Zika virus infection in a traveller returning to Europe from Brazil, March 2015

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We report a case of laboratory-confirmed Zika virus infection imported into Europe from the Americas. The patient developed fever, rash, and oedema of hands and feet after returning to Italy from Brazil in late March 2015. The case highlights that, together with chikungunya virus and dengue virus, three major arboviruses are now co-circulating in Brazil. These arboviruses represent a burden for the healthcare systems in Brazil and other countries where competent mosquito vectors are present.

Case presentation

A male Italian traveller in his early 60s presented to the Infectious and Tropical Diseases Unit, Azienda Ospedaliero Universitaria Careggi, Florence (Italy), four days after his return from a 12-day holiday in Salvador de Bahia, Brazil at the end of March 2015. The patient had a four-day history of confluent slightly-pruritic erythematous rash, diffused on the face, trunk, arms, and legs, accompanied by fever (maximum temperature 38 °C), conjunctivitis, general weakness, and painful oedema of both hands and feet. Blood tests revealed a normal white blood cell count (6,180 cells/µL; reference: 4,000–10,000/µL) with normal differential count, but some activated lymphocytes, thrombocytopenia (112,000/µL; reference: 140,000–440,000/µL) and slightly elevated C-reactive protein (10 mg/L, reference: ‹9 mg/L). Serum transaminases and creatinine were normal. Because of the clinical presentation and the travel history, a viral infection was suspected, and patient serum was tested for antibodies against chikungunya virus (CHIKV), dengue virus (DENV), Zika virus (ZIKV), Yellow fever virus, West Nile virus, Japanese encephalitis virus, Parvovirus B19, human herpes virus 6 (HHV6), and HIV [1]. The serum sample taken four days after symptom onset showed a positive result for anti-ZIKV-IgM and -IgG antibodies, suggesting an acute or recent ZIKV-infection. Results of the serological tests for the other viruses tested were negative (Table). A follow up sample, taken 26 days after symptoms onset, showed a threefold increase of the anti-ZIKV-IgM and -IgG antibody titres (Table). In addition, a low-titre DENV IgG was now observed (Table), most likely representing a serological cross-reaction of the anti-ZIKV-IgG antibodies (Table). ZIKV-specific real-time reverse transcription-PCR [1] was negative from both samples. Generic flavivirus and alphavirus RT-PCR [1] were also negative. The presence of ZIKV-specific neutralising antibodies in the second serum sample was confirmed by a virus neutralisation assay (Table). The patient was discharged, managed and followed-up in the outpatient department. The patient was recommended symptomatic treatment with paracetamol. The symptoms rapidly resolved in the following week (fever and rash lasted for only four days).

Background

ZIKV is an arbovirus belonging to the flavivirus genus that was first isolated from a rhesus monkey in the Zika forest in Uganda [2]. It is transmitted by different species of *Aedes* mosquitoes. Clinical manifestations of ZIKV infection are very similar to those of DENV and CHIKV infections, but usually milder [3]. Human infections have been documented in several African and south-eastern Asian countries [4]. ZIKV was responsible for several outbreaks on islands in the Pacific Ocean, such as Yap Island (Federated States of Micronesia in 2007 [4]) and more recently in French Polynesia, New Caledonia, Easter Island and the Cook Islands in 2013 [5,6]. In several non-endemic countries including Japan, Germany, Italy, Canada, Australia and the United States (US), the infection has been diagnosed in returning travellers [1,7-11].

ZIKV infections have recently been reported in Brazil, where the virus has probably been circulating since 2014 [12]. So far, 16 cases have been confirmed in accordance to the Ministry of Health of Brazil [13].The emergence of ZIKV in Brazil is of concern since Brazil is the country with the highest number of DENV infections

Table

Serological test results and virological data of a case of Zika virus infection imported from Brazil into Italy, March 2015

Antibody or antigen tested	Serum samples taken after symptom onset (days)	
	4	26
Anti-ZIKV-IgG[a]	1:160	1:1,280
Anti-ZIKV-IgM[a]	1:160	1:1,280
ZIKV NAb[b]	ND	1:640
Anti-DENV-IgG[a]	<1:20	1:20
Anti-DENV-IgM[a]	<1:20	<1:20
DENV-2 NAb[b]	ND	<1:20
DENV-4 NAb[b]	ND	<1:20
DENV NS1[c]	Negative (0.1 arbitrary units)	Negative (0.1 arbitrary units)
Anti-JEV-IgG[a]	<1:20	<1:20
Anti-JEV-IgM[a]	<1:20	<1:20
Anti-WNV-IgG[a]	<1:20	<1:20
Anti-WNV-IgM[a]	<1:20	<1:20
Anti-YFV-IgG[a]	<1:20	<1:20
Anti-YFV-IgM[a]	<1:20	<1:20
Anti-CHIKV-IgG[a]	<1:20	<1:20
Anti-CHIKV-IgM[a]	<1:20	<1:20

CHIKV: chikungunya virus; DENV: dengue virus; DENV-2: dengue virus serotype 2; DENV-4: dengue virus serotype 4; JEV: Japanese encephalitis virus; NAb: neutralising antibodies; ND: not done; NS1: nonstructural protein-1; WNV: West Nile virus; YFV: yellow fever virus; ZIKV: Zika virus.

[a] Indirect immunofluorescence assay (IIFA) titres <1:20 for serum were considered negative [1].

[b] Virus neutralisation test (VNT) titres <1:20 for serum were considered negative [1].

[c] SD BIOLINE Dengue Duo NS1 Ag + Ab Combo and Bio-Rad Platelia Dengue NS1 Ag.

world-wide [14]. Moreover, CHIKV has been introduced to South America as well with more than one million of cases diagnosed since 2013 to date [15].

Discussion and conclusions

The ongoing outbreak of now two major mosquito-borne infections in addition to endemic DENV infections has the potential of posing a serious threat to local and supra-national South American healthcare systems, as observed in the Pacific region in recent years [16].

In endemic areas, but also in the setting of travel medicine, ZIKV infection represents both a clinical and diagnostic challenge since the symptoms are very similar to other arboviral diseases, no specific commercial serological tests are available, and cross-reactive DENV serology (IgG or IgM) during ZIKV infection has been described in previously reported cases [11] which may lead to incorrect diagnoses. Recently, neurological complications possibly related to coinfections or sequential infections with dengue virus have been reported in French Polynesia [17].The European Centre for Disease Prevention and Control (ECDC) published a Rapid Risk Assessment on ZIKV in the Americas on 25 May 2015, with the aim of increasing awareness and enhancing vigilance towards the detection of imported cases of ZIKV infection in Europe [18]. This case is, to the best of our knowledge, the first laboratory-confirmed case of a ZIKV infection acquired in the Americas and imported into Europe. The patient had returned to Italy, his home country, where *Aedes albopictus*, a potential competent vector, is widely distributed. Considering the extensive airline travel between Latin America and other parts of the world where the viruses have not yet been established, but competent vectors are present, such as southern Europe and the southern part of the US, the surveillance systems have to be aware of the appearance of ZIKV in Brazil to avoid further dissemination of the disease. In order to prevent seeding of ZIKV into local mosquito populations, as it happened for CHIKV in Italy in 2007 and in France in 2010 and 2014 [19, 20, 21], screening of febrile returning travellers for arboviral infections, especially in the summer months, is highly advised.

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Conflict of interest

None declared.

Authors' contributions

Wrote the manuscript: LZ, DT, JSC, GV; performed laboratory investigations: DT, CF, MER, JSC, GV, SG; revised the manuscript: AB, JSC; managed the patient: LZ.

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