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# Neuroinvasive West Nile Virus Infections in the Trakya Region of Türkiye

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In August 2024, we detected an unusual outbreak of acute meningoencephalitis. When clinicians were cautioned by the national associations of Infectious Diseases and the National Arboviruses and Viral Zoonoses Reference Laboratory (Ankara, Türkiye) detected West Nile virus (WNV) in serum and/or urine samples employing the polymerase chain reaction (PCR) technique, the etiology could be determined.

The WNV is a neurotropic virus that cycles between mosquitoes and birds.[1,2] Individuals become infected because of mosquito bites. In eighty percent of patients, their infection with WNV is asymptomatic. In 20% of patients, a mild disease with high fever develops. Less than 1% of patients present with neuroinvasive disease.[2,3] West Nile Neuroinvasive disease (WNND) includes meningitis, encephalitis, and acute flaccid paralysis/poliomyelitis. Older adults and immunocompromised individuals are at a higher risk of developing severe or neuroinvasive disease.[2-4]

WNV is endemo-epidemic in countries located in southern, eastern, and western Europe.[5] Greece exhibited one of the highest notification rates in Europe. Human cases have been recorded every year in Greece since the first outbreak in 2010.[5,6] In 2018, the overall WNND notification rate was 2.2 cases per 100,000 population. In 2022, the overall WNND notification rate was 1.7 cases per 100,000 population.[6] The Meriç River divides the Trakya region into two distinct regions: Western Trakya is in Greece, while Eastern Trakya is in Türkiye.

Türkiye reported 47 human cases of WNV infection in 2010, with 12 laboratory-confirmed and 35 probable cases.[7] Most patients hailed from the western region of the country, and the incidence was 0.19 cases per 100,000 population. Forty of 47 patients presented with neuroinvasive manifestations. As of April 2011, WNV infections have been included in the national list of notifiable diseases of Türkiye. As a result of the occurrence of WNV infection-related cases in 2010 and 2011, it is considered to be among the endemic diseases.[7] The first patient diagnosed as WNV encephalitis in Trakya region was in 2012.[8] Subsequently, no case could be identified.

In August 2024, ten patients with high fever, headache, delirium, sluggish speech, slow movements and rapidly deteriorating level of consciousness were admitted to the Infectious Diseases and Neurology Clinics of Trakya University Hospital in Türkiye. All patients were over 60 years of age, and seven out of the ten patients were males. The most significant clinical findings were high fever, headache, malaise, fatigue, myalgias, nausea, vomiting, diarrhea, memory impairment, balance problems, and altered levels of consciousness. Neck rigidity was observed in only two patients during the physical examination.

Lumbar puncture could be performed on nine patients. The cerebrospinal fluid (CSF) examination detected high protein concentrations in all nine patients and CSF pleocytosis in seven patients, with a preponderance of neutrophils in five of them. The CSF glucose level was approximately half that of the blood glucose level. When we detected a predominance of neutrophils in CSF, we were unable to exclude acute bacterial meningitis. Hence, we initiated the administration of antimicrobial chemotherapy (ceftriaxone, ampicillin, vancomycin) and dexamethasone. We also initiated acyclovir therapy when the neurologist specifically recommended it to the patients in response to suspicions of encephalitis. Within 48-72 hours of dexamethasone therapy, severe mental dullness and altered consciousness levels began to improve.

The patients' blood and urine samples were submitted to the National Arboviruses and Viral Zoonoses Reference Laboratory (Ankara, Türkiye) for diagnosing arboviral infections. Five patients' serum samples and nine patients' urine samples tested positive for WNV using the WNV real-time PCR assay [Bosphore Geneworks West Nile Virus Quantification Kit v2 (Anatolia Geneworks, İstanbul,

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Türkiye), Bio-Rad CFX96 Touch™ (Bio-Rad Laboratories, Inc., USA)]. By the Immun Floresan Antibody method, serum samples of seven patients were found to be positive for WNV immunoglobulin M (IgM) antibody, and six patients were found to be positive for IgG antibody [IIFT Flavivirus Mosaic 1 (IgM) (Euroimmun, Germany), IIFT Flavivirus Mosaic 1 (IgG) (Euroimmun, Germany)]. The Plaque Reduction Neutralization test (worked manually with the microneutralization method) was performed for two patients to verify the seropositivity. As there was no specific treatment, supportive treatment was administered.

Aerobic culture of blood and CSF was conducted. Additionally, the following laboratory tests were performed for all patients: PCR for tuberculosis DNA and herpes simplex virus DNA; IgM and IgG antibody tests for dengue virus; all of these test results were negative.

Brain computed tomography (CT) and magnetic resonance imaging (MRI) were conducted for all patients to verify central nervous system involvement and to exclude other pathologies. The images were evaluated by specialists in both radiology and neurology. Only one patient exhibited MRI and CT findings (ventriculitis) consistent with the clinical presentation. This letter evaluates the clinical, laboratory, and diagnostic characteristics of these patients (Table 1).

We wish to report that the Trakya region experienced an acute meningoencephalitis outbreak in August 2024, which was caused by WNV. Preventive and control measures must be implemented as soon as feasible in the Trakya region, which is home to extensive rice fields, rivers, and streams that are conducive to mosquito breeding. It is anticipated that the mosquitoes may remain active until the end of October and new cases may continue to emerge. Consequently, neuroinvasive WNV infections must be considered in the differential diagnosis of acute meningoencephalitis.

**TABLE 1.** Summary of Cases with WNV Neuroinvasive Disease Admitted in August-September 2024.

| P | Sex, age (years) | Clinical presentations | CSF cells count/µl | CSF protein (mg/dl) | CSF/ blood glucose (mg/dl) | Serum PCR | Urine PCR | IgM (serum) | IgG (serum) | PRNT | CT | MRI |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | M, 70 | Myoclonus, tremor, fasciculation, balance problems | 72 70% lymphocyte | 106 | 80/117 | Negative | Positive | Positive | Positive | | Cerebral lacuna | Ventriculitis |
| 2 | M, 63 | Neck stifness, mental dullnes ICU admission | 352 70% neutrophil | 143 | 143/260 | Negative | Positive | Positive | Positive | | Normal | Normal |
| 3 | F, 78 | TIA, myoclonus, fasciculation | 120 80% neutrophil | 104 | 57/96 | Negative | Positive | Positive | Positive | Positive | Sequel changes | Normal |
| 4 | M, 69 | Memory impairment, neck stifness, changes in the level of consciousness | 448 60% neutrophil | 118 | 43/120 | Positive | Positive | Positive | Positive | | - | Normal |
| 5 | M, 70 | Myoclonus, fasciculation, changes in the level of consciousness | 688 80% lymphocyte | 169 | 48/92 | Negative | Positive | Positive | Positive | Positive | Normal | Normal |
| 6 | F, 63 | Right peripheral facial paralysis, mental dullnes | - | - | - | Positive | Positive | Gray Zone | Gray Zone | | Normal | Normal |
| 7 | F, 65 | Memory impairment, tremor, balance problems | 0 | 89 | 58/120 | Positive | Negative | Gray Zone | Gray Zone | | Normal | Normal |
| 8 | M, 64 | Slow spech Changes in the level of consciousness | 176 85% neutrophil | 138.9 | 153/304 | Positive | Positive | | | | - | Normal |

**TABLE 1.** Continued

| P | Sex, age (years) | Clinical presentations | CSF cells count/µl | CSF protein (mg/dl) | CSF/ blood glucose (mg/dl) | Serum PCR | Urine PCR | IgM (serum) | IgG (serum) | PRNT | CT | MRI |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 9 | M, 86 | Memory impairment, drowsiness ICU admission | 386 80% neutrophil | 145 | 100/166 | Positive | Positive | Positive | Positive | | Sequel changes | Normal |
| 10 | M, 66 | Changes in behavior Mental dullnes | 6 | 117.2 | 131/380 | Negative | Positive | Positive | Positive | | Normal | Normal |

P, patient; F, female; M, male; CSF, cerebrospinal fluid; PCR, polymerase chain reaction; CT, computerized tomography; PRNT, Plaque Reduction Neutralization test; MRI, magnetic rezonans imaging; ICU, intensive care unit, TIA, transitional ischemic attack; WNV, West Nile virus; IgM, immunoglobulin M; IgG, immunoglobulin G.

**Informed Consent:** Informed consent was obtained from all cases.

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