

INVITED SUBMISSION

Zika without symptoms in returning travellers: What are the implications?



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Summary Against the background of the emergence and rapid spread of Zika virus (ZIKV) in the Americas, we report the case of an afebrile ZIKV infection in a traveller returning from Central America to highlight relevant clinical and diagnostic aspects. ZIKV should be considered in the differential diagnosis of patients with clinical symptoms suggestive of dengue or chikungunya fever. Given the frequent subfebrile and afebrile manifestations of ZIKV infections, we propose abstaining from the term “Zika fever (ZF)” in favour of “Zika virus disease (ZVD)”. Owing to its unspecific clinical presentation and cross-reactivity in serological assays, ZVD may easily be missed or misdiagnosed as dengue fever. Until conclusive data on the currently suspected link between ZIKV infection in pregnancy and foetal microcephaly become available, pregnant women and women who are trying to become pregnant should be advised against travelling to regions with ongoing ZIKV transmission. In addition, male travellers returning from regions with ongoing transmission should be informed of the potential risk of sexual transmission until conclusive data on the significance of this mode of transmission become available. Although probably low and seasonally restricted, there is a risk of ZIKV importation to *Aedes* mosquito-infested regions in temperate climates (including regions of North America and Europe) with consecutive autochthonous transmission.

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1. Background

Like DENV, yellow fever virus, West Nile virus and Japanese encephalitis virus, ZIKV is a medically important mosquito-transmitted virus belonging to the flavivirus family. Similar to other flavivirus infections, asymptomatic infections are common, with only one in five infected individuals developing unspecific symptoms (mild fever, rash, conjunctivitis, and arthralgia) and the clinical presentation may easily be confused with other viral infections, such as DENV and CHIKV [1]. Since the virus's discovery in a sentinel Rhesus monkey in Uganda's Zika forest in 1947, human infections have only sporadically been reported in Asia and Africa. In 2007, ZIKV emerged outside its known endemic boundaries for the first time and caused an epidemic on Yap Island in the Federated States of Micronesia [1], followed by a large epidemic in French Polynesia in 2013–14 [2] and subsequent spread to several countries in Oceania, including New Caledonia and the Cook Islands [3]. While ZIKV was generally considered to only cause mild human disease, the outbreak in French Polynesia revealed the virus's potential to cause neurological complications (i.e. Guillain-Barré syndrome and meningoencephalitis) [4].

On May 7, 2015, the Pan American Health Organization issued an alert about potential ZIKV transmission in northeastern Brazil [5]. Following this first detection of ZIKV on the American continent, autochthonous ZIKV transmission has been confirmed throughout Central and South America (Fig. 2). The number of cases observed in Brazil alone was estimated at 440'000–1'300'000 [6]. Following the emergence and rapid spread of CHIKV in the Americas since 2013 [7,8], ZIKV is now the second arbovirus to emerge on the American continent in recent years. As ZIKV shares the *Aedes* mosquito vector with DENV and CHIKV, and half of the world's population lives in *Aedes*-infested regions, the

possibility of ZIKV epidemics are a major public health concern [9]. Furthermore, data suggest that ZIKV may be sexually [10] as well as transplacentally transmissible [11,12]. The latter form of transmission in particular raises concerns, especially after October 2015, when the Brazilian ministry of health reported a twentyfold increase in the number of microcephaly cases among newborns compared with previous years [12]. Maternal–foetal transmission of ZIKV has been documented throughout pregnancy and the detection of ZIKV RNA in pathologic specimens of foetal losses as well as confirmed ZIKV infections in infants with microcephaly suggest a link between ZIKV infection in pregnancy and microcephaly of the foetus. However, the incidence of ZIKV infection in pregnant women is currently unknown and the definitive proof of a causal link is still pending [13].

2. Case description

A 51-year-old female Swiss traveller presented to our outpatient department six days after returning from a two-week holiday to Guatemala and El Salvador in November 2015. Four days after returning, the patient noticed a slightly pruritic maculopapular rash on the face, trunk, and extremities without accompanying symptoms (neither fever nor symptoms suggestive of a systemic infection). On the next day, the rash worsened and a non-purulent conjunctivitis developed. We saw the patient another day later when additionally painful oedemas of the hands, elbows, knees and feet (Fig. 1) had developed. Besides the rash, the conjunctivitis, the oedemas and a generalized lymphadenopathy, the physical examination was unremarkable. Laboratory tests included complete blood count, hepatic transaminases, creatinine, C-reactive protein and rapid tests for dengue virus (DENV) (NS1-Ag, IgM, IgG [SD Dengue

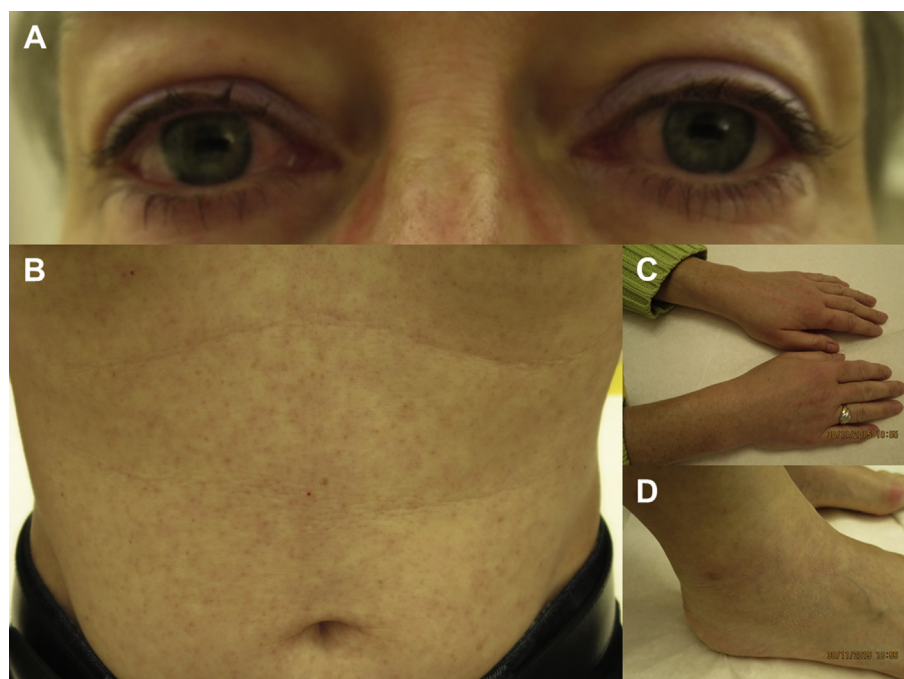


Figure 1 Clinical features of Zika virus disease: (A) conjunctivitis, (B) maculopapular rash, (C–D) peripheral oedemas.

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