Clinical Infectious Diseases

BRIEF REPORT

Dilemmas in Managing Pregnant Women With Ebola: 2 Case Reports

Séverine Caluwaerts,[1,2] Tessy Fautsch,[1] Daphne Lagrou,[1] Michel Moreau,[3] Alseny Modet Camara,[4] Stephan Günther,[5,6] Antonino Di Caro,[5,7] Benny Borremans,[5,8] Fara Raymond Koundouno,[5,9,10] Joseph Akoi Bore,[5,9,10] Christopher H. Logue,[5,11] Martin Richter,[5,12] Roman Wölfel,[5,13] Eeva Kuisma,[5,11] Andreas Kurth,[5,12] Stephen Thomas,[5,11] Gillian Burkhardt,[14] Elin Erland,[14] Fanshen Lionetto,[14] Patricia Lledo Weber,[14] Olimpia de la Rosa,[14] Hassan Macpherson,[15] and Michel Van Herp[1]

[1]Médecins Sans Frontières, Operational Centre Brussels, [2]Institute of Tropical Medicine, Antwerp, and [3]Department of Emergency Medicine, Centre Hospitalier Chrétien, Liège, Belgium; [4]Médecins Sans Frontières, Guéckedou, Guinea; [5]The European Mobile Laboratory Consortium, and [6]Bernhard Nocht Institute for Tropical Medicine, World Health Organization Collaborating Centre for Arboviruses and Hemorrhagic Fever Reference and Research, Hamburg, Germany; [7]National Institute for Infectious Diseases "L. Spallanzani", Rome, Italy; [8]Evolutionary Ecology Group, University of Antwerp, Belgium; [9]Laboratoire des Fièvres Hémorragiques en Guinée, Université Gamal Abdel Nasser de Conakry, and [10]Institut National de Santé Publique, Conakry, Guinea; [11]Public Health England, Porton Down, United Kingdom; [12]Robert Koch Institute, Berlin, and [13]Bundeswehr Institute of Microbiology, Munich, Germany; [14]Médecins Sans Frontières, Operational Centre Barcelona, Spain; and [15]Ministry of Health and Sanitation, Freetown, Sierra Leone

We report 2 cases of Ebola viral disease (EVD) in pregnant women who survived, initially with intact pregnancies. Respectively 31–32 days after negativation of the maternal blood EVD-polymerase chain reaction (PCR) both patients delivered a stillborn fetus with persistent EVD-PCR amniotic fluid positivity.

Keywords. pregnancy; Ebola; EVD.

In March 2014, the World Health Organization declared an Ebola virus disease (EVD) outbreak in Guinea, Guéckédou. The outbreak, which subsequently spread to Sierra Leone, Liberia, Senegal, Mali, and Nigeria, is the largest in history, currently with 27c965 cases and 11c298 deaths reported [1]. The Zaire strain is responsible for the current outbreak [2], with a 64.3% case fatality rate in the 3 most affected countries, Liberia, Sierra Leone, and Guinea, during the first 9 months of this epidemic [3]. In the literature, mortality in pregnant women is extremely high. Case series from prior epidemics report an 89%–93% case fatality rate among pregnant women [4, 5], and perinatal mortality is 100%. No reports have been published of neonates surviving transplacental EVD for longer than 19 days [6].

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Correspondence: S. Caluwaerts, Rue de l'arbre bénit 46, 1050 Brussels, Belgium (severine.caluwaerts@brussels.msf.org).

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Ebola virus (EBOV) transmission occurs through direct contact with body fluids [7]. EBOV has been detected in a variety of body fluids including blood, saliva, urine, sperm, tears, sweat, breast milk, vomit, and excreta [8]. There is a paucity of data on virus persistence in pregnant mothers who survive the infection. Here, we report the cases of 2 pregnant women, one from Guinea (Guéckédou) and one from Sierra Leone (Kissi, Freetown), who had a stillbirth after recovering from infection and in whom EBOV RNA in amniotic fluid, umbilical cord blood, and placenta was detected 32 and 31 days, respectively, after disappearance of EBOV RNA from maternal blood.

Case 1 Description

In September 2014, a 40-year-old G11P10 4-month pregnant woman with only term normal births in her history was admitted to an Médecins Sans Frontières (MSF)-managed Ebola treatment center (ETC) in Guéckédou, Guinea. She complained of several days of abdominal pain and diarrhea and was febrile (39°C). A real-time reverse transcription–polymerase chain reaction (RT–PCR) for EBOV RNA (L gene, Realstar filovirus screen, RT–PCR kit 1.0, Altona Diagnostics, Hamburg, Germany) on whole blood was positive on 9 September 2014 (Table 1). Two malaria rapid diagnostic tests (RDTs) were negative. The patient recovered without complications. Five days after admission, the EBOV RT–PCR on maternal blood was twice negative (Table 1). During admission, she described daily fetal movements. The fetal heart rate was repeatedly checked with Doppler sonography and remained within the normal range. As she was afebrile and the RT–PCR for EBOV RNA in maternal blood was twice negative, she was technically eligible for discharge from the ETC. However, the treating health workers were concerned about possible EBOV persistence in the placenta or amniotic fluid based on previous experience with EBOV-positive pregnant women [9]. Many women in Guinea deliver at home with a traditional birth attendant (TBA), so the potential danger of infecting the TBA, healthcare workers, or other family members if the amniotic fluid were to remain infectious was critical in development of a delivery plan. One option that the treatment team proposed was to terminate the pregnancy, for public health reasons, in an ETC with staff wearing full personal protective equipment in order not to risk her delivering at home or in an inadequately equipped primary healthcare facility. The patient and family declined. As an alternative solution, the team proposed that the patient remain near the ETC until delivery. During subsequent weeks, the patient repeatedly reported normal fetal movements. However, on 16 October 2014, 32 days after maternal blood first tested negative using EBOV RT–PCR, the patient started to bleed vaginally. She was transferred

Table 1. Ebola Virus Real-Time Reverse Transcription–Polymerase Chain Reaction Results for Case 1

Date Sample Taken (2014)	Specimen	Result (Cycle Threshold Value)
9 September	Maternal blood	Positive (22.3)
14 September	Maternal blood	Negative
15 September	Maternal blood	Negative
6 October	Vaginal swab after rupture of amniotic sac	Positive (28.9)
17 October	Amniotic fluid	Positive (22.2)
17 October	Placental swab	Positive (18.4)
17 October	Cord blood	Positive (15.8)

The lower the cycle threshold (Ct) value, the higher the virus load. A Ct value of 20 roughly corresponds to 10^8 EBOV RNA copies/mL of specimen.

Abbreviation: EBOV, Ebola virus.

back to the ETC and had a spontaneous delivery of a 5-month stillborn fetus. After administration of 10 IU oxytocin, blood loss in the postpartum was normal. EBOV RT–PCR on placenta, umbilical cord blood, and amniotic fluid after rupturing of membranes were all highly positive (Table 1). The mother left the ETC 1 week later in good condition and with condoms as a component of family planning.

Case 2 Description

On 7 March 2015, a 22-year-old G3P0 woman approximately 5 months pregnant was admitted from a quarantine home to an MSF-managed ETC in Kissi, Freetown, Sierra Leone. Per Sierra Leone national Ebola response policy, the patient's household had been placed under quarantine for 21 days due to an in-house confirmed Ebola death. Her obstetric history consisted of 2 first trimester miscarriages.

On admission, the patient complained of anorexia, muscle pain, and joint pain. The patient tested negative on malaria RDT. She denied vaginal bleeding, uterine contractions, or loss of fluid and reported good fetal movement. The patient was initially afebrile but later had a temperature of 38.3°C during the first 24 hours of her hospital stay. Blood samples were taken on 8 March and 9 March, and RT–PCR for EBOV RNA (L gene, Realstar filovirus screen, RT–PCR kit 1.0) was positive (see Supplementary Materials). She had an uncomplicated recovery during her hospital stay and reported frequent fetal movements. Fetal heart rate was auscultated by Doppler and found to be within normal range.

Following a negative RT–PCR test on 14 March, the patient and her family were counseled extensively on the risk of a stillbirth and that her fetus, placenta, and amniotic fluid may remain positive for the EBOV. The patient opted for expectant management with routine care and initially agreed to remain in the ETC for surveillance. On 21 March 2015 the patient requested to leave the ETC and was discharged against medical advice to her home, which was still under quarantine.

Upon discharge, the woman and her family were advised to self-isolate and to call in the event of any abdominal pain, vaginal bleeding, discharge, or leaking of amniotic fluid while at home. The patient was called twice daily by a trained healthcare worker and was asked to present weekly to the ETC for an examination by the clinical staff.

On 13 April, 3 weeks post-discharge, the patient presented to the ETC. An ultrasound confirmed an intrauterine fetal death. The patient initially declined intervention. On the morning of 14 April the patient reported abdominal pain and was noted to have leaking fluid. Misoprostol 200 µg buccal was given every 4 hours. The patient expelled the placenta and fetus within the amniotic sac approximately 30 minutes after the second dose of misoprostol. The maternal surfaces of the placenta and amniotic sac were swabbed for the EBOV RT–PCR assay; only the placenta tested positive. Maternal blood tested negative for EBOV RNA on 15 April and 17 April, and the patient was discharged from the ETC on 17 April in good condition.

Ethics

The National Committee of Ethics inMedical Research of Guinea approved the use of diagnostic leftover samples and corresponding patient data for this study (permit N°11/CNERS/14). As the samples had been collected as part of the public health response to contain the outbreak in Guinea, informed consent was not obtained from patients.

DISCUSSION

These 2 cases highlight several challenges in caring for pregnant women with EVD. Both patients survived EVD and initially had live second trimester fetuses in utero following cure. Limited published MSF data show a persistence of EBOV in amniotic fluid for an unknown duration after negative RT–PCR tests for EBOV in maternal blood [9]. Thus, at the moment of rupture of membranes, delivery, or in the postpartum, convalescent pregnant women could be possible sources of infection for health staff and those in the community. There is also a paucity of data on duration of fetal survival in utero, and a neonate surviving transplacental EVD has not been documented [6]. These cases from Guinea and Sierra Leone also posed difficult ethical dilemmas for the treating healthcare workers. If these patients were to be discharged and subsequently delivered at home or in a health center, they could have infected their family members, TBAs, or healthcare providers at the moment of membrane rupture or during delivery. The TBA or healthcare provider attending the delivery could have become a source of secondary EBOV transmission and enhance the further spread of EVD [10]. After long discussions of these 2 cases, one option proposed was termination of the pregnancy for public health reasons. In both cases, the family and the patient declined termination, and other solutions were necessary. In Guinea a small wooden house was built next to the ETC where the family visited the

patient and where the patient remained until her labor started. In Sierra Leone it was originally proposed that the patient remain hospitalized until delivery. She later declined and returned to her home. The team called her twice a day by phone.

These 2 cases add to the growing data on EBOV persistence in the body for more than 1 month after disappearance of EBOV RNA from blood. At the beginning of the epidemic, routine pregnancy testing was not standard at ETC entry, which meant that some early pregnancies may have passed unnoticed and thus potentially became a risk for infection in the community if a convalescent woman miscarried at home following discharge.

CONCLUSION

Managing pregnant women in an Ebola epidemic remains extremely complex. Research on possible infectivity of amniotic fluid after convalescence of the mother should be prioritized. We strongly urge healthcare workers who care for EBOV-positive pregnant women to advocate for delivery in an ETC, even after the convalescence of the mother, in order to prevent cross-infection due to EBOV persistence in amniotic fluid.

Supplementary Data

Supplementary materials are available at http://cid.oxfordjournals.org. Consisting of data provided by the author to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the author, so questions or comments should be addressed to the author.

Notes

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References

1. World Health Organisation 2015. Ebola Situation Report—9th of August 2015. Available at: http://apps.who.int/ebola/ebola-situation-reports. Accessed 9 August 2015.
2. Baize S, Pannetier D, Oesterreich L, et al. Emergence of Zaire Ebola virus disease in Guinea. N Engl J Med **2014**; 371:1418–25.
3. WHO Ebola Response Team. Ebola virus disease in West Africa—the first 9 months of the epidemic and forward projections. N Engl J Med **2014**; 371:1481–95.
4. Mupapa K, Mukundu W, Bwaka MA, et al. Ebola hemorrhagic fever and pregnancy. J Infect Dis **1999**; 179(suppl 1):S11–2.
5. Johnson KM. Ebola hemorrhagic fever in Zaire, 1976. Bull World Health Organ **1978**; 56:271–93.
6. Jamieson DJ, Uyeki TM, Callahan WM, Meaney-Delman D, Rasmussen SA. What every obstetrician should know about Ebola. Obstet Gynecol **2014**; 24:1005–10.
7. Centers of Disease Control and Prevention. Ebola Transmission 2014. Available at: http://www.cdc.gov/vhf/ebola/transmission/qas.html. Accessed 18 November 2014.
8. Bausch DG, Towner JS, Dowell SF, et al. Assessment of the risk of Ebola virus transmission from bodily fluids and fomites. J Infect Dis **2007**; 196:S142–7.
9. Baggi F, Taybi A, Kurth A, et al. Management of pregnant women infected with Ebola virus in a treatment centre in Guinea, June 2014. Eurosurveillance **2014**; 19: pii:20983.
10. Feldmann H, Geisbert TW. Ebola haemorrhagic fever. Lancet **2011**; 377:849–62.