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Letter to the Editor

Zika virus infection in pregnant women in Barcelona, Spain

We describe here the first pregnant women described with Zika virus (ZIKV) infection in Europe. One of the cases was a probable coinfection with dengue virus (DENV) and the most prolonged viraemia ever reported. We communicate the protocol established in our setting as a response for the international emergency.

The first patient was a Colombian woman in her 40s living in Spain who had travelled to Colombia in the months of December 2015 and January 2016. Three days after her return, at approximately 10 weeks' gestation, she observed a maculopapular, nonconfluent rash affecting her trunk and limbs, with no fever or other concurrent symptoms. Fifteen days later, she contacted the outpatient service of the International Health Unit at Vall d'Hebron Hospital, Barcelona, where an arboviral infection was suspected and a serum sample was taken. To confirm ZIKV diagnosis, anti-ZIKV immunoglobulin (Ig) M and IgG antibodies (Arboviral Fever Mosaic, Euroimmun, Germany) and specific retrotranscriptase (RT) PCR, RealStar ZIKV RT-PCR Kit and a modification from Balm *et al.* [1]) were performed at the Spanish National Microbiology Center at Instituto Carlos III, Madrid. RT-PCR and ZIKV IgG were positive and ZIKV IgM was negative. Anti–chikungunya virus (CHKV) antibodies were negative. Anti-DENV IgM and IgG (Dengue VirClia Monotest, Vircell, Granada, Spain) showed positive results. It was considered a confirmed case of ZIKV infection according to approved diagnostic criteria.

The second patient was a Spanish woman in her 30s who had traveled to Colombia during similar dates. Ten days after her arrival to Colombia, at 22 weeks' gestation, she experienced a rash on the face and trunk that was self-limited in 12 hours, with no other concurrent symptoms. She contacted the Unit of International Health upon her return, 20 days later, and a serum sample was obtained for DENV, CHKV and ZIKV serology. Anti-CHKV IgG/IgM and anti-DENV IgM were negative, but anti-DENV IgG was positive. For ZIKV, both IgM and IgG were positive, and serum neutralization confirmed the positive results, discarding cross-reaction with other viruses. It was considered a case of ZIKV infection according to the approved diagnostic criteria.

The same day the results were known, obstetricians assessed both patients. Prenatal ultrasounds, including neurosonography, were performed. The gestational age of the women's fetuses were 14 and 27 weeks, respectively; no apparent foetal malformations were detected. Both pregnant women are currently under strict supervision.

The working group designed and launched a protocol to diagnose and follow up all pregnant women coming from endemic ZIKV areas in order to be able to promptly detect foetal microcephaly and ZIKV infection among women at risk. The protocol is described in Fig. 1.

In the first case, specific RT-PCR detected viraemia 15 days after the onset of symptoms; this was confirmed by a second RT-PCR. Viraemia for ZIKV is usually shorter [2]; further studies are needed to assess the likely time ranges. DENV IgM was also positive; coinfection cannot be excluded. Further studies are needed to determine if these circumstances may be risk factors for foetal involvement. In the second case, in which RT-PCR was not performed and DENV IgG was also positive, seroneutralization was performed in order to confirm the case, as serologic cross-reactivity between ZIKV and DENV has been reported [3].

A complete follow-up has been set until delivery because the impact on the foetus is not yet well established [4]. Moreover, these women live in Europe, far from the endemic areas for arbovirosis. These cases provide information about the evolution of the infection without reexposure to the virus. Key points to complete the appropriate diagnosis are a good clinical history adapted to every moment to the changing situation, laboratory capacity to quickly implement new techniques and a timely and appropriate follow-up of the affected women.

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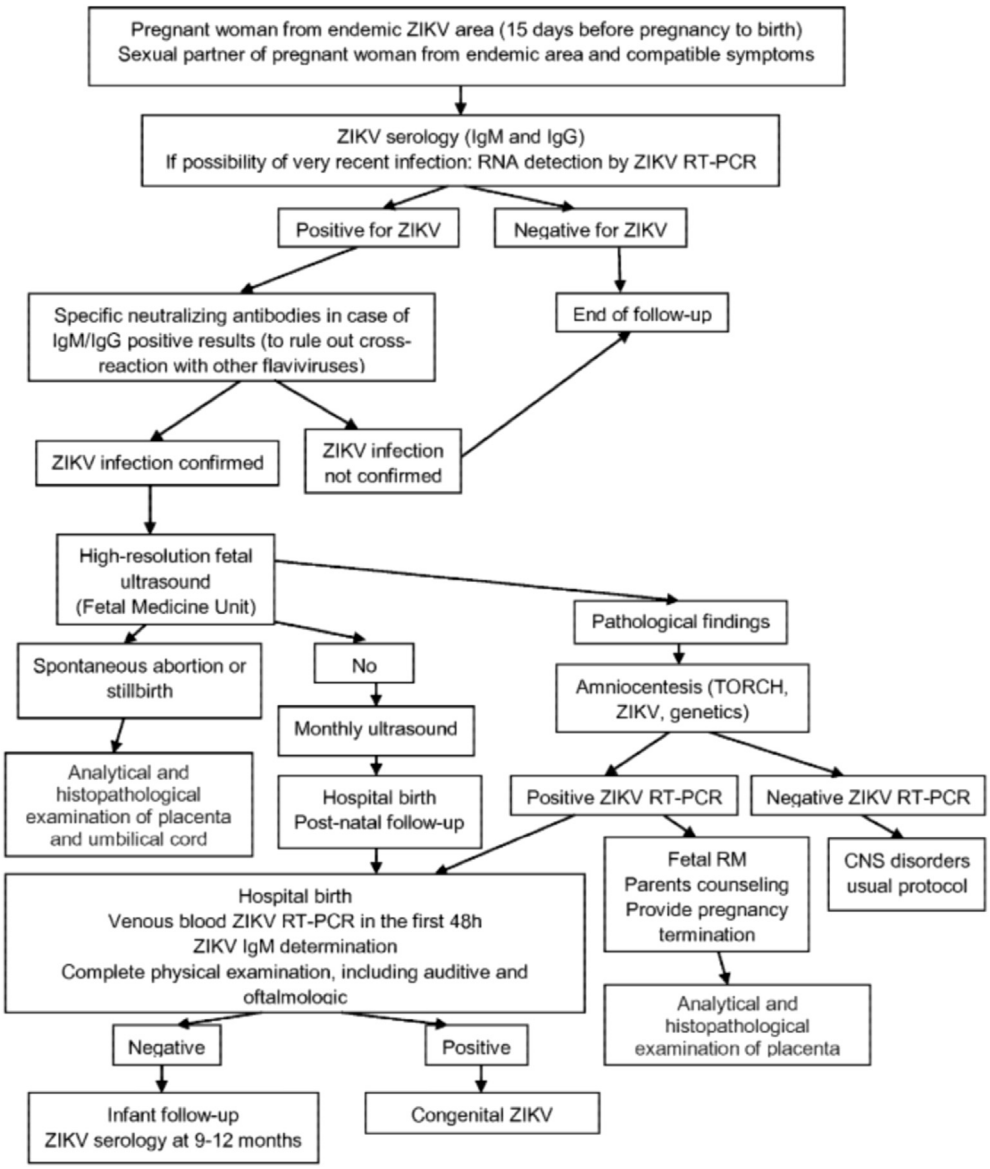

Fig. 1. Algorithm for diagnosis of pregnant women with suspected ZIKV infection. ZIKV, Zika virus.

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Transparency Declaration

All authors report no conflicts of interest relevant to this article.

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