CORRESPONDENCE

Three Cases of Vertical Transmission of Clade Ib Mpox Virus

TO THE EDITOR: Mpox (formerly known as monkeypox), which is caused by the virus MPXV, has been associated with adverse pregnancy outcomes, but evidence of vertical transmission remains limited.[1-3] Concerns regarding transplacental transmission are heightened by the ongoing clade Ib mpox epidemic, which often affects persons of reproductive age.[4] We report three cases of clade Ib MPXV infection in pregnant women in whom we assessed molecular and histopathological evidence of transplacental transmission across all trimesters. Details of the methods, clinical presentation, and histopathological testing are provided in the Supplementary Appendix, available with the full text of this letter at NEJM.org.

The first case involved a woman at 6 weeks' gestation who had fever, generalized rash, inguinal adenopathy, and painful genital discharge and edema. She tested positive for clade Ib MPXV. Despite supportive therapy, she had a spontaneous abortion. MPXV DNA was detected in placental and embryonic tissues, with cycle threshold (Ct) values of 20.1 and 13.4, respectively (Table 1). Histopathological testing of these tissues showed MPXV antigen colocalized with CD68-positive placental villous macrophages (Hofbauer cells) and alpha-fetoprotein–positive embryonic cells, a finding indicating transplacental transmission (Fig. S1A through S1K in the Supplementary Appendix).

The second case involved a woman with human immunodeficiency virus (HIV) infection who presented at 16 weeks' gestation with widespread vesiculopustular lesions (most prominently in the genital area), fever, adenopathy, and dysphagia. Fifteen days after she tested positive for clade Ib MPXV, fetal movements ceased, and ultrasonography confirmed intrauterine fetal death. A cesarean delivery was performed after unsuccessful induction of labor. The fetus had several mpox-like lesions on the face, chest, abdomen, and upper limbs. MPXV DNA was detected in placental and fetal tissues, with Ct values of 19.3 and 18.3, respectively (Table 1).

The third case involved an HIV-positive woman at 34 weeks' gestation who presented with fever, dysphagia, generalized mpox lesions, and genital ulcers and tested positive for clade Ib MPXV (Table 1). She was admitted to the hospital with hypotension but recovered and was discharged after 29 days. Thirteen days later, at 40 weeks' gestation, she delivered a live infant who had multiple ulcerative skin lesions (Fig. S2). MPXV DNA was detected in a placental swab (Ct value, 23.7) and in an oropharyngeal swab obtained from the newborn (Ct value, 38.2). Histopathological testing showed MPXV antigen within the placental villi, colocalized with CD68-positive cells (Fig. S1L through S1P). Three months later, the mother reported the infant's death, which was considered by the team of clinicians at Kamituga Hospital to have been probably unrelated to mpox.

These findings provide evidence that clade Ib MPXV can be vertically transmitted, resulting in pregnancy loss or congenital infection — data consistent with isolated previous reports regarding clade Ia MPXV.[1,2] These findings support the

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Table 1. Clinical Characteristics, Virologic Test Results, and Pregnancy Outcomes in Women with MPXV Infection.*

Variable	Case 1	Case 2	Case 3
Age range — yr†	20–30	25–35	20–30
Gestational age at diagnosis of infection — wk	6	16	34
HIV infection status	Unknown	Positive	Positive
Receiving ART	Not applicable	Yes	No
Mode of MPXV transmission	Sexual contact	Sexual contact	Skin-to-skin contact
Symptoms and signs	Fever, generalized and genital skin lesions, inguinal adenopathy, pruritus, genital pain, vaginal discharge, labial edema	Fever, generalized and genital skin lesions, inguinal adenopathy, genital pain, dysphagia	Fever, dysphagia, dehydration, hypotension, generalized skin lesions, ulcerative genital lesions, generalized pruritus
No. of lesions	100–250	>250	>250
WHO severity score‡	Severe	Grave	Grave
Pregnancy outcome	Spontaneous abortion	Intrauterine fetal death	Live neonate with congenital mpox
PCR test for MPXV DNA (Ct value)			
Maternal skin lesion	Positive (23.5)	NA	Positive (21.8)
Maternal oropharyngeal swab	Positive (30.5)	Positive (38.6)	Positive (30.5)
Maternal vaginal swab	NA	Positive (35.1)	NA
Maternal blood	Positive (33.1)	Negative	NA
Breast milk	NA	Positive (39.0)	Negative
Placental swab	Positive (20.1)	Positive (19.3)	Positive (23.7)
Swab of embryonic or fetal products or live newborn	Positive (13.4)	Positive (18.3)	Positive (38.2)
MPXV clade identification	Ib	Ib	Ib

* ART denotes antiretroviral therapy, Ct cycle threshold, HIV human immunodeficiency virus, MPXV mpox virus, NA not available, and PCR polymerase chain reaction.
† Age ranges are provided to protect the identities of the women involved.
‡ The World Health Organization (WHO) severity score is based on number of lesions: mild (<25 lesions), moderate (25 to 99 lesions), severe (100 to 250 lesions), or grave (>250 lesions).

importance of preventive interventions, including vaccination, in pregnant women. Prospective large-scale studies are necessary to better understand perinatal outcomes associated with mpox in pregnancy and to guide clinical management.

Emmanuel Hasivirwe Vakaniaki, M.D.,[1] Nono-Raymond Swar Kuispond, M.D.,[1] Yuichiro Hirata, M.D., Ph.D.,[2] Eugene Bangwen, M.P.H.,[3] Isabel Brosius, M.D.,[3] Eddy Kinganda-Lusamaki, M.D., Ph.D.,[1] Seiya Ozono, Ph.D.,[2] Harutaka Katano, D.D.S., Ph.D.,[2] Laurent Gabanga Ndunge, B.Sc.,[1] Noella Mulopo-Mukanya, B.Sc.,[4] Jean-Claude Tshomba, B.Sc.,[4] Elise De Vos, M.Sc.,[3] Christophe Van Dijck, M.D., Ph.D.,[3] Papy Munganga, M.D.,[1] Guy Mukari, M.D.,[1] Yves Mujula, B.Sc.,[1] Divin Mazambi Mambo, M.D.,[5] Steeven Bilembo Kitwanda, M.D.,[5] Nadine Maliyamungu-Bubala, B.Sc.,[5] Léandre Mutimbwa-Mambo, M.D., M.P.H.,[6] Ian Crozier, M.D.,[7] Lori E. Dodd, Ph.D.,[8] Olivier Tshiani-Mbaya, M.D.,[7] Bienvenu Massamba Lebwaze, M.D., Ph.D.,[9] Espoir Bwenge Malembaka, M.D., Ph.D.,[10] Isaac Barhishindi, M.D.,[10] Susanne Krasemann, Ph.D.,[11] Robert Colebunders, M.D., Ph.D.,[12] Patrick D.M.C. Katoto, M.D., Ph.D.,[10] Sheila Makiala-Mandanda, M.D., Ph.D.,[1] Jason Kindrachuk, Ph.D.,[13] Anne W. Rimoin, Ph.D.,[14] Jean-Jacques Muyembe-Tamfum, M.D., Ph.D.,[1] Daniel Mukadi-Bamuleka, M.D., Ph.D.,[4] Tony Wawina-Bokalanga, M.D., Ph.D.,[1] Sabin Sabiti Nundu, M.D., Ph.D.,[1] Tadaki Suzuki, M.D., Ph.D.,[15]

Raphaël Bulakali Chirimwami, M.D., Ph.D.,[9] Laurens Liesenborghs, M.D., Ph.D.,[3] and Placide Mbala-Kingebeni, M.D., Ph.D.[1]

[1] Institut National de Recherche Biomédicale, Kinshasa, Democratic Republic of Congo; [2] Japan Institute for Health Security, Tokyo; [3] Institute of Tropical Medicine, Antwerp, Belgium; [4] Rodolphe Mérieux Institut National de Recherche Biomédicale, Goma, Democratic Republic of Congo; [5] Kamituga General Hospital, Kamituga, Democratic Republic of Congo; [6] Kamituga Health Zone, Kamituga, Democratic Republic of Congo; [7] Frederick National Laboratory for Cancer Research, Frederick, MD; [8] National Institute of Allergy and Infectious Diseases, Bethesda, MD; [9] University of Kinshasa, Kinshasa, Democratic Republic of Congo; [10] Catholic University of Bukavu, Bukavu, Democratic Republic of Congo; [11] University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [12] University of Antwerp, Antwerp, Belgium; [13] University of Manitoba, Winnipeg, Canada; [14] University of California, Los Angeles, Los Angeles; [15] Chiba University, Chiba, Japan.

Dr. Liesenborghs can be contacted at lliesenborghs@itg.be.

Drs. Vakaniaki, Kuispond, and Hirata and Drs. Suzuki, Chirimwami, Liesenborghs, and Mbala-Kingebeni contributed equally to this letter.

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Oral Infigratinib Therapy in Children with Achondroplasia

TO THE EDITOR: In their article on the PROPEL2 trial, Savarirayan and colleagues (Feb. 27 issue)[1] describe the results of a phase 2 dose-finding trial of infigratinib in children with achondroplasia between the ages of 3 and 11 years. This condition is caused by variants in the gene encoding fibroblast growth receptor 3 (*FGFR3*). In an editorial accompanying the article, Hoyer-Kuhn[2] interpreted the results of this trial as a "valuable milestone" in the treatment of achondroplasia, pending the results of the phase 3 PROPEL3 trial (ClinicalTrials.gov number, NCT06164951).

However, infigratinib, a selective tyrosine kinase inhibitor, has effects on FGFRs other than FGFR3. The half-maximal inhibitory concentrations of the drug are 0.9 nmol per liter, 1.4 nmol per liter, 1 nmol per liter, and 60 nmol per liter for FGFR1, FGFR2, FGFR3, and FGFR4, respectively. Adverse reactions that have been reported in patients receiving infigratinib include stomatitis, dry eye, fatigue, alopecia, palmar–plantar erythrodysesthesia syndrome, arthralgia, dysgeusia, constipation, abdominal pain, dry mouth, diarrhea, decreased appetite, blurred vision, and vomiting.[3] In the trial by Savarirayan et al., the investigators report that the majority of children had adverse events that were either mild (in 54%) or moderate (in 39%) and that no patients discontinued treatment because of an adverse event. However, it seems that infigratinib is not selective enough to treat achondroplasia without the risk of such side effects.

TYRA-300, which was developed by Robert Hudkins[4] as an FGFR3-selective inhibitor, may avoid some of the toxic effects associated with the inhibition of FGFR1, FGFR2, and FGFR4. Another FGFR3-selective drug under development, LY3866288 (LOXO-435), was described in the initial results from the FORAGER-1 trial.[5] Future research should focus on FGFR3-selective inhibitors for the treatment of achondroplasia, treatments that do not have side effects caused by influence on FGFR pathways other than the FGFR3 signaling pathway.