Agri 2024;36(3):198–201
doi: 10.14744/agri.2021.35492

CASE REPORT

West Nile virus meningitis presenting with migrainous headache

Migrenöz baş ağrısıyla prezente olan batı Nil virüsü menenjiti

Esra KOÇHAN KIZILKILIÇ,[1] Merve AKTAN SÜZGÜN,[1] İlker İnanç BALKAN,[2] Sabahattin SALP[1]

Summary

West Nile Virus (WNV) infection is a clinical picture that is transmitted from wild birds, its natural host, to humans through mosquitoes and generally shows an asymptomatic course. Influenza-like WNV fever is frequently seen in symptomatic individuals, and a neuroinvasive course is more rarely observed. Neuroinvasive WNV has a broad-spectrum profile of neurological signs and symptoms. WNV meningitis is one of the most common neuroinvasive forms of WNV, and it does not differ clinically and radiologically from other viral meningitis. Secondary headaches, which can mimic primary headaches, are an infectious factor that should be kept in mind in the etiology, especially in cases presenting in the summer months. In this study, a case of WNV meningitis presenting with a headache of migrainous character is presented.

Keywords: Headache; migraine; west Nile virus.

Özet

Batı Nil virüsü (BNV) enfeksiyonu, doğal konağı olan vahşi kuşlardan sivrisinekler aracılığıyla insanlara bulaşan ve genellikle asemptomatik seyir gösteren bir klinik tablodur. Semptomatik olan bireylerde sıklıkla gribal enfeksiyon benzeri BNV ateşi görülmekte, daha nadiren ise nöroinvazif seyir izlenmektedir. Nöroinvazif BNV, geniş spektrumlu bir nörolojik belirti ve bulgu profiline sahiptir. BNV menenjiti, en sık görülen nöroinvazif BNV formlarından biridir ve diğer viral menenjitlerden klinik ve radyolojik olarak belirgin farklılığı bulunmamaktadır. Primer baş ağrılarını taklit edebilen sekonder baş ağrıları etiyolojisinde, özellikle yaz aylarında başvuran olgularda akılda tutulması gereken bir enfeksiyon etkenidir. Bu çalışmada migrenöz karakterde baş ağrısıyla prezente olan BNV menenjiti vakası sunulmuştur.

Anahtar sözcükler: Baş ağrısı; batı Nil virüsü; migren.

Introduction

West Nile virus (BNV) is a positive polarity, single-stranded RNA virus belonging to the genus Flavivirus of the Flaviviridae family.[1] Arthropod (ticks and mosquitoes) mediated transmission causes disease, especially in horses and humans.[2] The most common route of transmission in humans is mosquito bite, followed by blood transfusion,[3] organ transplantation,[4] transplacental transmission,[5] breast milk transmission,[6] and occupational exposure in laboratory workers.[7] Acute signs of infection may occur in 20–40% of infected individuals 2–14 days after virus transmission.[8] The clinical manifestations of the disease are like those of classical influenza infection, including fever, headache, myalgia, anorexia, nausea and vomiting, and abdominal pain.[9,10]

The neuroinvasive form, which is the rarest involvement pattern and is encountered in approximately 1–5% of all WNV infections, occurs by direct viral invasion of endothelial cells in the cerebral microcirculation or by the virus reaching the central nervous system via the olfactory bulb via the trans neuronal route.[11] Neuroinvasive disease can lead to clinical conditions such as meningitis, encephalitis, and acute flaccid paralysis, confusion, and coma accompanied by systemic fever, which can cause serious morbidity and mortality.[12] It has been reported in the literature that encephalitis is more common in the older age group, while meningitis is more common in the child and young adult age group.[13,14] Less common clinical presentations during neuroinvasive disease are brainstem encephalitis, cerebellitis, cranial neuropathies, polyneuropathy/radiculopathy,

[1]Department of Neurology, İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, İstanbul, Türkiye
[2]Department of Infectious Diseases and Clinical Microbiology, İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, İstanbul, Türkiye

Submitted *(Başvuru):* **06.09.2021** **Revised** *(Revize):* **23.09.2021** **Accepted** *(Kabul):* **15.11.2021** **Available online** *(Online yayımlanma):* **04.07.2024**

Correspondence: Dr. Esra Koçhan Kızılkılıç. İstanbul Üniversitesi-Cerrahpaşa, Cerrahpaşa Tıp Fakültesi, Nöroloji Anabilim Dalı, İstanbul, Türkiye.
Phone: +90 - 553 - 285 29 44 **e-mail:** dr.kochanesra@gmail.com

chorioretinitis, optic neuritis, parkinsonism findings, tremor, and myoclonus.[15] Almost all deaths due to WNV infection reported in the literature are secondary to neuroinvasion.[16] Morbidity is particularly high in immunocompromised and elderly individuals.[17]

In this study, a case of WNV meningitis is presented, the first symptom of which was a typical migrainous headache and in which central nervous system infection was suspected and diagnosed during the disease.

Case Report

A 24-year-old female patient without any chronic disease presented to the emergency department with a headache. The patient described a bifrontal and throbbing pain that had been ongoing for two days, accompanied by phonophobia, photophobia, osmophobia, and nausea and vomiting. The headache, which could reach a severity of 10/10 intermittently but was generally 5–6/10, was partially responsive to nonsteroidal anti-inflammatory treatment. It did not exhibit positional characteristics and was not accompanied by autonomic findings. It was learned that the patient had been evaluated for similar headache attacks one month before her emergency presentation and was started on duloxetine with a preliminary diagnosis of tension-type headache. The patient had a history of oral contraceptive use and smoking.

The patient, whose neurological examination was normal and in whom no acute pathology was detected in the non-contrast cranial CT examination, was initially considered to have a migraine headache attack without aura and was followed up with symptomatic treatment. During the follow-up period, the patient's cranial imaging was updated in detail due to the worsening of the headaches, the addition of positional character, and the emergence of meningeal irritation findings in the repeated neurological examination. Non-contrast cranial CT, diffusion MR, contrast cranial MR, and MR venography examinations were within normal limits. Lumbar puncture was performed on the patient with the preliminary diagnoses of subarachnoid hemorrhage and venous sinus thrombosis. CSF opening pressure was 36 cm H_2O, CSF protein was 110 mg/dl, and CSF glucose was measured within normal limits. In the CSF, while no erythrocytes were observed, 320/mm^3 leukocytes were seen with lymphocyte dominance. Although her vital signs were stable and fever-free, the patient was diagnosed with meningitis and started on empirical vancomycin and ceftriaxone treatment with clinical and CSF findings. Routine hemogram, liver and kidney function tests, and electrolyte levels were within normal limits. Hepatitis and HIV serology, aerobic and anaerobic bacterial cultures, viral meningitis panel (adenovirus, EBV, CMV, HSV-1, HSV-2, VZV, HHV-6, HHV-7, enterovirus, parvovirus B19), TBC PCR, and TBC culture were negative.

The patient's clinical findings regressed in the first days under empirical antibiotic therapy, and the second clinical worsening episode occurred on the 10th day after the end of the treatments. No pathology was observed in the renewed cranial imaging of the patient, whose headache complaints recurred and who had widespread myalgia complaints. A second lumbar puncture was performed for the differential diagnosis of infectious etiologies. CSF opening pressure was 20 cm H_2O, CSF protein was 73 mg/dl, and CSF glucose was measured within normal limits. CSF sample showed 30/mm^3 leukocytes with a neutrophil predominance. Routine CSF microbiology panels were negative for viral, bacterial, and fungal infections. Since the patient's anamnesis included a travel history to the Aegean Region 15 days ago and intense mosquito exposure, it was planned to investigate for possible West Nile virus infection. Serum samples were sent to the T.R. Ministry of Health, General Directorate of Public Health, National Arbovirus and Viral Zoonotic Diseases Laboratory for BNV serology and molecular (polymerase chain reaction-PCR) screening tests. In the serum sample, BNV IgM and IgG antibodies (IFA method) were positive, and BNV PCR was negative. In the tests repeated eight days later, it was seen that IgM antibodies became negative and IgG antibody positivity continued. It was planned to study BNV serology in the CSF sample for laboratory confirmation of neuroinvasion, but since the patient refused lumbar puncture, BNV IgM could not be studied in the CSF sample. The patient, who was evaluated as having BNV meningitis with the serum BNV serology results, was given symptomatic pain palliation and hydration treatment. Complete regression was observed in the patient's current symptoms within a period of one month. No clinical relapse was detected in the two-year follow-up.

Discussion

In our country, WNV was first detected in August 2010 in cases that applied to Manisa State Hospital with high fever, and confusion. WNV infection causes small epidemics every summer and can cause variable, severe, and fatal clinical findings with its neuroinvasive form seen in 1–5% of cases.[18] The first WNV meningoencephalitis case from Istanbul was reported in 2017, and 7 cases were reported from Istanbul until August 2019, when the case we presented applied to our hospital.[19] Our case was presented because the patient applied to the neurology clinic with a migraine headache and reminded us of the importance of WNV as a seasonal viral meningitis-encephalitis agent in addition to routine infectious agents among secondary headache causes.

WNV meningitis is characterized by fever, headache, meningeal irritation findings, and photophobia, as in other viral meningitis. Headache alone is not a distinguishing feature and may resemble all secondary headaches. Acute/subacute onset and accompanying systemic infection findings are warning signs and should be evaluated as red flags of headache. Nonspecific cranial MRI findings that may be detected during WNV meningitis vary according to the level of meningeal involvement and parenchymal involvement and are no different from other infectious meningitis involvements.[20] In West Nile virus central nervous system involvement, increased protein titer (<150 mg/dl) in CSF, moderate pleocytosis (<500 cells/mm^3) with lymphocyte dominance, and plasmacytoid lymphocytes or large monocytic cells can be detected in cytological examination.[21,22]

The basis of the diagnostic workup is the detection of WNV IgM antibodies in serum or CSF. A positive WNV IgM result is often sufficient for diagnosis. Neutralization tests are performed in the presence of suspicion of cross-reactivity with other flavivirus infection agents.[23] If the initial antibody test is negative but clinical suspicion persists, it is recommended to repeat the antibody test after 10 days.[23] WNV IgG antibodies have no role in the diagnosis of acute WNV infection. Seroconversion from WNV IgM antibodies to WNV IgG antibodies occurs between days 4 and 10 of viremia.[24] Demonstration of antibody presence in CSF is necessary to confirm the presence of neuroinvasive disease.[24]

WNV meningitis is often a self-limiting clinical condition and has no specific treatment. Symptomatic pain palliation and hydration practices and close clinical follow-up are recommended to prevent secondary bacterial infections and complications related to hospitalization/mobilization restriction.[25] It has been reported that fatigue, forgetfulness, balance problems, and headache complaints may persist for many years in patients after the acute infection period.[26] There is no licensed vaccine formulation that can be applied to humans for protection against WNV infection.

In conclusion, WNV meningitis, like all other secondary headache etiologies, can mimic primary headache forms and cause diagnostic difficulties. In cases presenting with acute-subacute onset headache, especially in the summer season, a history of mosquito contact should be questioned in the presence of concomitant systemic infection findings. It is a clinical entity that should be kept in mind in endemic regions and certain seasons, and reference laboratories should be contacted, and diagnosis should be made with serological and molecular examination of serum and CSF samples.

Conflict-of-interest issues regarding the authorship or article: None declared.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Use of AI for Writing Assistance: Not declared.

Peer-rewiew: Externally peer-reviewed.

References

1. Smithburn KC, Hughes TP, Burke AW, Paul JH. A neurotropic virus isolated from the blood of a native of Uganda. Am J Trop Med 1940;20:471–92. [CrossRef]
2. Rossi SL, Ross TM, Evans JD. West Nile virus. Clin Lab Med 2010;30:47–65. [CrossRef]
3. Stramer SL, Fang CT, Foster GA, Wagner AG, Brodsky JP, Dodd RY. West Nile virus among blood donors in the United States, 2003 and 2004. N Engl J Med 2005;353:451–9. [CrossRef]
4. Winston DJ, Vikram HR, Rabe IB, Dhillon G, Mulligan D, Hong JC, et al. Donor-derived West Nile virus infection in solid organ transplant recipients: Report of four additional cases and review of clinical, diagnostic, and therapeutic features. Transplantation 2014;97:881–9. [CrossRef]
5. Centers for Disease Control and Prevention (CDC). Possible West Nile virus transmission to an infant through breastfeeding--Michigan, 2002. MMWR Morb Mortal Wkly Rep 2002;51:877–8.

6. Centers for Disease Control and Prevention (CDC). Intrauterine West Nile virus infection--New York, 2002. MMWR Morb Mortal Wkly Rep 2002;51:1135–6.
7. Centers for Disease Control and Prevention (CDC). Laboratory-acquired West Nile virus infections--United States, 2002. MMWR Morb Mortal Wkly Rep 2002;51:1133–5.
8. Gorsche R, Tilley P. The rash of West Nile virus infection. CMAJ 2005;172:1440. [CrossRef]
9. Weiss D, Carr D, Kellachan J, Tan C, Phillips M, Bresnitz E, et al. Clinical findings of West Nile virus infection in hospitalized patients, New York and New Jersey, 2000. Emerg Infect Dis 2001;7:654–8. [CrossRef]
10. Sejvar JJ. Clinical manifestations and outcomes of West Nile virus infection. Viruses 2014;6:606–23. [CrossRef]
11. Davis LE, DeBiasi R, Goade DE, Haaland KY, Harrington JA, Harnar JB, et al. West Nile virus neuroinvasive disease. Ann Neurol 2006;60:286–300. [CrossRef]
12. Campbell GL, Marfin AA, Lanciotti RS, Gubler DJ. West Nile virus. Lancet Infect Dis 2002;2:519–29. [CrossRef]
13. Lindsey NP, Hayes EB, Staples JE, Fischer M. West Nile virus disease in children, United States, 1999-2007. Pediatrics 2009;123:e1084–9. [CrossRef]
14. Lindsey NP, Staples JE, Lehman JA, Fischer M. Surveillance for human West Nile virus disease- United States, 1999-2008. MMWR Surveill Summ 2010;59:1–17.
15. Sejvar JJ, Haddad MB, Tierney BC, Campbell GL, Marfin AA, Van Gerpen JA, et al. Neurologic manifestations and outcome of West Nile virus infection. JAMA 2003;290:511–5. [CrossRef]
16. Debiasi RL. West nile virus neuroinvasive disease. Curr Infect Dis Rep 2011;13:350–9. [CrossRef]
17. David S, Abraham AM. Epidemiological and clinical aspects on West Nile virus, a globally emerging pathogen. Infect Dis (Lond) 2016;48:571–86. [CrossRef]
18. Tosun S. Batı Nil virüs enfeksiyonu. J Exp Clin Med [Article in Turkish] 2013;29:183–92. [CrossRef]
19. Türk Klinik Mikrobiyoloji ve İnfeksiyon Hastalıkları Derneği. Batı Nil virüsü infeksiyonları hakkında sağlık çalışanlarına yönelik bilgi notu. Available at: https://www.klimik.org.tr/2019/07/26/80897/. Accessed May 28, 2024.
20. Ali M, Safriel Y, Sohi J, Llave A, Weathers S. West Nile virus infection: MR imaging findings in the nervous system. AJNR Am J Neuroradiol 2005;26:289–97.
21. Petersen LR, Brault AC, Nasci RS. West Nile virus: Review of the literature. JAMA 2013;310:308–15. [CrossRef]
22. Procop GW, Yen-Lieberman B, Prayson RA, Gordon SM. Mollaret-like cells in patients with West Nile virus infection. Emerg Infect Dis 2004;10:753–4. [CrossRef]
23. Barzon L, Pacenti M, Ulbert S, Palù G. Latest developments and challenges in the diagnosis of human West Nile virus infection. Expert Rev Anti Infect Ther 2015;13:327–42. [CrossRef]
24. Busch MP, Kleinman SH, Tobler LH, Kamel HT, Norris PJ, Walsh I, et al. Virus and antibody dynamics in acute west Nile virus infection. J Infect Dis 2008;198:984–93. [CrossRef]
25. Murray KO, Garcia MN, Rahbar MH, Martinez D, Khuwaja SA, Arafat RR, et al. Survival analysis, long-term outcomes, and percentage of recovery up to 8 years post-infection among the Houston West Nile virus cohort. PLoS One 2014;9:e102953. [CrossRef]
26. Patnaik JL, Harmon H, Vogt RL. Follow-up of 2003 human West Nile virus infections, Denver, Colorado. Emerg Infect Dis 2006;12:1129–31. [CrossRef]