Fever and Rash in a Husband and Wife Returning From the Cook Islands
(See page 1445 for the Photo Quiz.)

Diagnosis: Zika virus infection.
Arboviral infection was suspected. Dengue virus (DENV) serology (Panbio Dengue immunoglobulin G [IgG] indirect enzyme-linked immunosorbent assay [ELISA], Alere; Panbio Dengue immunoglobulin M [IgM] capture ELISA, Alere; Plate- lia Dengue NS1Ag ELISA, Bio-Rad) and pan-flavivirus reverse transcription polymerase chain reaction (PCR) using hemi-nested primers that amplify a conserved sequence in the NS5 gene (modified from Scaramozzino et al [1]) was requested on day 1 of illness for both patients. Acute DENV serology, including NS1 antigen, was negative in both patients. Both patients had positive IgG antibody and negative IgM antibody for measles, indicating past immunity or previous vaccination. The initial patient’s pan-flavivirus PCR was positive by conventional PCR. The initial extracted complementary DNA was then tested using a DENV type-specific real-time TaqMan PCR assay and was negative. The amplified product from the pan-flavivirus PCR (215 bp in length) was sequenced, and a BLAST search confirmed Zika virus (ZIKV). Interestingly, despite similar epidemiology and symptoms, ZIKV was not identified in the husband’s sample. Convalescent DENV serology in the initial patient demonstrated a low positive seroconversion in DENV IgG, suggestive of cross-reacting antibodies. Both patients made a complete recovery over 5 days with no specific treatment.

ZIKV infection is caused by an RNA virus endemic to Southeast Asia and Africa that is transmitted by Aedes species mosquitoes. ZIKV was initially isolated in 1947 from a rhesus monkey in Zika Forest, Uganda [2]. Confirmed cases were rare until recent epidemics in Micronesia, French Polynesia, and the Cook Islands [3]. Clinical manifestations are similar to other arboviral infections, such as DENV and chikungunya, and are characterized by fever, maculopapular rash, myalgias, and headache. Investigations are nonspecific. Diagnostic clues that may help distinguish ZIKV from DENV include conjunctivitis [4–6] (17/31 [55%] of ZIKV patients [5] vs 14/148 [9%] DENV patients [7]; P < .0001) and an absence of thrombocytopenia [6]. Rash was also more commonly reported in ZIKV (28/31 [90%] ZIKV patients [5] vs 44/148 [30%] DENV patients [7];

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Figure 1. Bilateral conjunctivitis secondary to Zika virus infection. Arrows indicate areas of conjunctivitis.

Figure 2. Papular rash on torso, secondary to Zika virus infection.
The illness is typically mild and self-limited with resolution over 1 week. In a previous outbreak with 49 confirmed cases of ZIKV, no deaths, hospitalizations, or hemorrhagic complications were reported [5], but neurological complications including Guillain-Barré syndrome have been described [8]. Diagnosis most commonly relies on PCR of acute serum samples or ELISA for IgM antibodies against ZIKV [5]. As seen in the second patient, laboratory diagnosis with PCR is challenging because of low viremia and a brief viremic phase of ZIKV infection; in addition, serological tests are only available in select laboratories [9]. Serologic cross-reactivity with other flaviviruses is common, in particular DENV [2].

ZIKV is an emerging pathogen and may have the potential to cause endemic transmission in areas such as the southern United States and Queensland, Australia. Endemic transmission of DENV, which shares the same mosquito vector, has been noted in these areas previously [10, 11], and the emergence of chikungunya fever in the Caribbean [12] and the Pacific [13] further underscores the threat posed by arboviral infection. Clinicians should consider ZIKV in the differential diagnosis of febrile returned travelers with a rash, and further study is needed to understand the more rare complications of ZIKV and its propensity to cause future outbreaks.

Notes

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Potential conflicts of interest. All authors: No potential conflicts of interest.

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References


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