Early maternal-fetal transmission of the chikungunya virus

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Summary

Introduction > Since the onset of the Chikungunya outbreak in Reunion Island, vertical maternal-fetal transmission of the virus has been observed in newborns, but no such transmission has been demonstrated early during pregnancy. We report here the first three cases of maternal-fetal transmission of the Chikungunya virus (CHIKV) before 16 weeks’ gestational age.

Cases > Maternal infections occurred at terms of 12 weeks and 4 days, 15 weeks and 5 days, and 15 weeks and were confirmed by positive findings for specific anti-CHIKV IgM. Fetal deaths were subsequently observed, and at that point, CHIKV RT-PCR was negative for all three maternal blood samples. Amniocentesis preceded rupture of membranes in all three cases. RT-PCR showed viral genome in the amniotic fluid of the three fetuses, in the placentas of two, and in the brains of two. Autopsy found no malformations, and all other bacterial and viral test results were negative.

Discussion > These findings demonstrate early maternal-fetal transmission of CHIKV, which is suspected to be directly linked to the fetal deaths. This vertical transmission, probably abortifacient, should be considered in the light of human and animal responses to other arboviruses.
Epidemic chikungunya has ravaged Reunion Island since March 2005 [1]. Chikungunya is an RNA virus belonging to the Alphavirus genus of the Togaviridae family. It is transmitted to humans by mosquitoes of either the Aedes or Culex genus. The principal vector in Reunion is very probably Aedes albopictus. Chikungunya virus is known to induce hyperthermia, arthralgia, headaches and rash [2, 3]. To our knowledge, no case of fetal Chikungunya infection inducing abortions has yet been published. We report here 3 cases for which virologic evidence proves maternal-fetal transmission of chikungunya and suggests the possibility that it played a direct role in these fetal deaths.

Cases

By March 31, 2006, an estimated 230000 cases of chikungunya on Reunion had infected 30% of the population. From December 1, 2005, to February 28, 2006, there were 1370 ongoing pregnancies in the southern basin of the island. The fetopathology laboratory of the South Reunion Hospital Group received for analysis fetal remains of 23 fetuses. Chikungunya serology was negative for 16 of the 23 mothers. Seven fetal deaths occurred while the mother was infected with chikungunya at a term of 12-18 weeks. Virologic testing showed evidence of maternal-fetal chikungunya transmission in 3 of these 7 cases.

Case 1

One 39-year-old patient had a fever of 39°C, arthralgia, headaches and rash at a term of 12 weeks and 4 days. Anti-chikungunya IgM serology was negative at that time but positive at 14 weeks. Fetal death was noted on the day amniocentesis (indicated because of maternal age) was scheduled, at 15 weeks. Chikungunya RT-PCR that day was negative. Amniocentesis was performed and the villi biopsied before rupture of membranes, and RT-PCR showed viral genome in the amniotic fluid and villi. The fetus, very macerated, was expelled at 19 weeks, in a fixed position with limbs flexed but with no malformation. Its measurements were those of a fetus with a gestational age of 16 weeks. Bacterial and other viral infections (herpes, CMV, and parvovirus) were ruled out.

Case 2

This 36-year-old patient had clinical signs of chikungunya at a term of 15 weeks and 5 days. Fetal death was noted at the ultrasound performed at 19 weeks and 5 days. Serum samples taken that day were positive for chikungunya IgM antibody titers, but RT-PCR for the virus was negative. Amniocentesis was performed and the villi biopsied before rupture of membranes, and RT-PCR showed viral genome in the amniotic fluid and the villi. The normally formed macerated fetus expelled at 20 weeks had measurements corresponding to a gestational age of 16 weeks. RT-PCR of brain tissue was also positive. Bacterial and other viral infections (herpes, CMV, and parvovirus) were ruled out.

Case 3

This 26-year-old patient had clinical signs of chikungunya at 15 weeks. In utero fetal death was observed at 18 weeks. Serum samples taken that day were positive for chikungunya IgM antibody titers, while RT-PCR for the virus was negative. Amniocentesis was performed before the membranes ruptured, and RT-PCR showed viral genome in the amniotic fluid. The fetus, expelled at 19 weeks, had no abnormalities except for edema of the head and neck. It was very macerated, and its measurements were those of a 15-week fetus. RT-PCR of brain tissue was also positive for the virus. Bacterial and other viral infections (herpes, CMV, and parvovirus) were ruled out.

Discussion

Vertical transmission in humans has been described in other arbovirus infections: in 2002, in the United States with West Nile virus (WNV), of the flavivirus group [4], and earlier, in 1953 and 1959 with western equine encephalitis virus (WEEV), of the alphavirus group [5, 6]. Observations and animal experiments have proved the existence of transplacental infections with three other alphaviruses, the Getah, Ross River (RRV) and Semliki Forest (SFV) viruses [7-10]. Inoculation of gestating mice by RRV and SFV showed that viral replication in the placenta depends on the term of the pregnancy, that it persists despite maternal IgM production and that fetal infection follows an “all or nothing” rule, depending on the speed of production and transplacental transfer of maternal IgG [10]. These data from the literature indicated that plausibility of vertical Chikungunya transmission but until now, to our knowledge, no reports have described early maternal-fetal transmission of this virus, which may be responsible for in utero death. These three cases appear to be the first such reports.

The fetal measurements provide evidence that death occurred around the time of the maternal clinical manifestations in cases 2 and 3, and more than 2 weeks later in case 1. Autopsies ruled out malformation as the cause of death. No other viral or bacterial cause was found. Karyotyping was not performed, however. We know that elevated fever in the mother can be lethal to the fetus, and this was not totally ruled out by our observations, despite the presence of the chikungunya genome. Chikungunya genome was found in the amniotic fluid and placenta, although it was no longer detectable in the maternal blood. This finding rules out contamination of amniotic fluid by maternal blood during the amniocentesis. The presence of viral genome in the placenta and amniotic fluid therefore confirmed transplacental transmission of chikungunya and its persistence after fetal death. The presence of viral genome in amniotic fluid...
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fluid is probably due to urinary excretion of the virus by the infected fetus. Its persistence in the placenta confirmed that viral replication there is not sensitive to the maternal immune reaction.

Because of the precautions taken for the macerated fetal brain samples (scalp rinsing, disinfection with alcohol and polyvidone iodine, change of scalpel at each stage), introduction of the viral genome into the brain by contamination is very improbable. Perinatal transmission of chikungunya has previously been reported, accompanied by serious neurological events and hemorrhage [11]. The 3 cases reported here prove that transplacental transmission of chikungunya can also occur before 16 weeks and suggest the virus played a direct role in these fetal deaths. This role may be confirmed either by the repetition of such observations or by the observation of intracellular viruses in well preserved fetal tissues (brain, liver, etc.). In particular the presence of the virus in neurons would confirm its neurotropism, already suggested by neurological events in newborns.

References


