Atypical presentation of West Nile encephalitis: a brief report and review of the current literature

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ABSTRACT

West Nile virus (WNV) causes both sporadic and epidemic infections, which may be accompanied by severe neurologic involvement. The infection is transmitted to humans primarily through mosquito bites, and the virus is maintained through a cycle in which birds serve as its primary host. The typical involvement of the central nervous system is indistinguishable from other pathogens' meningitis and encephalitis. In this report, we describe an atypical presentation of WNV meningoencephalitis in an 81-year-old female patient who initially displayed psychiatric symptoms. Anamnestic information was crucial for diagnosing the correct condition. Upon learning that the patient lived near a natural bird reserve, the search for the agent responsible for meningoencephalitis was directed.

Introduction

West Nile virus (WNV) is a single-stranded RNA virus of the genus Flavivirus, a member of the Japanese encephalitis virus antigenic complex, which causes both sporadic and epidemic infections that may be associated with severe neurologic involvement.[1,2] The majority of human infections are asymptomatic, with only 20 percent exhibiting flu-like symptoms and 1 percent progressing to forms of meningoencephalitis, primarily among the elderly and immunocompromised.[3,4]

The first major outbreak in Europe was reported in 1996, and the number of human cases increased significantly in the years that followed. From 2002 to 2009, WNV outbreaks were reported in a number of European and neighboring countries, and since 2005, the transmission cycle has become endemic in some countries of southeast and eastern Europe, with annual outbreaks originating primarily from WNV lineage 2 strains belonging to the Hungarian and Volgograd clades.[5-11] The infection is transmitted to humans primarily through mosquito bites, and the virus is maintained in a cycle where birds serve as the primary host.[12]

In 1998, the first outbreak in Italy was discovered in Tuscany; since 2008, there has been an increase in the spread of WNV throughout Italy, and as a result, surveillance and monitoring systems have been established,[13,14] demonstrating a widespread virus circulation in mosquitoes, birds, and horses across a vast territory.

The typical manifestation of WNV infection is a febrile manifestation with flu-like symptoms.[15] The involvement of the central nervous system is indistinguishable from other pathogens' meningitis and encephalitis.[16,17]

In this manuscript, we describe the case of an 81-year-old female patient with WNV encephalitis whose initial manifestations were indistinguishable from psychiatric symptoms. Due to the lack of specificity of the patient's symptoms, anamnestic information was required for a proper diagnosis. Particularly, the targeted

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search for the causative agent of meningoencephalitis was refined after it was discovered that the patient resided near a nature reserve.

Case Report

In this brief report, an atypical and subtle presentation of WNV meningoencephalitis is described. Careful analysis of the clinical presentation, meticulous anamnestic collection of key elements of the patient's personal history, and the emergency room physicians' intuition regarding a rare but endemic pathology all contributed to the correct diagnosis.

An 81-year-old female presented to the emergency room with a disorder that initially manifested as a panic attack and progressively worsened into psychomotor agitation and a state of confusion.

Upon initial evaluation, the patient appeared agitated, anxious, and confused, with widespread upper limb tremors. When questioned about the nature of the disorder, she provided vague and contradictory responses. The family members who accompanied the patient to the Emergency Room (ER) believed that the neurological disturbance was a recurrence of similar anxiety attacks from the past.

In terms of previous clinical history, the patient had an ischemic stroke that was not complicated by neurological relics. The patient was prescribed anxiolytics and antipsychotics for a history of bipolar disorder and panic attacks and underwent regular specialist follow-up.

Due to the patient's uncooperative nature and cognitive impairment, the physical examination was severely hampered. She demonstrated hypertension (170/90 mmHg), tachycardia (110 beats per minute), and tachypnea (20 acts per minute). The patient denied having headaches, dyspnea, or angina. Temperature of the body was normal. Both cardiac and pulmonary objectivity were normal. On examination of the abdomen, neither acuteness nor peritonism were detected. On neurological examination, no signs of meningitis or other significant alterations were detected.

With the exception of a very slight leukopenia, blood tests were unaffected except for a very slight leukopenia. The inflammation indices are negative (Table 1).

To rule out organic neurological lesions, a direct computed tomography of the skull/brain was performed; despite the previous ischemic outcomes, no acute lesions were detected.

The patient was evaluated by a psychiatric specialist, and symptomatic treatment with benzodiazepines was then initiated. Patient was observed in the emergency room due to lack of improvement.

In the 12 hours following admission, the patient's clinical condition deteriorated. She developed fever, shivering, and a mild case of meningitis. Asthenia affected the upper limbs, particularly the right side. The tremor intensified, and drowsiness ensued.

Therefore, we performed a lumbar puncture to collect cerebrospinal fluid, repeated blood examinations (Table 1), and gathered blood cultures.

Neutrophil count and C-reactive protein levels were found to have increased marginally compared to initial levels. Table 2 displays the physicochemical characteristics of the liquor, and the polymerase chain reaction analysis of the most prevalent pathogens was negative (*Escherichia coli K1*, *Haemophilus influenzae*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Streptococcus agalactiae*, *Streptococcus pneumoniae*, *Cytomegalovirus*, *Enterovirus*, *Herpes simplex virus 1*, *Herpes simplex virus 2*, *Human herpesvirus 6*, *Human parechovirus*, *Varicella zoster virus*, *Cryptococcus neoformans*).

A suitable form of supportive care was initiated. In addition, we prescribed empiric antibiotic and antiviral therapy with levofloxacin and aciclovir, as recom-

Table 1. Blood exams at baseline and after 6 hours from admission.

Parameter	Baseline	After 12 hours
WBC, 1000/mm^3	4.12	7.96
Neutrophils, %	65	83
Platelets, 1000/mm^3	144	167
C-reactive protein, mg/dL	0.62	1.13
Procalcitonin, ng/ML	0.06	0.29
Creatinine, mg/dL	0.6	0.7
Fibrinogen, mg/dL	450	544
ALT, U/L	40	40
AST, U/L	42	42

WBC, white blood cells; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Table 2. Chemical-physical characteristics of the liquor.

Parameter	Value
Total protein, mg/dL	90
Glucose, mg/dL	91.9
Chloride, mEq/L	118
Lactate, mg/dL	3889
Cells, cells/mm^3	540
Color	Colorless
Appearance	Clear
Mononuclear cells	13.9%
Polynuclear cells	86.1%
Meningitidis score, normal value <2	4
Glycorrhachia/glycemia ratio	0.6

mended by the infectious disease consultation, in the event that meningoencephalitis was suspected.

In the absence of culture results, initiating early empirical therapy against treatable meningoencephalitis improves prognosis and reduces neurological sequelae.[18,19] Considering that the patient reported a severe allergic reaction to beta-lactamines and cephalosporins, quinolones were a suitable alternative.[20]

We learned crucial information after questioning the patient's family members more thoroughly.

The patient presented with fever and diarrhea the week prior, which resolved spontaneously. In addition, she lived near a bird sanctuary, which was a marsh. Therefore, a viral infection transmitted by vectors such as sand flies and mosquitoes was hypothesized; WNV disease was compatible with the clinical course of the patient, and it was endemic in this region.

It was decided to conduct further research on cerebrospinal fluid samples. Because our reference laboratory (S Jacopo Hospital, Pistoia; SS Cosma e Damiano Hospital, Pescia; Usl Toscana Centro) does not perform these specific analyses, we sent biological samples to Careggi Hospital, Florence. The research on alcohol and WNV was positive.

The patient was transferred to the infectious disease department after the diagnosis was established. Therapy and monitoring of vital functions were administered. Cognitive functions improved gradually, and vital signs remained normal. At the conclusion of her hospitalization, she was sent home with outpatient care.

Discussion and Conclusions

Up to forty percent of WNV infection cases are asymptomatic. The incubation period is typically between 2 and 14 days, but in immunocompromised hosts it can last longer.[15] The typical manifestation of the infection is identical to that of other viral syndromes.

The disorder manifests initially as fever, headache, diffuse malaise, and myalgia. Occasionally, the fever may be absent or very mild.[21] Eye pain, pharyngitis, gastrointestinal symptoms including nausea, vomiting, diarrhea, and abdominal pain are uncommon manifestations.[15] A morbilliform skin rash, occasionally maculopapular, is associated with the defervescence phases of the infection and is unrelated to neuroinvasive complications.[22]

Typically, a neuroinvasive infection manifests as a fever with mixed symptoms of meningitis, encephalitis, and flaccid paralysis.[23]

Particularly, the forms that progress to encephalitis appear to be more prevalent in elderly patients and have a 10% mortality rate.

The encephalitic manifestations range from a mild, self-limiting confusional state to widespread and severe neurological manifestations that result in coma and death.[17]

Extrapyramidal neurological manifestations are suggestive of WNV infection. Particularly, coarse tremor and myoclonus, primarily affecting the upper extremities, as well as parkinsonian-type symptoms including rigidity and bradykinesia, have been described.[24]

Figure 1 depicts a timeline of the patient's clinical presentation.

The febrile presentation accompanied by gastrointestinal symptoms suggested a viral syndrome with nonspecific features; the literature describes a one-week incubation period for the neuroinvasive manifestations of WNV infections.

Although difficult to interpret, motor disturbances, particularly asthenia of the upper limbs, are regarded as typical of WNV encephalitis forms.[24]

In addition, advanced age is considered a major risk factor for the development of neuroinvasive disease caused by WNV, specifically encephalitis.[25]

WNV was also suggested by several anamnestic data.

Summer is a typical time for vectors such as mosquitoes to spread. Toscana virus, an arbovirus that is also transmitted by sand flies, has also been considered in differential diagnostics.[26] However, the results of this study were negative.

In addition, the patient resided in close proximity to the 'Padule di Fucecchio', the largest inland Italian swamp. This habitat is a natural reserve for numerous species of birds, the primary hosts of WNV infection. Tuscany is also an endemic region for WNV, and several outbreaks have been described.

Attention to clinical and anamnestic details is crucial for a timely and accurate diagnosis. This difficulty

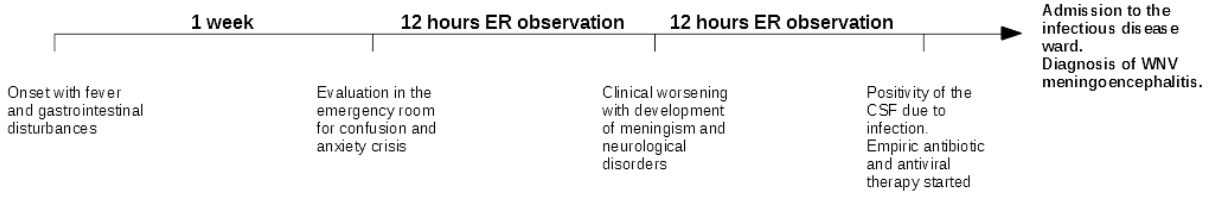

Figure 1. Timeline of clinical presentation and management during emergency evaluation. ER, Emergency Room; WNV, West Nile virus; CSF, cerebrospinal fluid.

is exacerbated in a chaotic and frenetic environment like the emergency room.

However, a meticulous approach to investigation not only yields optimal results, but also saves time and money.

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