West Nile virus retinitis in a patient with neuroinvasive disease

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Dear Editor:

The West Nile virus (WNV) is a widely distributed emerging mosquito-borne arbovirus. Although the majority of WNV infections are asymptomatic (80%), some infected individuals (20%) present with non-specific febrile disease (WNV fever) and less than 1% develop neuroinvasive diseases (meningitis, encephalitis, and myelitis). Several atypical or rare presentations of WNV infection such as cerebellitis, myocarditis, hepatitis, pancreatitis, and rhabdomyolysis have been described in case reports or small case series. Although rare, ocular manifestations, including monofocal or multifocal WNV chorioretinitis are the most commonly reported clinical manifestations of WNV infection after fever and neuroinvasive disease.

We herein report the first case of retinitis detected in a patient with WNV neuroinvasive disease in Croatia. In August 2018, a 68-year-old patient with type II diabetes mellitus was admitted to the infectious disease department with a six-day history of fever (temperature up to 38.9°C), shivering, chills, vertigo, frontal headache, and fatigue. The patient came on holiday in a touristic area on the Adriatic Coast from the continental part of Croatia where autochthonous WNV infections have already been registered continuously from 2012, as well as in the 2018 transmission season (unpublished data of the Reference Centre for Diagnosis and Surveillance of Viral Zoonoses, Croatian Ministry of Health, Croatian Institute of Public Health). In the coastal area, autochthonous human WNV infections had not been detected so far. According to the epidemiological history (arbovirus transmission season, living in the area with documented arbovirus circulation, and reported mosquito bites), an arboviral etiology was suspected.

On physical examination, the patient was confused, restless with slight tremors of the hands, and had conjunctival hyperemia. On the lower extremities, there were multiple mosquito bites. Routine blood laboratory parameters were within normal ranges except for an elevated glucose level (9.0 mmol/L, reference range 4.4–6.4 mmol/L). Cerebrospinal fluid analysis showed pleocytosis (437 × 10⁶/L cells) with lymphocyte predominance (67%), elevated protein level (1.40 g/L; reference range 0.17–0.37 g/L), and elevated glucose level (5.7 mmol/L, reference range 2.5–3.3 mmol/L). An electroencephalogram showed nonspecific changes while a brain computed tomography scan showed normal findings.

On the 9th day after disease onset, he developed sudden decreased visual acuity in both eyes. Ophthalmologic examination revealed conjunctival injection, while other parts of the anterior segment of the eye were unremarkable. The visual acuity in both eyes was classified using the semiquantitative scale of “hand motion”. Intraocular pressure was normal. In the
posterior segment of the eye, vasculitis, edema, and hemorrhage of the entire retina were found (Figure 1). Fluorescent angiography showed bilateral occlusion of the retinal blood vessels with centrally located ischemic areas.

Repeated blood cultures showed negative results. Serological tests were performed using commercial enzyme-linked immunosorbent assays (Euroimmun, Lübeck, Germany). The diagnosis of WNV neuroinvasive disease was confirmed by seroconversion in samples obtained during the acute and convalescent phases. In the first sample tested on day 8, positive IgM antibody assay results (ratio 1.25; >1.1 positive) were found while IgG antibody assay results were negative (10.58 RU/ml; >22 positive). In the second sample tested on day 27, both IgM (ratio 1.48) and IgG (142.10 RU/ml) antibodies were found. IgG antibodies showed low avidity (24%; <40% low avidity index) indicating acute WNV infection. To rule out cross-reactivity with other flaviviruses, serology for tick-borne encephalitis virus and Usutu virus was also performed. Antibody cross-reactivity with other flaviviruses, serology for tick-borne encephalitis virus and Usutu virus was also performed. The diagnosis of WNV neuroinvasive disease was confirmed by seroconversion in samples obtained during the acute and convalescent phases. In the first sample tested on day 8, positive IgM antibody assay results (ratio 1.25; >1.1 positive) were found while IgG antibody assay results were negative (10.58 RU/ml; >22 positive). In the second sample tested on day 27, both IgM (ratio 1.48) and IgG (142.10 RU/ml) antibodies were found. IgG antibodies showed low avidity (24%; <40% low avidity index) indicating acute WNV infection. To rule out cross-reactivity with other flaviviruses, serology for tick-borne encephalitis virus and Usutu virus was also performed. Antibody cross-reactivity with other flaviviruses, serology for tick-borne encephalitis virus and Usutu virus was also performed.

In conclusion, the case presented in this report highlights the need for awareness of the possibility of WNV-related retinitis during the arbovirus transmission season. In addition, routine ophthalmological examination should be considered, especially in patients presenting with severe WNV encephalitis.

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**Conflict of interest**

The authors declare that there is no conflict of interest.

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