Neuropsychiatric Manifestations of Mpox (monkeypox) Virus Amidst a Global Outbreak

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Mpox (formerly monkeypox) is a zoonotic virus in the *Poxviridae* family and *Orthopoxvirus* genus that has recently been implicated in outbreaks worldwide.[1] The *Orthopoxvirus* genus contains other viruses including the variola virus and vaccinia virus that cause diseases such as smallpox, cowpox, horsepox, and camelpox.[2] The World Health Organization[3] recently announced that they will begin using the new preferred term *mpox* to reduce stigma associated with the term *monkeypox*.

Transmission of mpox is through contact with infected body fluids, respiratory droplets, or skin directly or indirectly through fomites.[1] Many cases have been identified in men who have sex with men.[4] Mpox human infection can be diagnostically confirmed via viral culture or polymerase chain reaction for mpox DNA. As noted with other viral illnesses, there is currently no known specific intervention proven to treat mpox infection in addition to supportive management.[1]

In this report, we discuss neuropsychiatric manifestations of mpox infection that providers may encounter in the setting of the worldwide mpox virus outbreak.

Epidemiology

Mpox is known to be endemic to western and central Africa, starting in the Democratic Republic of the Congo in the 1970s. Within the past year, there have been multiple reports of mpox virus infection linked to the West African clade among individuals involved in international travel from Africa or African animal imports. By June 10, 2022, over 1,500 cases of mpox virus had been reported transcontinentally in nonendemic countries.[5] By the end of July, over 66,471 cases of mpox virus had been reported in 106 countries, with 25,341 cases in the United States.[6] Many of these countries have not had a confirmed case of mpox virus in 30 to 40 years.[7]

Production of smallpox vaccines, involving the vaccinia virus in the *Orthopoxvirus* genus, was discontinued in 1982 after smallpox was globally eradicated.[8] The smallpox vaccine carried cross-immunity to the mpox virus, as they both share the *Orthopoxvirus* genus.[9] Therefore, the overall population has waning immunity to smallpox, which may contribute to the recent surge in mpox virus cases. The international spread of mpox to nonendemic areas with waning smallpox immunity stresses the importance of understanding manifestations, management, and prevention of this disease.[7]

Somatic Manifestations

Manifestations of mpox infection in endemic locations have been well documented in the literature. Four to 17 days after mpox virus exposure, patients develop a febrile prodrome with headache, myalgia, fatigue, and lymphadenopathy. After 1 to 2 days, diffuse maculopapular or vesiculopustular lesions erupt on mucosal regions followed by the face and extremities, including the palms and soles. The lesions remain pustular for 5–7 days before crusting and desquamating over 1 to 2 weeks. Once the lesions have crusted and fallen off, the individual is considered noninfectious. Mpox infection duration lasts 2–4 weeks and is associated with low mortality.[1,3]

Complications of mpox infection include permanent skin scarring, hyperpigmentation or hypopigmentation, corneal scarring, pneumonia, dehydration, sepsis, and encephalitis.[1] The recent mpox virus outbreak, characterized by the West African clade, may have missing or delayed prodromal symptoms. The rash has also been seen to first develop in oral, genital, and anal mucosal areas without spread to other areas.[3]

Neuropsychiatric Symptoms

Little is known about the neuropsychiatric effects of mpox infection at this time. Neurologically, mpox virus has been associated with dangerous encephalitis complications. In 2022, there were 2 described fatal cases of neuroinvasive mpox virus disease in immunocompetent adult men.[3] Other neurologic manifestations of mpox virus include headache, weakness, stiff neck, and confusion.[2,3] Neurologic workup may include magnetic resonance imaging (MRI), electroencephalogram (EEG), and cerebrospinal (CSF) analysis. Cortical MRIs have demonstrated diffuse edema, meningeal amplification, and signal abnormalities. EEG findings have demonstrated diffuse slowing. CSF findings include predominantly polymorphonuclear pleocytosis and lymphocytes with normal glucose and protein levels.[2]

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Prim Care Companion CNS Disord 2022;24(6):22br03429

To cite: Mittal R, Pathak M, Jain A. Neuropsychiatric manifestations of mpox (monkeypox) virus amidst a global outbreak. *Prim Care Companion CNS Disord.* 2022;24(6):22br03429.

To share: https://doi.org/10.4088/PCC.22br03429

A meta-analysis[10] examined data from 19 studies including 1,030 participants with confirmed mpox virus infection. The most prevalent neuropsychiatric symptoms of mpox infection were myalgia (55.5%), headache (53.8%), fatigue (36.2%), seizure (2.7%), confusion (2.4%), and encephalitis (2.0%).[10] There were not enough data to report on the prevalence of psychiatric symptoms including anxiety and depression. However, facial scarring is a potential complication of mpox virus infection that can be associated with persistent anxiety and depression. The emotional toll of infection may also lead to reduced self-esteem and loss of identity[10] and has been described in other studies[11] of previous outbreaks of mpox virus infection in Africa. Psychosocial disturbances involving hospitalization and social isolation may be related to reported symptoms of anxiety and depression. Individuals with preexisting mental illness may be more susceptible to psychiatric symptoms from mpox virus infection.

Recent psychiatric manifestations of mpox infection described in the literature include mood disturbance, emotional lability, depression, and acute alcohol withdrawal.[12,13] Previous documented outbreaks of mpox virus provide valuable information regarding psychiatric manifestations as well. In Nigeria from September 2018 to December 2019, 11 of 40 (27.5%) hospitalized patients with confirmed mpox virus developed anxiety and depression symptoms necessitating psychotherapy.[14] A 2017 case of a Nigerian man with no preexisting psychiatric disease admitted to the hospital for mpox infection emphasizes the psychological toll of the disease.[15] The 34-year-old businessman reported mild anxiety regarding implications of his disease without reported suicidal ideation at admission. On his fourth day of admission, he completed suicide via hanging.[15] This case emphasizes the need for greater attention to the psychological toll and psychiatric complications manifesting from mpox infection during the current global outbreak.

CONCLUSION

With the recent worldwide surge in confirmed mpox virus cases, providers should be aware that neuropsychiatric manifestations of mpox virus infection can be debilitating. Neuropsychiatric symptoms include headache, weakness, fatigue, anxiety, depression, and worsening of preexisting psychiatric symptoms. More research is needed to understand the prevalence of psychiatric complications associated with mpox virus infection.

Submitted: October 3, 2022; accepted October 18, 2022.
Published online: December 20, 2022.
Relevant financial relationships: None.
Funding/support: None.

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