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Mpx: What Practicing Gastroenterologists Need to Know

The World Health Organization declared human monkeypox virus (HMPXV) infection, or Mpx, a global health emergency on July 23, 2022.\(^1\)\(^-\)\(^3\) Although new case counts are declining, early diagnosis remains essential. This commentary provides a brief overview of Mpx infection and reviews the presentations of infection because gastroenterologists are uniquely positioned to detect Mpx during routine examination of the perianal region and during endoscopic evaluation.

Our Current Understanding of Mpx

What Is the HMPXV?

HMPXV is an enveloped double-stranded DNA virus. It is a member of the Orthopoxvirus genus of the Poxviridae family, the same family as Variola (smallpox) virus. Several rodents and small mammals are the suspected natural reservoirs of this zoonotic virus. HMPXV, first described in humans in 1970, is considered endemic in central and western Africa.\(^4\)

There are 2 circulating HMPXV clades (genetic groups). Clade 2 is associated with milder disease and fewer deaths. Before 2022, almost all nonendemic HMPXV cases were linked to international travel to endemic countries or through imported animals. In contrast, most HMPXV cases associated with the 2022 outbreak occurred by local transmission in the United States and other nonendemic regions.

How Does HMPXV Spread and Who Gets Infected?

Transmission occurs through close or direct contact with skin lesions or bodily fluids, through contaminated fomites (porous surfaces like clothes and bedding, or surfaces that have been in contact with fluid from lesions), and possibly through large respiratory droplets. There is also evidence of vertical transmission.\(^2\) During the 2022 outbreak, most new cases occurred in gay, bisexual, and other men who have sex with men. The Centers for Disease Control and Prevention (CDC) identified these groups as most likely to benefit from enhanced vaccination efforts.\(^3\)

Although vaccination against smallpox may be protective, segments of the population younger than ages 40–50 years may be more susceptible to Mpx because of the cessation of smallpox vaccination campaigns by the mid-1970s. Because of the risk of waning vaccination protection, the CDC recommends repeat vaccination for at-risk individuals whose last vaccine was more than 3 years ago.\(^3\)

What Is the Clinical Presentation of Mpx?

Classically, infected persons present with prodromal symptoms (fever, headache, myalgia, lymphadenopathy, upper respiratory symptoms) followed by a characteristic rash that starts in the mouth and then spreads to the face and extremities, including the palms and soles. Lesions, ranging from tens to hundreds, begin as macules and progress to papules, vesicles, and pustules, eventually scabbing over and falling off with new skin underneath. During the current outbreak, the presentation of Mpx has differed from the classic presentation. For example, skin lesions may be limited to only the oral, genital, perigenital, and perianal areas and may present as a single lesion or ulcer; different stages of development may be present side by side; or individuals may present with only mild or absent prodromal symptoms that may begin after the onset of the skin lesion(s).

Based on a systematic review of 46 articles, describing 1984 confirmed cases (48 from case reports and 1937 from observational cohort studies), anogenital lesions were the most observed skin manifestations in up to 66% of cases.\(^5\) The lesions were vesiculopustular, vesicular-umbilicated, or pseudopustular lesions with less than 10 lesions per patient. Almost all patients reported systemic manifestations, including fever, lymphadenopathy, fatigue, myalgia, and headaches.\(^5\) In ~20% cases, pharyngitis or dysphagia was reported. The incidence of proctitis and/or proctalgia ranged from 22% to 37% in different case series.\(^6\)\(^-\)\(^9\) There is documentation of ulcers in the rectum and oropharynx, based on at least 1 publication.\(^10\) In 1 study of 70 men who have sex with men, 26 (37.1%) had signs and symptoms of proctitis with anal pain as the most common presenting symptom.\(^9\) In 11 patients (42.3%), proctitis preceded the skin rash, appearing a median of 3 days (range, 1–7) before the rash. In 6 patients (23%) proctitis was the only clinical manifestation. Three patients with proctitis (11.5%) were found to have a protruding anal mass (positive polymerase chain reaction [PCR] test on rectal swab) accompanied by excruciating pain. Another 3 patients complained of having a feeling of a new anal mass, but no mass was found on inspection. One patient with proctitis had a pelvic computed tomography performed that demonstrated diffuse rectal wall thickening surrounded by infiltrated fat with associated lymphadenopathy. The cause of proctitis was believed to be direct inoculation of the virus into the rectal mucosa. All patients were sexually active men who have sex with men. More than one-fourth were HIV positive.

How Long Is an Individual With Mpx Considered Infectious?

The CDC currently recommends that individuals isolate at home for the duration of their illness, which can be up to 4 weeks.\(^3\) Patients are infectious from the time prodromal symptoms start until the lesions scab and fall off, with a new layer of skin formation underneath. The extent to which asymptomatic infection may occur is unknown. To date, positive PCRs have been detected from rectal swabs (including in asymptomatic persons), stool, saliva, and semen in addition to the lesions themselves (including scabs). Detection of
viral DNA is variably associated with infectious virus.\textsuperscript{11,12} The US Food and Drug Administration has advised that HMPXV may be transmitted through fecal microbiota transplantation products (although the risk of such transmission is unknown) and that additional protections were needed for the investigational or clinical use of fecal microbiota transplantation (such as updated donor-screening processes and development of an efficacious and reliable test to detect HMPXV viral DNA in fecal matter).\textsuperscript{13}

**How Is the Diagnosis of Mpox Made?**

In a patient with suspected active Mpox infection, a diagnosis can be made by obtaining a specimen from a skin lesion. Certain laboratories can perform specific PCR testing, whereas others perform generic orthopox virus testing (which may detect other orthopox pathogens, such as vaccinia or cowpox). Although some laboratories perform PCR testing of pharyngeal and rectal swabs, current US Food and Drug Administration–approved assays are intended only for swabs from lesions. Turnaround times vary. It is important to check with your local health department regarding reporting requirements for diagnosed and suspected Mpox and testing information.

**Is There a Vaccine to Prevent Mpox?**

Two vaccines, both designed for smallpox, are recommended for Mpox: ACAM2000 and Jynneos.\textsuperscript{14-16} These vaccines are currently targeted for prevention in individuals at high risk of exposure and can also be used as postexposure prophylaxis up to 14 days after exposure. ACAM2000, a second-generation smallpox vaccine, is a live virus vaccine that requires 1 shot using the multiple puncture technique. Because of concern over secondary spread of vaccinia infection, ACAM2000 has not yet been used during the 2022 Mpox outbreak. Jynneos (modified vaccinia Ankara, MVA), a third-generation smallpox vaccination, is a live nonreplicating vaccine that requires 1 subcutaneous shot 4 weeks apart. MVA is generally considered safe. The most notable side effect is injection site reaction. However, myocarditis and pericarditis are rare side effects (1/10,000 vaccinated individuals), occurring up to 6 weeks after vaccination.\textsuperscript{17}

During the 2022 outbreak an emergency use authorization allowed MVA to be given in smaller doses intradermally to expand availability. MVA, as a nonreplicating vaccine, does not cause disease in humans and is safe in immunocompromised individuals, including those receiving immunosuppressing medications. ACAM2000, a live virus vaccine, is contraindicated in immunocompromised individuals. Vaccines for Mpox are expected to be 85% effective, based on data from first-generation smallpox vaccines.\textsuperscript{15} Pre-exposure prophylaxis is currently recommended for certain occupational exposure risk groups (laboratory personnel handling orthopox viruses; gay, bisexual, and other men who have sex with men; and people who have sex in a commercial sex venue).\textsuperscript{16}

**What Is the Recommended Treatment for Mpox?**

Mpox is a self-limited infection, and most patients will improve without specific treatment. Supportive care including topical agents, stool softeners, and over-the-counter and prescription pain control may benefit patients. Patients with severe disease or individuals at risk of severe disease may benefit from specific antiviral therapy, which can be started empirically while testing is pending.

Tecovirimat (TPOXX\textsuperscript{®} or ST-246\textsuperscript{®}, SIGA Technologies) is a novel antiviral that inhibits the VP37 protein, preventing the formation of intracellular enveloped virus and stopping viral development. In a safety study, tecovirimat was not associated with any serious adverse events; however, efficacy data are extremely limited. No randomized control trials have been completed, although several are ongoing.\textsuperscript{18} Tecovirimat has been used as a first-line therapy during the 2022 outbreak. In the United States, this drug is currently only available through an expanded-access investigational drug process through the CDC. Cidofovir and brincidofovir likely have activity against orthopox viruses by acting as competitive inhibitors that are incorporated into growing DNA strands and blocking DNA synthesis. However, their use is limited because of toxicity. Cidofovir is associated with nephrotoxicity, whereas brincidofovir administration is frequently associated with elevated liver enzymes.\textsuperscript{19} These have been used as second-line agents during the 2022 outbreak, reserved for individuals with severe or progressive disease.

**What Is the Prognosis for Patients With Mpox?**

Classically, Mpox infection has been considered a self-limited disease; however, young children and immunocompromised persons, including persons living with HIV infection, have been reported to be at increased risk for severe outcomes. Complications of Mpox are rare but can include secondary infections, bronchopneumonia, sepsis, encephalitis, and conjunctivitis/keratitis with ensuing loss of vision.

Published reports of the 2022 Mpox outbreak have highlighted that mortality is rare; however, many patients have presented with severe disease including proctitis with tenesmus, urethritis, and pharyngitis. In a case series of 528 persons, 70 persons required hospitalization for severe rectal pain (n = 21), soft tissue infections (n = 18), or sore throat and difficulty swallowing (n = 5).\textsuperscript{10} In another case series from the United Kingdom of 196 men with confirmed Mpox, all presented with mucocutaneous lesions in the genital or perianal area, and reasons for admission included perianal or rectal pain (8/20) or penile swelling (5/20).\textsuperscript{20} Long-term outcomes of infection remain unknown.

**What Practicing Gastroenterologists Need to Know**

**Recognition of Potential Mpox Infection**

When seeing patients with new anal or perianal lesions or new
symptoms of proctitis, gastroenterologists should consider Mpx, especially in male patients who have sex with men. Inquiries about potential prodromal symptoms and a careful skin examination are essential (Figure 1). Prodromal symptoms (fever, headache, fatigue, muscle aches) may occur concurrently with skin lesions or may be absent. The differential diagnosis includes varicella zoster virus, molluscum contagiosum, herpes simplex virus, syphilis, impetigo, measles in the early stages, and rickettsial diseases. For anogenital ulcers, the differential includes gonorrhea and lymphogranuloma venereum. Of note, lymphadenopathy is a distinctive feature of Mpx compared with other diseases. When presented with a possible case, gastroenterologists should notify their local infection prevention and control department and local department of health.

In the current outbreak, rectal pain, especially in the setting of proctitis, is one of the most common presentations of Mpx. Although reports of endoscopy for Mpx proctitis are limited, imaging studies (computed tomography) have demonstrated severe circumferential thickening of the anorectal wall with broad discrete nonenhancing hypointense zones because of intramural ulceration. When severe, it may be associated with rectal bleeding, tenesmus, and the need for hospital admission. Pharyngitis leading to dysphagia and nausea and vomiting in the setting of pain may limit eating and drinking and lead to dehydration. Patients are prone to pharyngeal superinfections.

**General Risk of Mpx to Healthcare Workers**

The risk for transmission of Mpx in a healthcare setting has not been formally studied. In general, Mpx is not easily transmissible, and the CDC
does not currently recommend pre-exposure vaccination for healthcare workers. Potential high-risk exposures for healthcare workers include direct exposure of the healthcare worker’s broken skin or mucous membranes to materials, skin, lesions, or bodily fluids of a patient or close contact during an aerosol-generating procedure when not wearing respiratory protection (N95 masks).21

What To Do After Exposure to a Known Patient With Mpox

Although the risk of HMPXV transmission to healthcare workers is low with appropriate precaution, healthcare workers who are exposed may benefit from postexposure prophylaxis. In healthcare providers with a low risk of exposure (ie, appropriate use of personal protective equipment), vigilance for symptom development for the next 21 days is recommended, and individuals can self-monitor for fever, chills, lymphadenopathy, and new skin rash.2

Specific Concerns With Endoscopy

To date, there have been no reports of endoscopic transmission of the virus, although contamination of surfaces in hospitals has been reported.22 All surfaces that come in contact with patients should be disinfected using standard hospital-approved disinfectants including both bleach and hydrogen peroxide–based products containing antiviral activity. Soiled laundry should be handled gently, and medical waste can be handled in the same manner as other medical waste. Appropriate use of personal protective equipment, including facemasks, should reduce transmission risk during endoscopy. This includes N95 or similar mask and eye protection for upper endoscopy where risk through aerosolized viral particles may be higher. The CDC recommends wet cleaning of rooms to minimize chance of resuspending settled particles.2 Standard endoscope cleaning and disinfection techniques may pose a risk to staff through aerosolization. Soaking endoscopes first in disinfecting solutions known to reduce vaccinia populations (eg, glutaraldehyde) before the standard cleaning cycle has been shown to be effective; however, there is no formal guidance for disinfection of HMPXV.25

Conclusions

Gastroenterologists are uniquely positioned to detect Mpx as mucocutaneous lesions around the anogenital and oral areas. Pharyngitis and proctitis are unique clinical presentations of the current outbreak. Having a high clinical suspicion for infection is critical to ensuring appropriate referral and treatment and minimizing risk to other individuals in the community.

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