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CASE REPORT

Fatal case of West Nile encephalitis associated with acute anteroseptal ST elevation myocardial infarction (STEMI): a case report

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SUMMARY

Cardiac involvement has rarely been reported in West Nile (WNV) infection. We report a fatal case of WNV encephalitis associated with an acute anteroseptal ST elevation myocardial infarction. The patient was hospitalized with a fever, headache, nausea and vomiting. The physical examination revealed positive meningeal signs and an altered level of consciousness. High levels of cardiac enzymes (creatine phosphokinase/MB fraction, lactate dehydrogenase, myoglobin and cardiac troponin I) and ST elevation on electrocardiogram were found. Both CSF and urine samples were positive for WNV RNA. This case highlights the need of awareness of the possibility of a WNV-related myocardial infection, including myocardial infarction.

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INTRODUCTION

West Nile virus (WNV) is a mosquito-borne arbovirus that belongs to the family *Flaviviridae*, genus *Flavivirus*. Birds are the reservoir hosts and mosquitoes of the genus *Culex* are the principal vectors of WNV. Due to low-level viremia, humans represent incidental or dead-end hosts for WNV. Although many WNV infections are asymptomatic (80%) or present as a mild febrile disease (WNV fever), some patients develop a neuroinvasive disease (meningitis, encephalitis, myelitis) (Sejvar *et al*., 2011). Cardiac involvement such as WNV myocarditis has been documented pathologically in mammals (van der Meulen *et al*., 2005) and birds (Gibbs *et al*., 2005; Khouzam, 2009), but has rarely been reported in humans (Kushawaha *et al*., 2009; Manov *et al*., 2014). Although cardiac arrhythmia is rare during WNV infection, it is more common in WNV encephalitis compared to WNV meningitis and WNV fever (Bode *et al*., 2006).

We present a fatal case of WNV encephalitis associated with an acute anteroseptal ST elevation myocardial infarction (STEMI).

Key words:
West Nile virus, encephalitis, myocardial infarction.

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CASE REPORT

A 77-year-old Croatian female patient was hospitalized in the late summer of 2017 on the second day of the illness manifested by fever up to 38.6°C, headache, nausea, vomiting and diarrhoea. The patient did not report any recent travel and tick bite, but recalled mosquito bites. Her past medical history included hypertension treated with ramipril 5 mg daily. Physical examination revealed neck stiffness, positive meningeal signs and an altered level of consciousness. Her blood pressure was 115/60 mm Hg, and heart rate was 79 bpm.

At admission, WBC count was 24.6 (reference range 3.4-9.7x10^9/L) with neutrophilia (92%, range 44-72%), elevated liver transaminases: aspartate-aminotransferase 278 (range 8-30) U/L, alanine-aminotransferase 597 (range 10-36) U/L and very high levels of cardiac enzymes: creatine phosphokinase 1856 (range 17-153) U/L, creatine phosphokinase MB fraction 14.4 (range 0.6-3.5) μg/L, lactate dehydrogenase 433 (range 2-241) U/L, myoglobin 3116 (range 20-80) μg/L and cardiac troponin I 17640 (range 0.000-0.056) μg/L. Electrocardiogram showed ST elevation. In the cardiac intensive care unit, an emergency coronary angiography was performed which confirmed the coronary artery stenosis. The patient's condition com-

plicated at the 4th day of the illness with progression to coma. Glasgow coma scale was 6. Computed tomography of the brain was normal. Cerebrospinal fluid (CSF) analysis showed a pleocytosis with 26 cells/mm^3, predominantly mononuclears (73%), elevated protein level (1.151, range 0.170-0.370 g/L) and slightly elevated glucose level (3.44, range 2.5-3.3 mmol/l). CSF and urine samples were tested for the presence of neuroinvasive viruses: enteroviruses, herpes simplex viruses, WNV, tick-borne encephalitis, Usutu, Toscana, Tahyna and lymphocytic choriomeningitis virus RNA using a reverse-transcriptase polymerase chain reaction (RT-PCR). Both CSF (Ct 32) and urine (Ct 26) were positive for WNV RNA by real-time and nested RT-PCR. Viral RNA was extracted from CSF and urine samples using a High Pure Viral Nucleic Acid Kit (Roche Diagnostics, Mannheim, Germany). A real-time RT-PCR for WNV was performed according to the protocol of Tang *et al*. (2006). Primers (FP: AAGTTGAGTAGACGGTGCTG, RP: AGACGGTTCTGAGGGCTTAC) were used to amplify a conserved 92-bp region spanning nucleotides 10,533-10,625 of the WNV 3'-noncoding region. Probe FAM-CTC AAC CCCAGG AGG ACT GG-BHQ1 was used to detect WNV PCR products. Nested RT-PCR for WNV was performed using external primers (FP: GARTGGATGACVACRGAAGACATGCT, RP: GGGGTCTCCTCTAACCTCTAGTCCTT) according to the protocol of Weissenböck *et al*. (2002) and internal primers (FP same as for real-time RT-PCR, RP: CTAGGGCCGCGTGGG) amplifying 224 bp region spanning nucleotides 10,533-10,756. The same primers were used for Sanger sequencing of the RT-PCR amplicon. A phylogenetic analysis of the detected strain showed WNV lineage 2 (*Figure 1*).

Serologic tests were performed using a commercial ELISA (Euroimmun, Lübeck, Germany). IgM antibodies for WNV were reported positive in the CSF (ratio 5.4, positive ≥1.1), while IgG antibodies were equivocal (17.21 RU/ml; negative <16, positive >22).

CSF culture was sterile. PCR testing of CSF for *Borrelia burgdorferi*, *Listeria monocytogenes*, *Streptococcus pneumoniae* and *Staphylococcus aureus* was negative.

The patient was initially treated with acyclovir, ampicillin and cefepime parenterally with supportive therapy (antiedematous, antiaggregation and antihypertensive therapy) until the completion of microbiology results. On the 8th day of the illness a respiratory insufficiency developed. The patient was intubated and mechanically ventilated, but developed hypotension and low oxygen saturation in spite of an adequate respiratory support. Despite cardiopulmonary resuscitation, the patient died due to cardiopulmonary arrest.

DISCUSSION

Cardiac involvement, including myocardial infarction, is documented in several flavivirus infections such as tick-borne encephalitis, dengue and Zika infection (Lin *et al*., 2016; Minhas *et al*., 2017). There have been many reports of myocarditis secondary to WNV infection in several mammalian species and birds, indicating a predilection for myocardial involvement (Gibbs *et al*., 2005; van der Meulen *et al*., 2005). In contrast, few published studies have documented cardiac involvement in human WNV infection (Platonov *et al*., 2001; Pergam *et al*., 2006; Kushawaha *et al*., 2009; Manov *et al*., 2014). During the large

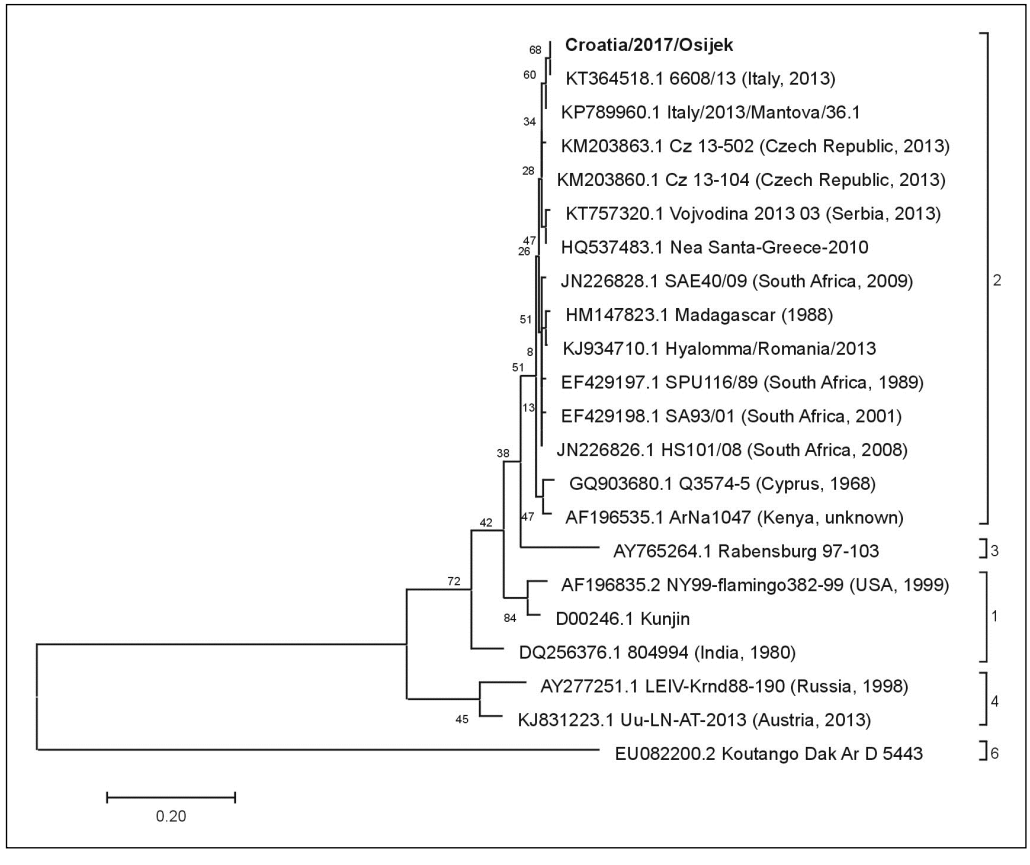

Figure 1 - *Phylogenetic tree based on 203 nucleotides long sequences of the West Nile virus (WNV) gene. The virus sequenced in this study is indicated in bold. Sequences available in the GenBank were used for comparison. Accession numbers precede virus strain designations. Location and year of detection are given next to the virus strain designation where appropriate. WNV lineages according to Rizzoli et al. (2015) are indicated next to the tree. The scale bar indicates nucleotide substitutions per site.*

Russian WNV outbreak (1999), cardiac findings on the autopsies of 40 laboratory confirmed fatal WNV meningoencephalitis cases revealed hydropericarditis with flabbiness of the cardiac muscle (Platonov *et al*., 2001). In 2004, a case of myocarditis in WNV infection was described in the US. The patient presented with cardiac arrhythmia, myocardial dysfunction and elevated cardiac enzymes (Pergam et al., 2006).

Another study conducted in the US showed that cardiac and pulmonary complications were the most common primary causes of death (35% and 25%, respectively) during WNV infection. Among cardiac complications, myocardial infarction was identified in 50% of patients. Although the pathophysiology and the role of WNV in these WNV-related fatalities are not clear, it is possible that the physiological stress of WNV infection or of exacerbated underlying medical conditions, such as acute myocardial infarction or cardiac arrhythmias, resulted in death in predisposed individuals, especially in the elderly (Sejvar *et al*., 2011). Cardiac complications were detected more commonly in patients with WNV encephalitis, compared to WNV meningitis and WNV fever (Bode *et al*., 2011). In 2016, the case of a patient with WNV encephalomyelitis with subsequent quadriplegia and who developed recurrent idioventricular rhythm requiring a permanent pacemaker was described (Espinosa *et al*., 2016). In a recently published study, sinus bradycardia and QT interval prolongation was described in a previously healthy patient with WNV encephalitis (Ajam *et al*., 2018). Myocarditis or autonomic dysfunction are the possible explanation for the observed arrhythmias (Bode *et al*., 2006).

The patient presented in this study developed WNV encephalitis (confirmed by detection of viral RNA in CSF and urine, as well as detection of WNV antibodies in CSF) complicated with STEMI which led to death on the 8th day after the disease onset. Since the antimicrobial therapy was initiated after the acute myocardial infarction was diagnosed at admission, possible reaction to drugs used was excluded. Although cardiac involvement is not frequently reported in the course of a WNV infection, this case highlights the need of awareness of the possibility of a WNV-related myocardial infection, including myocardial infarction.

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Conflicts of interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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