

West Nile virus encephalitis outbreak in the Guadalquivir river basin area: experience and results in patients admitted to the intensive care unit[☆]



Brote de encefalitis por virus del Nilo Occidental en el área de la cuenca del río Guadalquivir: experiencia y resultados en los pacientes ingresados en cuidados intensivos

Dear Editor,

West Nile virus (WNV), an RNA virus of the genus *Flavivirus*, family *Flaviviridae*,^{1,2} is a zoonotic arbovirus transmitted by a mosquito of the genus *Culex*,^{2,3} and has a considerable worldwide public health impact.⁴

It was isolated for the first time in 1937 from a woman living in the West Nile region, in Uganda, and since then cases have been reported all over the world,⁵⁻⁷ including wide regions in western Europe.⁸ In Spain, the infection was confirmed in 2004, and since then cases have been reported mainly in Andalusia.³

In late July 2020, a WNV encephalitis epidemic was declared in the provinces of Seville, Cádiz and Badajoz. The Spanish National Center of Epidemiology was informed of 69 cases of WNV fever (35 confirmed and 34 probable): 56 in the province of Seville, 12 in Cádiz and one Badajoz – with 41 hospital admissions during the epidemic, 17 admissions to the Intensive Care Unit (ICU) and 7 deaths.⁹ Hospital Virgen del Rocío assisted 35 patients, with 9 individuals requiring admission to the ICU because of severe encephalitis. All the patients lived in the geographical setting of the Guadalquivir river basin, in the towns of Coria and Puebla del Río. No common exposures of the patients were identified, though all the affected individuals were involved in open-air activities. The demographic data are reported in [Table 1](#).

The reason for ICU admission was impaired consciousness and respiratory failure in all cases. The mean duration of the symptoms before hospital admission was four days, versus 5 days until ICU admission. All of the patients suffered severe neurological deterioration, with a mean Glasgow Coma Score (GCS) of 8 points (range 6–11). The most common symptom was fever (90%), followed by weakness (88%), neck stiffness (44%), vomiting (33%), headache (33%) and diplopia (22%). Muscle involvement was very prevalent, with extrapyramidal symptoms in 66% of the cases, flaccid paralysis with lower limb weakness in 55%, spastic muscle stiffness in 44% and hyporeflexia in 32%.

The blood count showed variable degrees of leukocytosis, with a mean count of 12,787/mL (interquartile range [IQR] 7020–20,900); there were no erythrocyte or platelet alterations. Two patients suffered acute renal failure and another two developed liver alterations.

The cerebrospinal fluid (CSF) puncture findings were suggestive of viral infection, showing pleocytosis with a mean leukocyte count of 257/mm³ (IQR 14-1275): 66.6% lymphocytes and 33.4% neutrophils. Cerebrospinal fluid protein elevation was observed, with a mean concentration of 97.56 mg/dl (IQR 38-899). None of the patients presented diminished CSF glucose levels.

A FilmArray[®] study was made in CSF, involving polymerase chain reaction testing for the most common pathogens causing community-acquired meningoencephalitis.¹⁰ The results proved negative in all cases. The CSF, serum and urine samples were sent to the National Microbiological Research Center in Granada, where they underwent indirect IgM and IgG capture ELISA testing, as well as real-time polymerase chain reaction (PCR) assay to detect antibodies against WNV. Confirmation diagnosis was performed in 100% of the patients: 8 involving IgM serological testing and one based on urine PCR testing.

All patients underwent brain computed tomography (CT) evaluation, with no acute alterations being observed in any of them. In view of the presence of neurological clinical manifestations without CT abnormalities, brain magnetic resonance imaging (MRI) was requested in 6 patients, with the identification of structural lesions in three of them ([Fig. 1](#)).

An electroencephalographic (EEG) study was made in 7 patients, of which four showed a moderate diffuse cerebral dysfunctional pattern – with no epileptic activity in any case. In turn, an electrophysiological study was carried out in three subjects, with the following findings: (1) peripheral nervous system involvement with severely decreased motor and sensory amplitudes and active denervation on the electromyogram; (2) predominantly motor axonal polyneuropathy with preservation of the sensory responses secondary to the possible involvement of the anterior horn of the spinal cord; and (3) altered auditory evoked potentials due to brainstem involvement.

Following admission to the ICU, all 9 patients required some ventilatory support measure, 7 required orotracheal intubation, and two needed high-flow oxygen with a nasal cannula. Vasoactive hemodynamic support proved necessary in 7 patients. None of the subjects required renal replacement therapy.

Methylprednisolone pulses were administered for 5 days in 8 patients. This was done early (within <24 h after admission to the ICU) in 5 patients, of which three presented a favorable neurological course. One patient received human immunoglobulin, with an unfavorable neurological outcome. In this case treatment was carried out late (after 18 days), due to delays in the microbiological diagnosis. At present, and even though various drugs were used to treat the WNV infection (corticosteroids, ribavirin, immunoglobulin, aciclovir, interferon), none proved to be effective.¹⁻³

The clinical course was variable ([Table 1](#)). The progressive and severe neurological deterioration, with variable GCS scores between 3 and 9 points, implied the need for orotracheal intubation in 7 patients. Those who did not require orotracheal intubation presented a favorable course, with early recovery of the GCS score to 14–15 points. The youngest patient showed a torpid clinical course, with recovery of the level of consciousness, left-side hemiple-

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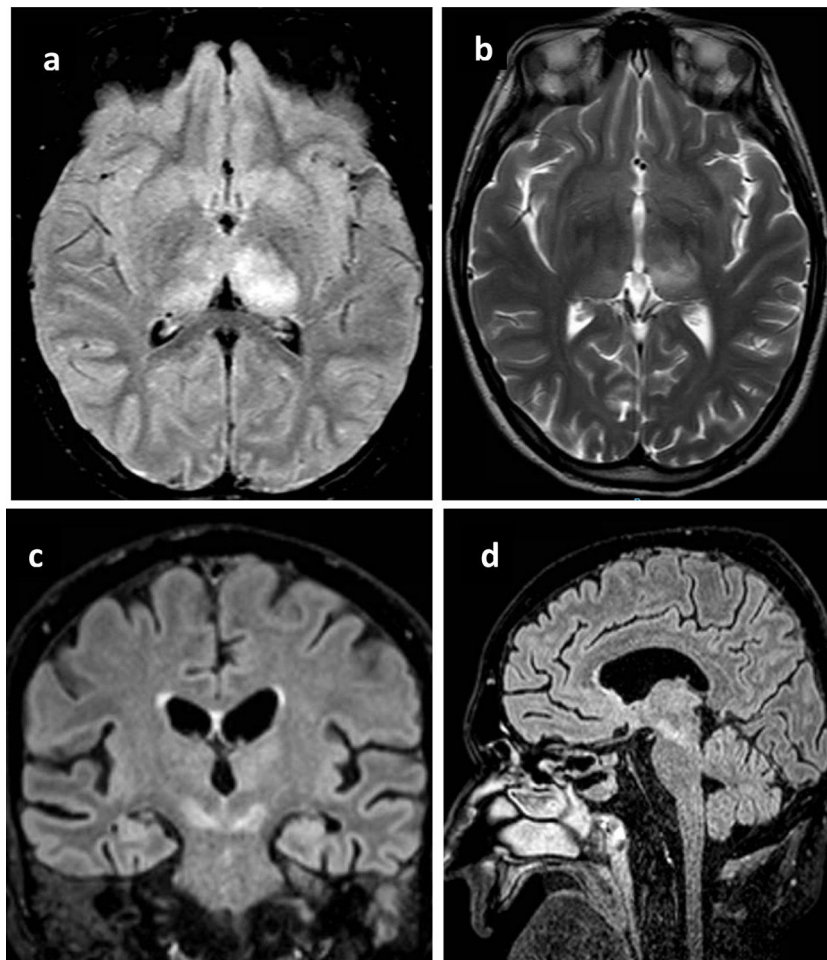


Figure 1 Principales hallazgos en RMN en pacientes con infección por Virus del Nilo Occidental. Paciente 1: a) Cambios en la intensidad de señal en el margen posterior de ambos tálamos, fundamentalmente el izquierdo con hipointensidad heterogénea en T1. b) hiperintensidad heterogénea en secuencia T2 en ambos tálamos principalmente izquierdo. Paciente 2: c) alteración del tronco del encéfalo con afectación hiperintensa marcada en banda en ambos pedúnculos cerebrales del mesencéfalo. Paciente 3: d) Lesión hiperintensa en la línea media del mesencéfalo que se extiende caudal hasta la protuberancia.

gia and right-side motor involvement with flaccid paralysis. Three patients evolved towards a vigil coma state, requiring tracheostomy; weaning from mechanical ventilation was achieved, and the patients were moved to the hospital ward. Two patients suffered rapidly progressing neurological deterioration, with severe brainstem involvement, and died during admission to the ICU.

Following discharge from the ICU, the three patients that evolved towards vigil coma without consciousness had died, with a mean survival of 2.1 months. The youngest patient (a minor) continued to present an important neurological deficit, though he was conscious, and the three patients that evolved favorably in the ICU recovered functional autonomy with no major neurological sequelae at one year of follow-up.

In conclusion, WNV infection in our setting must be taken into account in the differential diagnosis of viral meningoencephalitis. Neurological involvement is usually severe, and diagnostic confirmation tends to be established late. These two factors, together with the lack of effective treatment, imply that management in the ICU essentially focuses on life

support, with poor clinical outcomes in the form of neurological damage and death. Faster diagnostic techniques and effective treatments are needed to act upon the virus or attenuate the brain damage, with a view to improving the patient prognosis.

Ethics Committee approval

The present study was evaluated and approved by the Ethics and Biomedical Research Portal of Andalusia, with designation of the Research Ethics Committees of Hospital Universitario Virgen Macarena and Hospital Universitario Virgen del Rocío (internal code: 0733-N-21), which issued a favorable opinion on 26 October 2021.

Acknowledgments

Special recognition must go to the patients and families affected by the WNV encephalitis outbreak, and particularly

Table 1 Demographic characteristics and hospital course of the patients admitted to the ICU due to West Nile virus infection in the region of the Guadalquivir river basin.

	Mean	n	Range/percentage
Median age (years)	66		14–77
Gender			
Female		4	44.4
Male		5	55.6
Age distribution (years)			
10–20		1	11.1
50–60		1	11.1
Over 60		7	77.7
Personal history		7	77.7
Patients with PDH		5	55.6
AHT		3	33.3
DM II		3	33.3
Lung disease		1	11.1
CKD		1	11.1
CVA		1	11.1
Liver transplantation			
Days from symptoms onset to ICU admission		5	3–7
GCS upon admission to ICU		8	6–11
GCS at discharge from ICU		12	8–15
Days of ICU stay		18	4–30
Diagnosis			
IgM		8	88.8
CRP in urine		1	11.1
Brain CT		9	100
Normal		6	66.7
Evidence of acute process		0	0
Atrophy or chronic ischemic changes		3	33.3
Brain MRI		6	66.6
Normal		3	33.3
Evidence of acute process		2	22.2
Atrophy or ischemic changes		1	11.1
EEG		7	77.8
Normal		4	44.4
Pathological		3	33.3
EPS		3	33.3
Normal		0	0
Pathological		3	33.3
Treatment			
None		2	22.2
Corticosteroids		7	77.8
Immunoglobulin		1	11.1
Tracheostomy		6	66.6
Death in ICU		2	22.2
Death during first year		3	33.3
Full recovery		3	33.3
Major disability		1	11.1

PDH, previous disease history; CVA, cerebrovascular accident; DM II, type II diabetes mellitus; GCS, Glasgow Coma Score; EPS, electro-physiological study; EEG, electroencephalographic study; CKD, chronic kidney disease; AHT, arterial hypertension; IgM, immunoglobulin M; n, number de cases; CRP, C-reactive protein; MRI, magnetic resonance imaging; CT, computed tomography; ICU, Intensive Care Unit.

to those who died of the disease. We hope that preventive strategies and adequate treatment will soon be available, allowing us to avoid severe involvement as a result of this disorder.

We thank the healthcare professionals of the ICU of Hospital Universitario Virgen del Rocío, who dedicate great

effort every day to the care of their patients, offering them the best conditions for overcoming their illnesses.

Likewise, thanks are due to the entire staff of Hospital Universitario Virgen del Rocío related to the diagnosis and management of patients in the emergency care setting, hospital wards and microbiology laboratory, since their

contributions made it possible to offer timely care for our patients.

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Perception of dysphagia in the ICU of Spain, diagnostic and therapeutic management[☆]



Percepción de la disfagia en las UCI de España, manejo diagnóstico y terapéutico

Dear Editor:

Oropharyngeal dysphagia (OPD) and its complications are problems often described in critically ill patients. However, the incidence rate of this entity is still unknown.^{1,2} Due to the scarce information available, different authors recommend conducting future studies to try to validate standardization in the diagnostic protocols of this problem.^{3–6}

Therefore, the authors of this study attempted to find out about the perception, diagnostic approach, and therapeutic management of OPD in Spanish intensive care units (ICU).

A cross-sectional descriptive study was conducted from a survey submitted to Spanish ICUs and translated into Spanish from the DICE study published by Zuercher Z et al. in Switzerland.⁷ This survey was submitted to physicians and nutrition experts—one per ICU—from June through November 2020.

A descriptive analysis of data and a bivariate analysis were conducted to study whether there were any differences among the different ICUs surveyed based on the *Number of patients treated each year* (< and >1500/year).

A total of 38 ICUs participated in the survey nationwide, 31 (81.5%) of them provides care to less than 1500 patients/year.

A total of 34 ICUs (89.5%) considered that swallowing disorders were a problem of ICU patients. However, only 10 ICUs (26.3%) had a normalized care procedure to treat this entity, while 8 of them (21.1%) were thinking of its implementation in the near future (Table 1).

Regarding screening, 17 ICUs (44.7%) performed it, although only 3 (7.9%) would do so systematically in all the patients. All ICUs > 1500 beds performed screening (Table 1). This screening was often performed by the nursing staff in 22 ICUs (57.9%) and mostly it was performed using the water swallowing test in 15 of these units (39.5%) (Table 2).

A total of 23 ICUs (60.5%) did not follow sequential approaches to assess OPD (screening test followed by an assessment by a dysphagia specialist and/or a confirmation procedure test). This percentage was higher in ICUs with <1500 patients/year [20 (64.5%).] In 39.5% of the ICUs no specific assessments to diagnose dysphagia were performed (41.9% in ICUs with <1500 patients/year vs 28.6% in ICUs with >1500 patients/year) and whenever these assessments would be performed, they were the responsibility of the ENT specialist in 8 ICUs (21.1%) (Table 2).

The most widely used diagnostic technique at the ICUs was the swallowing test (52.6%) followed by the clinical suspicion of aspiration (47.4%) (Table 2). Fiber endoscopy of swallowing was the most commonly used procedural test for diagnostic purposes. However, it was only used in 23.7% of the ICUs (19.4% in ICUs with <1500 patients/year vs 42.9% in >1500). No ICU ever used video fluoroscopy of swallowing or manometry for study purposes.

Regarding treatment, it was mainly based on changing diet, the size of the bolus, and the consistency of food in 24

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