Title:

Report on the first two confirmed autochthonous cases of West Nile virus encephalitis in Catalonia, Spain.

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Abstract:

Background: West Nile virus (WNV) is a mosquito-borne flavivirus that can cause Central Nervous System infection in humans. Previous autochthonous cases of WNV encephalitis have been described in Spain, but none in Catalonia.

Materials and methods: We report on the first two autochthonous cases of encephalitis in humans caused by the West Nile virus (WNV) diagnosed in Catalonia (northeastern region of Spain).

Results: An old married couple presented with clinical and biological signs compatible with viral encephalitis. Acute and convalescent serum samples showed IgM and IgG positivity for WNV. In addition, IgM was also detected in cerebrospinal fluid in the male patient. The serological results were later confirmed by microneutralization assays.

Conclusions: WNV infection must be considered in patients presenting with meningoencephalitis with viral CSF characteristics when common pathogens are excluded.

Keywords:

West Nile virus, Arboviruses, Encephalitis, Viruses.

Introduction:

West Nile virus (WNV) is a mosquito-borne and bird-borne flavivirus that can infect humans, horses, and other mammals (1). Human infection has been described in Europe, Africa, North America, Asia, and Australia (1,2). Of all infected people, 20-25% develop fever and unspecified symptoms, and only 0.4-0.6% develop a neuroinvasive disease such as meningitis, encephalitis, or acute flaccid paralysis (1,2). Full recovery is the norm, with 10% case fatality if Central Nervous System (CNS) infection (2) is present. The diagnosis is based on detecting ribonucleic acid (RNA) in Cerebrospinal Fluid (CSF) or urine and WNV–specific IgM antibody in serum and CSF. Because IgM antibody does not cross the blood-brain barrier, its presence in CSF indicates CNS infection (2). Due to cross-reactions with other flavivirus, a positive enzyme-linked immunosorbent assay (ELISA)-IgM in serum is usually needed to prove seroconversion with convalescence serum, with the confirmation of microneutralization assays (3). Treatment of WNV infection is supportive (2). Previous autochthonous cases of WNV encephalitis have been described in Spain (3–6), but none in Catalonia.

Materials and methods:

We report on the first two autochthonous cases of encephalitis in humans caused by the West Nile virus (WNV) diagnosed in Catalonia (northeastern region of Spain).

Results:

In September 2022, a married couple presented with fever and a decreased level of consciousness in the Emergency Room of the "Hospital Universitari Sant Joan de Reus", southern Catalonia (Spain). The first patient was an 86-year-old woman with diabetes mellitus and cognitive impairment who had fever and somnolence for four days, with an episode compatible with a seizure. Blood tests and a cranial computed tomography (CT) were performed without significant findings. Therefore, a lumbar puncture was performed, revealing a clear CSF with 37 white blood cells/ml (of which 73% where lymphocytes), 52 mg/dl proteins, and 99 mg/dl glucose. Her husband was a 92-year-old man with arthrosis, chronic monocytosis, and gallstones who presented with fever and somnolence for 24 hours. Cranial CT and blood tests were performed, with a high leukocyte count (11850/ml) as the only finding. A lumbar puncture was also performed, obtaining a clear CSF with 89 white blood cells/ml (of which 95% were

lymphocytes), 87 mg/dl proteins, and 78 mg/dl glucose. Both patients were stable. Infectious meningoencephalitis was suspected. Empirical antibiotics and acyclovir were initiated in both patients, and they were admitted to the Internal Medicine ward. Clinical evolution was satisfactory in both patients, with no complications, and they were discharged after two weeks.

Gram stain, CSF cultures, and Multiplex polymerase chain reaction (PCR) for bacterial and viral meningitis were negative; thus, antibiotics and acyclovir were interrupted. Moreover, less common causes of meningoencephalitis were investigated*Brucella*, *Rickettsia conorii¸ Borrellia burgdorferi*, *Toxoplasma gondii*, *Treponema pallidum*, Human Immunodeficiency Virus, and Epstein-Barr virus serologic tests were all negative. Although there were no relevant epidemiological data because they lived in an urban zone in Reus, both reported a recent history of mosquito bites, so acute and convalescence serum, urine, and CSF were sent to the referral center (Hospital Clinic de Barcelona) to detect an arbovirus infection. The samples were analyzed with the ELISA to detect IgM and IgG for Dengue, Chikungunya, Zika, Toscana and West Nile (WNV) viruses. A PCR for arboviruses in CSF and urine was also performed.

In both patients, acute serum showed IgM positivity for WNV, and convalescence serum showed IgG positivity for the same virus. Moreover, the male patient had a positive PCR in urine and a positive IgM in CSF for WNV. These results were later confirmed by microneutralization assays in the Spanish referral center (Instituto de Salud Carlos III, Majadahonda, Madrid).

Discussion:

These are the first two confirmed cases of autochthonous WNV encephalitis in the region of Catalonia in the northeast of Spain. The virus had been previously detected in horses and birds in various regions of Spain(7). The first human encephalitis case was diagnosed in Barcelona, Catalonia in 2007 (3), but the patient had travelled to the southwestern region of Spain first (where seroprevalence of WNV was previously found in birds) (8). Two outbreaks of human WNV infection were later declared in the region of Andalusia (southern Spain) in 2016 (6) and in a study from 2020 (5). WNV seroprevalence was previously described in horses and birds in Catalonia from 2010 to

2019 (9), and even seroprevalence in humans in the southern Catalonia, but with no confirmed symptomatic cases (10).

Recently, in September 2021, the national animal and vector surveillance detected again WNV in horses within a radius of 5 km from Reus (7). Nevertheless, no clear autochthonous symptomatic infections have been diagnosed in our region. These patients had not travelled out of Reus, and so the transmission must have been local. No other human cases have been detected.

In conclusion, these are the first confirmed cases of autochthonous WNV encephalitis in Catalonia. Because there is local presence of WNV in horses and birds in Catalonia, this etiology must be considered in patients presenting with meningoencephalitis with viral CSF characteristics when common pathogens are excluded.

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Declaration of interest statement

The authors declare that there are no conflicts of interest.

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