, or sick contact.

On presentation, the patient was noted to have a fever of 100.9° Fahrenheit and sinus tachycardia (110–120 beats per minute) with normal respiratory rate and oxygen saturation. Physical examination was unremarkable except for slight tenderness in the right shoulder joint at the site of the previous arthroscopy.

Laboratory diagnostics demonstrated no leukocytosis, elevated acute phase reactants (C-reactive

Received 22 July 2023; revised 12 October 2023; accepted 20 October 2023.
Available online 12 January 2024

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https://doi.org/10.55729/2000-9666.1287

protein: 67.82 mg/L, reference range: 0–10 mg/L; erythrocyte sedimentation rate: 38 mm/h reference range: 0–30 mm/h). His HIV viral load was undetectable with normal absolute CD4 count (673 cells/Ul, reference range: 404–1612 cells/UL). Blood, urine, and stool studies for infectious pathogens were negative. Cytomegalovirus PCR, respiratory viral panel, and tests for sexually transmitted infections, including nucleic acid amplification testing for chlamydia/gonorrhea, were negative. Chest X-ray was unremarkable. His electrocardiogram showed sinus tachycardia with ventricular rate of 110 beats per minute, and echocardiogram showed left ventricular function of 60%–65% with no obvious valvular vegetation or pericardial effusion. Troponin T 5th-generation test was negative. A 7-day cardiac monitor showed sinus rhythm with average rate of 104 beats per minute.

The patient's diarrhea resolved within a week while the patient was under evaluation for tachycardia and fever, but he started having progressively worsening pain and swelling of the left knee and ankle joint, restricting mobility. On examination, his left knee was red, swollen, and warm with positive tenderness in the left medial knee and 1+ pitting edema extending from the left foot to the knee. A complete duplex ultrasound of the left lower extremity was negative for deep vein thrombosis. MRI left knee without contrast showed grade 2 tear to the origin of the medial collateral ligament with some underlying medial femoral condyle edema and knee effusion. He underwent aspiration of the left knee effusion, yielding 50 cc of clear fluid with slightly elevated white blood cell count and protein level suggestive of inflammatory arthritis (Table 1). Antinuclear antibody, rheumatoid factors, and HLAB27 were negative. Joint fluid crystals, cultures, and Lyme PCR testing were negative.

The patient subsequently developed migratory arthritis (left elbow, right knee, bilateral temporomandibular joints) and redness in the left eye with floater spots and decreased vision. Eye examination (Table 2) showed normal fundus with reduced visual acuity, circum-corneal congestion, keratin precipitate, irregular pupil, and anterior chamber cells suggestive of anterior uveitis (Fig. 1). He was started on prednisone eye drops every 1 h and cyclopentolate twice a day. It was considered unlikely that his extensive left knee swelling with effusion and pitting edema distally was associated with the small meniscal tear. The patient's diarrhea, asymmetric arthritis, dysuria, and uveitis were believed to be due to reactive arthritis. After septic arthritis was ruled out, he was started on methylprednisolone for 2 weeks. His arthralgia improved when he was taking methylprednisolone, but it returned after he finished the course. He started taking NSAIDs three times daily with minimal benefit.

Given the diminished visual field and migratory arthritis unresponsive to NSAIDs, he was re-started on prednisone 20 mg daily for 1 week followed by 10 mg daily with meloxicam 15 mg daily. One month after treatment with steroids and NSAIDs, his arthralgia was well controlled and acute phase reactants returned to baseline. His visual field defect persisted.

Table 1. Left knee synovial fluid analysis.

Parameters	Normal range	Laboratory result
Clarity	Transparent	Transparent
Color	Clear	Clear
Viscosity	High	Low
WBC/mm3	<200	1751
PMN leukocyte cells %	<25	30
Glucose mg/dL	70–110	119
Protein gm/dL	1.5–2.5	5.3
Crystal	Negative	Negative
Culture	Negative	Negative
Lyme PCR	Negative	Negative

WBC: white blood cells; PMN: polymorphonuclear.

3. Discussion

Mpox is a highly contagious infectious disease with sporadic outbreaks outside its endemic areas of the African continent. It spreads through droplets, sexual contact, and direct or indirect contact with rash or contaminated articles. Higher numbers of mpox cases have been documented among people with multiple sexual partners and men who have sex with men.[4]

Mpox affects people of any age and has three phases: incubation, prodrome, and eruptive stage. The incubation period ranges from 3 to 34 days followed by the prodromal phase that lasts for 1–4 days. Symptoms include fever, headache, fatigue, cervical lymphadenopathy, and centrifugal umbilicated rashes with complications such as cutaneous scars, respiratory tract infections, corneal ulcerations, and even death.[5] The first suspected case of mpox in the US was reported on May 17, 2022, with a total of 30,505 probable and confirmed cases and 43 deaths by June 21, 2023.[6]

One study found that patients with mpox can be co-infected with hepatitis C, HIV, or other sexually transmitted infections.[7] The authors speculated that concomitant HIV infection alters the natural course of mpox infection due to the resulting immunosuppressed state.[7] In a series of 528 mpox cases, 216 (41%) had concomitant HIV and 205 of those patients (95%) were on antiretroviral therapy.[8]

Table 2. Eye examination.

Parameters	Normal reference	Right eye	Left eye
Visual acuity (Snellen-Linear)	20/20	20/20	20/50
Tonometry mmHg	10–21	15	10
Pupil reaction	Brisk	Brisk	Sluggish
Pupil shape	Round	Round	Irregular
Lids/Lashes	Normal	Normal	Normal
Conjunctiva/Sclera	White and quiet	White and quiet	1+ injection 360
Cornea	Clear	Clear	Mild desc folds, no NaFl staining
Anterior chamber	Deep and quiet, no cell	Deep and quiet, no cell	2 +cell, no hypopyon
Iris	Normal	Normal	Scattered posterior synechiae
Lens	Clear	Clear	Scattered pigment on anterior capsule
Vitreous	Normal	Normal	1+ vitreous cells

Desc folds: descemet folds; NaFl staining: sodium fluorescein staining.

Vaccination, quarantine measures, screening of travelers from endemic countries, personal hygiene, and use of personal protective measures are the common approaches to reduce transmission and halt outbreaks.[1]

Reactive arthritis is an inflammatory condition characterized by a constellation of symptoms including asymmetric arthritis, urethritis/diarrhea, and conjunctivitis/keratitis/uveitis.[9] It usually follows infection with salmonella, shigella, campylobacter, yersinia, and chlamydia.[10] In our case, diagnosis of enteritis-associated reactive arthritis was not likely because of the absence of recent hospitalization/sick contact, antibiotics usage, prior gastrointestinal infection or associated gastrointestinal symptoms (abdominal pain, nausea/vomiting, loss of appetite), and negative stool culture and toxin assay.

HIV-positive patients have a high risk of developing rheumatic disease due to the twofold inflammatory effect of HIV on synovial tissue.[11] The incidence of reactive arthritis in pre-combined antiretroviral therapy HIV patients ranges from 0% to 11%.[12] Our patient's HIV viral load was undetectable for five years and he was on daily antiretroviral therapy, for 10 years, which suggested low risk for reactive arthritis due to HIV.

Autoimmune inflammatory reaction is an uncommon adverse event after vaccinations, occurring in less than 0.01% of people worldwide.[13] This reaction has been associated with a combination of genetic, familial, and environmental factors, molecular mimicry between human and viral proteins, and positive HLA-B27. The JYNNEOS vaccine is a replication-deficient virus vaccine. Only 13 (1%) of the 1350 JYNNEOS reports to the vaccine adverse

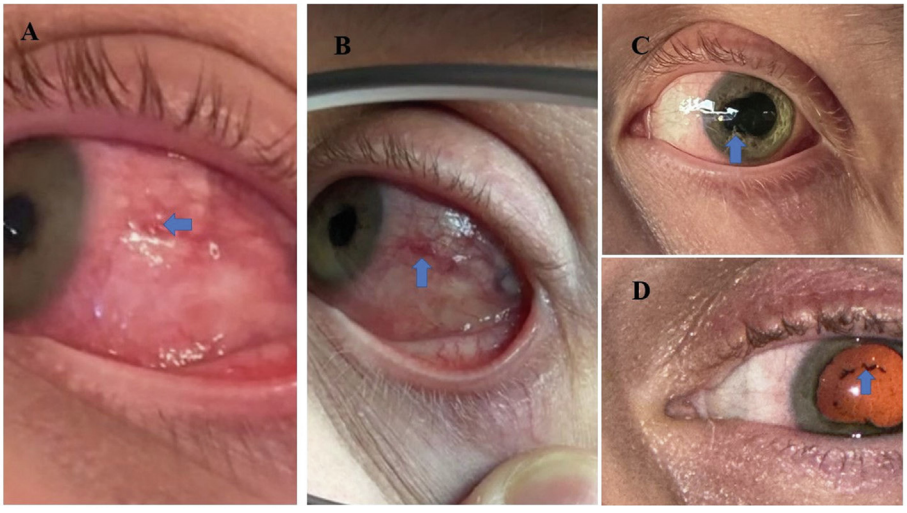

Fig. 1. Left eye examination. (A) Gross eye examination demonstrates left eye circumciliary congestion (arrow). (B) Speculum examination demonstrates the same circumciliary congestion (arrow) in left eye. (C) Slit lamp examination of left eye demonstrates irregular pupil (arrow) due to presence of posterior synechiae. (D) Slit lamp examination of left eye after a release of posterior synechiae demonstrates pigments (arrow) on the anterior capsule of the left lens.

event reporting system (VAERS) are for severe side effects.[14] We reported this case to VAERS because of rapid onset of symptoms within 2 h of receiving vaccination and because several clinical features (unrelenting fever, diarrhea accompanied by migratory arthritis and anterior uveitis, absence of rash on the body) were considered to be consistent with a diagnosis of reactive arthritis secondary to mpox vaccination.

There is no evidence of the benefit of antibiotic therapy in the diminution of clinical course in the noninfective form of reactive arthritis. Sulfasalazine and NSAIDs may be used for chronic cases lasting more than 6 months, and other biological disease-modifying antirheumatic drugs (DMARDs) or anti-TNF agents can be used in cases of poor response.[11] In addition to other treatments, physical therapy and local measures like cold compression can be used as supportive modalities for joint pain.[13] Uveitis is treated with topical steroids, mydriatics, and systemic corticosteroids in severe cases.[9] Short courses of systemic corticosteroids (up to 4 months) are used for peripheral joint symptoms not responsive to NSAIDs.[15]

Reactive arthritis has a good prognosis in general, with most people having a complete recovery within a year.[10] However, there is a high recurrence rate of joint and eye inflammation, and 20%–70% of patients develop other joint problems such as ankylosing spondylitis.[10]

4. Conclusion

The advantage of vaccination in emerging outbreaks is considered to surpass the potential risk of autoimmune inflammatory response in predisposed individuals. However, this case of autoimmune inflammatory response after mpox vaccination shows the importance of vigilance for this reaction, continued study to identify individuals at higher risk of this complication, and persistent effort to report to VAERS to improve the available data from which vaccine formulators may derive identifiable biomarkers to further inform efforts to improve the safety of vaccine formulations in the future.

Funding

No outside funding was received for this study.

Conflict of interest

The authors have no potential conflict of interest related to this article.

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