People With Advanced HIV Can Have Very Severe Mpox

More than a quarter of HIV-positive people with a CD4 count below 100 died of mpox complications.

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Mpox (formerly known as monkeypox) can be much more severe in people living with HIV who have a very low CD4 count, according to a case series presented at the 30th Conference on Retroviruses and Opportunistic Infections in Seattle and published simultaneously in The Lancet.

The presentation of mpox is "very starkly different" among HIV-positive people with severe immune suppression, so much so that it should be classified as an AIDS-defining opportunistic infection, said presenter Chloe Orkin, MD, of Queen Mary University of London.

The series included nearly 400 cases of mpox among people with HIV who had a CD4 T-cell count below 350. Many patients had severe necrotizing lesions resulting in tissue death, and some had lung involvement and sepsis. The overall mortality rate was 7%, rising to 27% among those with a CD4 count below 100.

The silver lining is that no one with well-controlled HIV and no one who was vaccinated against mpox vaccine died, suggesting that antiretroviral treatment can prevent severe outcomes. However, Orkin advised clinicians who care for untreated patients with severe mpox to be alert for immune reconstitution inflammatory syndrome (IRIS), a worsening of symptoms that can occur when people start antiretrovirals with a very low CD4 count.

Mpox and HIV

The 2022 mpox outbreak in countries outside of Africa was first identified in England last May. To date, the Centers for Disease Control and Prevention (CDC) has identified more than 30,000 cases of mpox in the United States and nearly 86,000 cases worldwide. The overwhelming majority of cases have been among gay men.

Mpox cases have declined dramatically since the outbreak peaked in late summer, likely due to a combination of behavior change, vaccination and natural immunity after infection. But mpox remains a risk for people living with HIV, who account for up to half of all cases in this outbreak.

Several studies have shown that HIV-positive people on antiretroviral therapy with an

undetectable viral load and an adequate CD4 count do not fare worse than their HIV-negative peers. But it's a different story for those with more advanced immune suppression.

For example, a smaller case series from the CDC, published in November, looked at 57 people hospitalized with mpox. More than 80% were living with HIV, but only four were on antiretroviral treatment, and 72% had a CD4 count below 50. All had severe skin manifestations, and some had involvement of the lungs, eyes and brain. Nearly a third required intensive care and 12 people died.

Now, a larger global analysis confirms this dire picture.

To characterize the worldwide mpox outbreak, Orkin and a large team of colleagues formed an international collaboration known as the SHARE-net Clinical Group. The group previously published studies that described the spectrum of mpox symptoms and mpox cases among women.

The new case series compiles data from 382 HIV-positive people with mpox in 19 countries. Most were cisgender men, four were cisgender women and 10 were transgender women. The median age was 35. Nearly three quarters of the case reports came from the Americas (individual countries were not specified), about one quarter from Europe and less than 2% from Africa. Only 7% had received an mpox vaccine.

Although about 90% of the patients were previously diagnosed with HIV, just 60% were on antiretroviral treatment and only half had an undetectable viral load. One third had a CD4 count between 200 and 300, one quarter between 100 and 200 and 22% below 100; 200 is the threshold for an AIDS diagnosis. Overall, 8% had a concurrent opportunistic illness, but this rose to 26% among those with the lowest CD4 counts.

Mpox looked like a very different disease among people with uncontrolled HIV, Orkin reported. Most people developed a skin rash, with the number, size and extent of the lesions increasing as CD4 counts fell. Nearly one quarter developed large necrotizing lesions, which in some cases coalesced, or merged. Many had disseminated lesions far from the site of viral entry, suggesting systemic infection carried through the bloodstream. Lesions were "teeming with virus," Orkin said, indicating that people with immunosuppression are unable to contain the infection.

Some patients experienced more severe complications, including inflamed tonsils, swollen lymph nodes that impeded swallowing or breathing, necrotic genital lesions, urinary obstruction or bowel perforation.

Internal organs were also affected. About 9% overall—but 29% of those with a CD4 count below 100—developed respiratory complications (including lung nodules), 5% had eye complications and 3% had neurological manifestations. Nearly one quarter developed secondary bacterial infections. All types of complications were much more common among those with the lowest CD4 counts.

Nearly 30% of the patients were hospitalized, including 9% who required intensive care. However, just 16% were treated with the antiviral drug TPOXX (tecovirimat), which was only available to

people in the United States, Brazil and Europe. Some people progressed and died despite repeated courses of TPOXX.

Overall, 27 people (7%) died, with mortality heavily concentrated among those with the most advanced immune suppression. No one with a CD4 count above 200 and just 4% of those with a count of 100 to 200 died, but the mortality rate rose to 27% for those with a count below 100. Most of those who died had multiple severe mpox complications and their median CD4 count was only 35. HIV viral load also played a role: Among those with a CD4 level below 100, the mortality rate was 7% for those with viral suppression versus 30% for those with a high viral load.

Orkin reported that 85 people either started antiretroviral treatment for the first time or restarted therapy. Of these, 25% had suspected IRIS. Among those with IRIS, the mortality rate was 57%. The patients who developed IRIS started antiretrovirals a median of 21 days after presenting with mpox symptoms. It is unknown whether starting HIV treatment earlier, when mpox symptoms first appear, would lead to better outcomes, she said.

The difference in outcomes between people with well-controlled and uncontrolled HIV clearly show the "huge advantage" of being on antiretroviral therapy, Orkin told reporters at a media briefing. "Late HIV treatment may be the main reason things were so bad." However, she added, "sometimes in very sick people, the timing of HIV treatment has to be carefully considered."

According to the study authors, mpox acts as an opportunistic infection in people with uncontrolled HIV, and the severe necrotizing form is an AIDS-defining illness. They called on the CDC and the World Health Organization (WHO) to add mpox to the 14 other opportunistic conditions in international disease classifications.

Already, the Department of Health and Human Services HIV treatment guidelines has noted in a September 2022 update that, "Some reports suggest that monkeypox could be an opportunistic infection in people with HIV."

Meg Doherty, MD, PhD, head of WHO's global HIV, hepatitis and sexually transmitted infection programs, said the agency will review the data and consider the researchers' recommendations. "The recent case series makes a very compelling case that in people living with HIV and with a CD4 count less than 200, the risk of severe disease and death from mpox is high and disseminated infection behaves like other opportunistic infections," she said in a statement.

This classification is important because in some countries—including the United States—having an AIDS diagnosis can unlock certain services and financial support.

The study findings paint a disturbing picture of inadequate health care for people living with HIV worldwide, many of whom do not know their status. The study authors advised that clinicians should be alert for mpox progression in people known to have HIV and that all people with mpox should be tested for HIV if their status is unknown.

"If there's someone in your life who hasn't had an HIV test and may have a low CD4 count without

knowing it, if they get mpox it could have catastrophic outcomes," Orkin said.

The authors also recommended that HIV-positive people with a CD4 count below 200 should be prioritized for mpox antivirals and vaccines—including in those countries where these resources are currently not available.

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