Simultaneous outbreaks of dengue, chikungunya and Zika virus infections: diagnosis challenge in the returning traveler with non-specific febrile illness

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Abstract

Zika virus is an emerging flavivirus that is following the path of dengue and chikungunya. The three *Aedes*-borne viruses cause simultaneous outbreaks with similar clinical manifestations which represents a diagnostic challenge in ill-returning travelers. We report the first Zika virus infection case imported in Switzerland and present a diagnostic algorithm.
Dear Editor,

On November 19th 2015, a 29-year-old woman attended our clinic with a four-day flu-like syndrome after a trip in Colombia from October 30th-November 15th. During her trip home, she developed a feverish feeling with diarrhoea; 24 hours later, she noted a pruritic rash on her trunk. Over the coming days, she presented retro-orbital headache and arthralgia involving her wrists and interphalangeal joints. On physical examination, there was a maculopapular rash on her trunk and limbs. Full blood count was normal. Because of her stay in a region with concurrent arbovirus epidemics, as well as clinical presentation and incubation time, differential diagnosis included dengue (DENV), chikungunya (CHIKV) and Zika (ZIKV) viruses infection. Given the absence of concerning clinical signs, the patient received symptomatic treatment and was followed up as an outpatient.

Blood smear, malaria (SD BIOLINE Malaria Ag P.f/Pan) and dengue rapid tests (SD BIOLINE Dengue Duo IgG/IgM/NS1Ag) were negative. On serum collected on November 20th (5 days after symptoms onset), chikungunya IgM/IgG (immunofluorescence commercial test CHIKV (Euroimmun, Germany)) was negative, but real-time ZIKV RT-PCR was positive (38 C_t; method developed by national reference center for arboviruses, service de santé des armées, Marseille, France). Urine collected 12 days after symptoms onset was positive for ZIKV by real-time RT-PCR with a higher viral load than in serum collected 7 days before (34 C_t). At the last medical visit, 20 days after symptoms onset, she described progressive relief from the arthralgia and urine real-time RT-PCR was negative. This was the first imported case of ZIKV infection in Switzerland.

Clinical manifestations of ZIKV infection are similar to dengue and chikungunya (fever, exanthema, conjunctivitis, retro-orbital headache and arthralgia) [1]. Identification of the virus has specific management implications for clinicians. In the case of dengue, a close follow-up for thrombocytes and haematocrit should be done. In the case of chikungunya, high prevalence of chronic arthralgia should be discussed. In the presence of ZIKV, potential sexual and materno-foetal transmission (risk of congenital microcephaly) should be presented [2].

A reliable immunochromatographic rapid diagnostic test makes DENV infection easy to rule out in acutely ill travellers [3]. NS1 antigen is highly specific but, in the presence of DENV IgM only, cross-reactivity between the two flaviviruses, DENV and ZIKV, has been described [4]. CHIKV can be detected by PCR in blood and serology by immunofluorescence is expected to be positive after ≥5 days of symptoms. Cross-reactivity between flaviviruses limits the use of serology for ZIKV diagnosis which relies on viral RNA detection by PCR in blood, preferably less than five days after symptoms onset (short viraemic period 3-5 days). As illustrated in our case, viral RNA in urine persists for longer periods (15-20 days) and can be useful to confirm infection [5]. Virus can
also be detected in saliva during the viraemic period [6]. To support clinicians in their diagnostic work-up, we present in the Figure a diagnostic algorithm for travelers with non-specific febrile illness returning from regions experiencing simultaneous outbreaks of DENV, CHIKV and ZIKV.

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Figure legend

Diagnostic algorithm for travelers with non-specific febrile illness returning from regions experiencing simultaneous outbreaks of dengue, chikungunya and Zika virus infections.

Abbreviation: RDT: rapid diagnostic test

References


Non-specific febrile illness in returning travelers from a region with simultaneous outbreaks of dengue, chikungunya and Zika virus infections

**Diagram:**

1. RDT dengue
   - Antigen NS1 positive
     - Confirmed dengue
     - IgM dengue negative
       - < 5 days of symptoms
         - PCR Zika virus in blood and/or PCR chikungunya in blood
           - Dengue, chikungunya, Zika unlikely
           - Confirmed Zika
           - Confirmed chikungunya
           - Confirmed Zika and chikungunya
       - ≥ 5 days of symptoms
         - IgM chikungunya
           - Confirmed Zika
           - Confirmed chikungunya
   - Antigen NS1 negative
     - IgM dengue positive*
       - PCR Zika virus in urine
         - Confirmed Zika
         - Dengue, chikungunya, Zika unlikely

*First, exclude malaria with a rapid diagnostic test.
*Cross-reactivity between flaviviruses.
*Sequential testing is an alternative in the absence of concerning clinical signs.