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Monkeypox and pregnancy

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In May 2022, the World Health Organization reported an emerging global outbreak of monkeypox virus infection. Clinical manifestations of monkeypox allow us to quickly suspect the disease. Until now, no pregnant women infected with this virus have been reported; however, because of its speed of spread worldwide, it is possible that we will soon observe such cases. Thus, it is necessary for obstetrician—gynecologists to know the disease, its clinical manifestations, and the experiences reported in the few previous cases in pregnant women.

Keywords: miscarriage, monkeypox virus, pregnancy, premature delivery, stillbirth

Monkeypox virus epidemiology

Monkeypox is a viral zoonosis caused by the monkeypox virus, which is a large double-stranded DNA virus of the genus *Orthopoxvirus*, family Poxviridae. It occurs mainly in tropical forest areas of Central and Western Africa and is sporadically exported to other regions, currently with an outbreak of >35,000 confirmed cases in >85 countries worldwide. The zoonotic virus is transmitted through bites or scratches from an infected animal, contact with fluid from active lesions, or sexual intercourse. Most of the initial cases in the current outbreak presented with anogenital lesions, lesions in the mouth, and proctitis, without a previous prodromal phase and with the common association of sexual intercourse among men; many public health experts believe that the current outbreak probably originated among men who had sex with men.

There are 2 "clades" or versions of the monkeypox virus: West African and Central African. The latter is more virulent, whereas the West African clade is milder, with a mortality of between 1% and 10%, and seems to be the one that is causing the current crisis.

Clinical manifestations

The clinical manifestations of monkeypox are usually mild to moderate. The first symptoms that patients experience are fever, intense headache, generalized weakness, arthralgia, and lymphadenopathy (absent in smallpox) at the neck or inguinal level, followed by lesions or skin rash. The rash evolves sequentially from macules to papules, vesicles, pustules, and crusts, all in the same stage, which differentiates it from chickenpox rash, in which the lesions occur in different stages. The lesions are most frequently located on the face, followed by the lower limbs and hands, and there may be lesions in the oral mucosa and corneal involvement.[1] The number of lesions correlates directly with the severity of the disease. In the current outbreak, the initial clinical manifestations in some people have been in the genital and/or perianal area, sometimes preceded by symptoms of proctitis,[1,2] and may be confused with a sexually transmitted disease. An Italian study isolated the monkeypox virus in the seminal fluid of 4 patients, suggesting sexual transmission, although more studies are needed in this regard.[2]

It is known from previous studies that the clinical course of the disease lasts 3 to 4 weeks and is generally self-limited. Severe cases occur more frequently among children, young adults, immunocompromised people, and pregnant women, and are related to the degree of exposure to the virus and the vulnerability of the person.

Complications and differential diagnosis

The most frequent complication is bacterial infection of skin lesions in up to 20% of cases. Other less frequent complications include bronchopneumonia, sepsis, inflammation of the central nervous system (encephalitis) (all in <1% of cases), and eye infection (4% of cases). The disease can be confused with various pathologies, including infectious exanthematous skin diseases (varicella, herpes zoster, measles, Zika, dengue fever, chikungunya, herpes simplex, bacterial skin infection, disseminated gonococcal infection, primary or secondary syphilis, chancroid, lymphogranuloma venereum) and dermatologic lesions of noninfectious etiology such as urticarial papules and plaques produced by dermatitis, acne, drug rashes, and others.[1–4]

Diagnosis

The diagnosis of the infection is based on clinical examination, electron microscopy, histologic examination, serologic tests, and polymerase chain reaction (PCR) analysis of skin scrapings. The diagnostic test of choice is the specific PCR. Multiple specimens from different lesions at different stages of infection should be taken to ensure an adequate sample for the laboratory and to decrease the chance of a false-negative result. Clinicians wishing to submit specimens should coordinate with their local health department and the institution that carries out epidemiologic control in their region or country.

Pregnancy

Historic studies show that smallpox is more serious in pregnant women than in nonpregnant women or in men, and the risks of severe hemorrhagic smallpox, miscarriage, stillbirth, and

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TABLE
Monkeypox during pregnancy

Severity in the mother	Antiviral treatment	Adverse course of pregnancy	Fetal/newborn complications	Delivery mode	Neonatal care	Samples from newborns
Potentially serious	Tecovirimat; CDC —recommended	Abortion, premature birth	Fetal death, stillbirth, congenital infection	No information on the correct route of birth delivery. Consider CD, especially if there are genital or perianal injuries.	Isolation in a separate room with caregivers. In a shared room if the RT-PCR of monkeypox virus in the newborn is positive.	RT-PCR: throat swab or skin lesions if present. From blood and urine if media are available.

CD, cesarean delivery; *CDC*, Centers for Disease Control and Prevention; *RT-PCR*, reverse transcription polymerase chain reaction.

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premature delivery are higher among women who have had smallpox.[3] Studies in pregnant women with monkeypox are limited, even in countries where the disease is endemic. A study[4] of 122 patients with the disease, conducted in the Democratic Republic of the Congo reported on the fetal outcomes of 4 pregnant women, of whom 1 carried a healthy infant to term, 2 had first-trimester miscarriages, and 1 had stillbirth. This stillborn infant was covered with diffuse maculopapular skin lesions affecting the head, trunk, and extremities, including palms of the hands and soles of the feet.[4] Only obstetrical maternal complications were described.

In the current monkeypox outbreak, no cases have been reported in pregnant women to date. However, it is important that health professionals in charge of caring for pregnant women become familiar with all aspects of the disease, including its behavior during pregnancy and its potential effect on the fetus and newborn Table.

Treatment: monkeypox vaccine and antiviral medications in pregnant women

Like other viral disease treatments, monkeypox treatment is based on symptom management and control of associated complications, especially skin and mucosal lesions. Treatment includes acetaminophen, adequate hydration, antihistamines to control pruritus, careful inspection of skin lesions for superimposed bacterial infection, and appropriate treatment with either topical or systemic antibiotics.

Paracetamol is used for fever management (500 mg−1 g every 6−8 hours) or ibuprofen (400 mg every 8 hours) or tramadol in case of pain (50−100 mg every 4−6 hours). Loratadine (10 mg every 24 hours) or hydroxyzine (25 mg every 24 hours) are used in case of intense itching. For bacterial superinfection, oral cephalexin (500 mg every 6 hours for 5 days) or oral clindamycin (300−600 mg every 6−8 hours for 7 days) are used.

To date, there has been no approved specific antiviral treatment for the management of monkeypox infection. However, it is proposed to apply one antiviral medication (tecovirimat) and a vaccine with immunoglobulin to prevent the spread of the virus, thus reducing infectiousness. This can be considered for pregnant women who are severely ill. The European Medicines Agency has approved tecovirimat for monkeypox, and the US Food and Drug Administration (FDA) prescribing information for tecovirimat confirms that no embryotoxic or teratogenic effects have been detected in animal studies. The oral dosage of tecovirimat would be 600 mg every 12 hours for 14 days in women weighing >40 kg.

Monkeypox vaccines

MVA-BN is a third-generation smallpox vaccine recently approved in the United States, Canada, and the European Union. Because of the high degree of attenuation, the vaccine virus has very little ability to replicate and should not pose a risk to the pregnant woman or her fetus. In the United States, where MVA-BN is marketed as JYNNEOS, it is approved by the FDA for vaccination against both smallpox and monkeypox. The JYNNEOS vaccine is 85% effective in protecting against monkeypox.

The ACAM2000 vaccine is contraindicated during pregnancy because it contains a live virus (vaccinia virus), and cases of fetal vaccinia have been documented after maternal vaccination.[5] The US Centers for Disease Control and Prevention indicates that this vaccine could be indicated in pregnant women in a national emergency such as a bioterrorist attack with the smallpox virus.

Conclusion

Because monkeypox is a disease unknown to most professionals in countries outside Africa, and may go unrecognized, a high index of suspicion is recommended, especially in people from countries affected by the outbreak or their contacts. For these people, when in doubt, all the logistics must be implemented to make the etiologic diagnosis as early as possible, isolate the patient, trace contacts, use personal

protective equipment, vaccinate if possible, and thus cut the chain of transmission. Although no pregnant women have been reported in the current outbreak, the possibility exists, and the risks associated with monkeypox infection during pregnancy are severe, especially for embryos, fetuses, and newborns. For this reason, we must be prepared to address cases among pregnant people through optimal measures should infection occur in this population. ■

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