

West-Nile virus encephalitis in immunocompetent pediatric patients : 2 case reports and review of the literature

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ABSTRACT

West Nile virus (WNV) is a zoonotic agent causing life-threatening encephalitis in a proportion of infected patients. Its neuro-invasive presentation, is an emerging disease in North Africa, with increasing rates of morbidity and mortality. Prompt clinical suspicion and recognition of this condition would benefit patients from a prompt management. WNV encephalitis is usually asymptomatic; however, it is known to cause clinically significant disease in immunocompromised hosts including severe persistent infection with fatal outcomes.

We report on two cases of West Nile encephalitis in recently-treated, different-aged, immunocompetent patients. The evolution of the older patient was fatal however the second patient had a complete recovery. Given its non-specific clinical presentation, the diffusion of WNV constitutes a crucial and emerging concern. Even though rare, neuro-invasive WNV infection should always be suspected in pediatric patients, living or traveling in endemic areas, presenting with meningitis, encephalitis or acute flaccid paralysis during the WNV transmission season.

Key words : west Nile Virus, encephalitis, immunocompetent

INTRODUCTION

West Nile virus (WNV) is an emerging virus responsible for an increasing number of neuro-invasive disease in Africa, North America, Europe, and neighboring countries. It belongs to the Flaviviridae family of the genus Flavivirus (1). West Nile disease in children is less common and associated with milder symptoms and better outcome than in elderly individuals, even though severe neuro-invasive disease and death have been reported also among children (2). However, the incidence of WNV infection and disease in children is probably underestimated and the disease clinical features are not fully understood because of lack of reporting cases in children.

In this report, we describe 2 cases of West-Nile virus encephalitis: one in a 6-years old immunocompetent child with fatal evolution and the other in a 2-year-old immunocompetent infant with a complete recovery.

OBSERVATION

Case 1 :

A 6-years old child presented to the Pediatric Emergency with gait disorders settling on one day. The child's mother reported that a few days before the

onset of symptoms he presented fever, headaches, rhinorrhea followed by altered general state. On preliminary examination, his vital signs were normal. His general examination found generalized hypotonia with abolition of osteo-tendinous reflexes. He was admitted to the pediatric intensive care unit. The initial laboratory tests were all normal. A lumbar puncture revealed 100 cells/mm³ with 84% of lymphocytes, cerebral spinal fluid protein was elevated (0.74 g/L), and glucose was normal (3.37 mmol/L). Because of the clinical suspect of viral encephalitis, acyclovir treatment was promptly started without improvement in his neurological condition. The electromyogram and the cerebral MRI were normal, whereas an electroencephalograph showed diffuse slow wave activity without paroxysm. Within 3 days, he became poorly responsive to verbal stimuli and diffusely hyporeflexic. He also developed mumps. A metabolic disorder was suspected but the dosage of lactate, pyruvate, and ammonemia returned negative. A normal rate of Anti-NMDA receptor antibodies has eliminated an autoimmune encephalitis. Polymerase chain reaction for WNV returned positive in the CSF with a detection of WNV-specific

IgM and IgG seroconversion. One month after his admission, he presented pancreatitis and secondary diabetes. Despite a prompt management, his mental status and weakness rapidly worsened. A mechanical ventilation was required and he died two months after his admission.

Case 2:

A 2-year-old boy was presented to the pediatric emergency department, because of fever, fatigue, dizziness, headache, and vomiting five days before hospital admission. The mother's infant brought him to a general practitioner who gave him symptomatic treatment and azithromycin. The infant didn't show any improvement, thus, his general state worsened and he presented seizures. So, the mother brought him to the pediatric emergency department. Upon admission, he was febrile, unconscious (Glasgow Coma Scale 12/15), with blood pressure 90/50 mm Hg, heart rate 144/min; the rest of physical examination did not show any abnormalities. Neurological examination did not show neck stiffness or symptoms of Kernig and Brudzinski at the time of hospitalization but did show axial hypotonia and impossible standing position. The main laboratory findings were as follows: white blood cell count 12130/L, platelets 437000/L, hemoglobin 9.6 g/dL, C-reactive protein 3.6 mg/L. Imaging investigations were done at the beginning of illness. Electrocardiogram, x-ray and cerebral scan did not show any abnormalities. A lumbar puncture revealed 86 cells/mm³ with 80% of lymphocytes, cerebral spinal fluid protein was normal (0.3 g/L), and glucose was normal (3.51 mmol/L). An electroencephalograph had shown slight brain damage. Antiviral drug therapy was started (Zovirax) with an antiepileptic treatment and immunoglobulin. The patient received supportive treatment as well. An MRI was performed and had shown: Flair and T2 hypersignal range signal abnormality at the level of the wall of V4, periaqueductal region and cerebellar peduncle, with no post-contrast enhancement. Specific WNV-IgM and WNV-IgG antibodies were detected in serum (Anti-WNV ELISA IgM, IgG). Neurological manifestations were reversible and in a few days the patient regained normal consciousness. After complex therapy, the patient was discharged. On three-month follow-up, the patient was free from any neurological complications.

DISCUSSION

WNV was first detected in the Western Hemisphere in 1999 during an outbreak of encephalitis in New York City. In the 2000s, WNV became a major public health problem in Africa and Europe and human cases of WNV neuroinvasive disease (WNID) were noted (3,4). Rural areas and low socioecono-

mic condition were found in most of the cases (5,6). The variations in the viral genome are responsible for the increasing virulence of WNV for humans (3). Mosquitoes become infected with WNV after biting a bird with high-level viremia and may then transmit it to humans following a blood meal from the host (5). Horses and humans are incidental dead-end hosts. The most important risk factor for acquiring WNV infection is exposure to infected mosquitoes (4). WNV can also be transmitted via transfused platelets, red blood cells, and fresh frozen plasma as well as through heart, liver, lung, and kidney transplants (2,4). WNV infections are asymptomatic or subclinical in 70% of cases. In the pediatric population, the most frequent clinical form is the West Nile Fever, while WNND occur in approximately 1% of all infections, presenting as meningitis, encephalitis or acute flaccid paralysis (7). The clinical presentation of the first patient was compatible with encephalitis. The incubation period for clinical illness generally ranges from 2 to 14 days, but it can be longer (up to 21 days) in immunocompromised patients (2,3)

WNV encephalitis, the most life-threatening aspect of WNV infection, can begin with a nonspecific systemic prodrome: high fever and neurologic symptoms such as somnolence, meningeal signs, tremor, myoclonus, seizures, paralysis and coma (3). As in our first case, the first symptoms were gait disorder and fever.

Although cerebral MRI and computed tomography are often normal in patients with WNV meningoencephalitis, MRI should be performed. Furthermore, the majority, up to 80% of cases with normal MRI findings may require only short periods of hospitalization and have complete recovery (8). However, in the first case the patient's condition was critical with a fatal outcome and the second case which has a pathological MRI have had a complete recovery.

Diagnostic tests including cerebrospinal fluid examination should be performed in order to differentiate WNV infection from stroke, myopathy, and Guillain-Barre Syndrome. The CSF profile in neuro-invasive disease may be characterized by a lymphocytic pleocytosis in up to half of the cases, as was the case in the two patients, a neutrophil pleocytosis in up to 45% of cases, or a noninflammatory profile in up to 5% of cases of neuro-invasive diseases (7).

The virus is present at very low levels in human blood and tissues. Thus, real-time PCR-based detection systems are used (9).

A case is considered probable if the patient meets any of the following clinical criteria: suggestive clinical presentation (encephalitis, meningitis, fever) in

the presence of WNV-specific immunoglobulin M or IgG in serum with IgG seroconversion, or a four-fold increase in IgG titer on two subsequent samples. A confirmed case is defined as meeting the previous clinical criteria and one or more of the following additional criteria: (1) Isolation of WNV from blood or cerebrospinal fluid, (2) detection of WNV RNA in blood and/or CSF, (3) WNV-specific IgM in CSF, and (4) detection of WNV IgM at a high titer and detection of WNV IgG, confirmed by a neutralization assay (3,7). According to these criteria, our patient could be considered a confirmed case of WNND due to the detection of WNV IgM in CSF, collected in the symptomatic phase of the neurological infection and the subsequent WNV IgG seroconversion. In most children with WNV, the disease is mild and self-limited, and thus supportive care only is required. However, WNV neuro-invasive disease can lead to death, and can cause permanent disability (10). Furthermore, there are no effective antiviral to combat WNV infection (3,11).

CONCLUSION

Since its discovery, the disease has continued to increase in vast areas of the world. Thus, it is considered the main cause of viral encephalitis in the world. Avoiding human exposure to WNV-infected mosquitoes remains the cornerstone for preventing WNV disease (4). Over the next few years, researches into new methods to reduce human exposure to mosquitoes is crucial and can help prevent other mosquito-borne illnesses

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