JGG 2024;72:108-110
doi: 10.36150/2499-6564-N602

Neurologic presentation of West Nile virus in patient with prostatitis and orchiepididymitis: difficult diagnosis

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West Nile Virus (WNV) infection in humans ranges from asymptomatic infection or mild febrile illness to severe neurological manifestations causing West Nile Neuroinvasive Disease (WNND) that, in some cases, may lead to death. Elderly and immunocompromised patients have a higher risk of developing WNND. We reported a case of very difficult diagnosis of WNND in an elderly patient hospitalized for fever and pollakiuria secondary to prostatitis and orchiepididymitis.

Key words: West Nile Virus, altered mental status, neurologic abnormalities, comorbidity

INTRODUCTION

Patients infected with West Nile Virus (WNV) may experience a wide range of symptoms, ranging from asymptomatic infection or mild febrile illness up to severe neurological manifestations that cause West Nile Neuroinvasive Disease (WNND). In some cases, WNND may lead to death. Elderly and immunocompromised patients have a higher risk of developing WNND. However, frail elderly patients with several comorbidities have many confounding factors that contribute to complicate and delay diagnosis. We herein report a case of difficult diagnosis of WNND in an elderly patient living at home with an active life.

CASE PRESENTATION

A 79-year-old male, suffering from benign prostatic hypertrophy and thyroid disease on home medication with tamsulosin 0,4 mg/day and levothyroxine 100 mcg/daydie, presented to the Emergency Room of Ospedale Civile SS Antonio e Biagio on 8 August 2022, complaining of fever and pollakiuria, already treated at home with ciproloxacin 500 mg p.o. b.i.d. for suspected Urinary Tract Infection (UTI). Ciprofloxacin was stopped after 2 days of treatment for skin rash. He was admitted again to the emergency room with fever (body temperature 38.9°C), confusion, ideo-motor slowdown, and mild muscle stiffness. Blood chemistry tests were performed with the following results: normal levels of procalcitonin (0.04 ng/ml, normal range (n.r.): < 0.500 ng/ml) and leukocytes, but increased levels of C-reactive protein (CRP) (1.22 mg/dl, n.r.: 0.00-0.80 mg/dl), aspartate transaminase (83 UI/L, n.r.: < 49 UI/L) and alanine transaminase (79 UI/L,

Received: December 2, 2022
Accepted: December 14, 2023
Published online: February 28, 2024

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How to cite this article: Furlani F, Marchegiani A, Campisi D, et al. Neurologic presentation of West Nile virus in patient with prostatitis and orchiepididymitis: difficult diagnosis. Journal of Gerontology andGeriatrics2024;72:108-110.https://doi.org/10.36150/2499-6564-N602

n.r. < 40 UI/L]). We excluded SARS-CoV-2 infection by SARS-CoV-2 real-time polymerase chain reaction (PCR) test/rapid antigen test. Urinalysis, urine culture and blood cultures came back negative. A head Computed Tomography (CT) showed no evidence of focal lesions, while a CT scan of the kidneys and urinary tract showed that the urinary excretory tracts were not dilated bilaterally, with no calcified stones detectable along their course. A Urology consult found an increased volume of the left epididymis. The patient was then treated with Cotrimoxazole (trimethoprim/sulfamethoxazole, TMP-SMX) 800/160 mg p.o. b.i.d. for 2 days and transferred to the Geriatrics Department of Ospedale Civile SS Antonio e Biagio. The day after after the admission, the patient experienced persistent hyperpyrexia, which was poorly responsive to antipyretics including acetaminophen and lysine acetylsalicylate, with a slight increase of inflammatory indices (PCR 3.21 mg/dl [v.n. 0.00-0.80 mg/dl]) and mild neutrophilic leukocytosis. A chest x-ray ruled out pneumonia. Cotrimoxazole was stopped and piperacillin-tazobactam 4.5 g intravenous infusion q6h for 10 days was started, with fever regression. However, neurological symptoms persisted, despite the patient was well-oriented and independent at home before the hospitalization. Finally, to explain neurological symptomes, we carried IgM tests for West Nile out on blood and urine, which were both positive.
In consideration of the persistent urinary symptoms, an echo of the testicles was performed, which confirmed left orichiepididymitis, that improved with antibiotic therapy and specific urological therapy. After 13 days of hospitalization the patient was discharged at home alert, oriented, able to cooperate, with controlled pain.

DISCUSSION

We described a clinical case of neurological manifestation of WNV infection, with a difficult diagnosis complicated by concomitant urological problems that could explain the fever and, consequently, the altered neurological status. No other cases of WNV infection were reported in the same geographical area. In this case, the persistence of neurological symptoms and the slight increase of the inflammation indices suggested to investigate WNV infection. WNV, named from the West Nile district of Uganda, is a mosquito-borne arbovirus belonging to the family *Flaviviridae* commonly found in Africa, Europe, the Middle East, North America, and western Asia and causes WNND. WNV infection epidemiology has evolved over the past few decades [1]. In humans, the clinical course of WNV infection ranges from asymptomatic infection (20%) or mild febrile illness up to severe neurological manifestations (< 1%) and even to death [2,3]. In uncomplicated WNV infection, most patients have an acute onset of fever, chills, nausea, weakness, fatigue, myalgia, arthralgia, and headache [3,4]. About 50% of patients may develop lymphadenopathy associated with a rash lasting about 7 days [1,3,5]. These symptoms are usually mild and resolve in less than a week, but prolonged fatigue is common [5]. In rare and severe cases, patients have neurological manifestations leading to WNND. WNND includes syndromes such as meningitis, encephalitis, acute flaccid paralysis (AFP)/poliomyelitis, and transverse myelitis [3,6]. In rare cases, cranial nerve paralysis, movement disorders and parkinsonian features have also been reported. The exact mechanism of neuro-invasion is unclear. Perhaps, an overactive immune response leads to increased permeability of the blood-brain barrier to the virus; however, if the immune system is delayed in eliminating the virus-infected cells, neuronal cell death may occur with severe manifestations [7]. Risk factors for encephalitis include advanced age, diabetes, alcohol abuse, and immunodepression [8]. Elderly and immunocompromised hosts are at increased risk of disseminated WNV infection and developing fatal encephalitis [7]. Among WNND cases in the United States, hospitalization rates were > 85% across all age groups, but were highest among patients aged ≥ 70 years (98%) [9]. Management for WNND is symptomatic with supportive care.
In Italy, the epidemiological surveillance of human cases of WNV is regulated by the "National Plan for the prevention, surveillance and response to Arbovirosis (PNA) 2020-2025" signed by the State, Regions and Autonomous Provinces Conference on January 15, 2020. Italy records an average of 60 locally acquired human cases each year, mainly in the north of the country. In 2018, as in others European countries [10,11], Italy experienced exceptionally early and intense WNV transmission in over 600 confirmed human infections [12]. In 2022, until August 24, the majority of cases (76%) and deaths (71%) associated with WNV infections in the EU and the European Economic Area (EEA) were reported from Italy [13]. From June 1st (beginning of surveillance) to August 24, 2022, 301 confirmed cases of WNV were reported in Italy, 160 of which showed neuro-invasive symptoms (2 in the province of Alessandria, 1 in a patient under 14 years of age and 1 in a patient over 75 years of age). The cases were all locally-acquired; 45 were identified in blood donors (2 Bologna, 1 Brescia, 1 Cremona, 1 Ferrara, 1 Lodi, 1 Mantova, 1 Milano, 3 Novara, 9 Padova, 1 Parma, 1 Pavia, 3 Piacenza, 1 Ravenna, 3 Reggio Emilia, 2 Rovigo, 8 Venezia, 2 Vercelli, 3 Verona, 1 Vicenza), 93 cases presented with fever (1 Asti, 1 Brescia, 2 Ferrara, 2 Lodi, 49 Padova, 2 Pordenone, 9 Rovigo, 6 Treviso, 1 Udine, 10 Venezia, 3 Verona, 5 Vicenza, 2 province not indicated) and 3 cases were symptomatic (2 Padova, 1 Vicenza) [14].

CONCLUSIONS

Elderly and immunocompromised patients have a higher risk of developing WNND. However, in frail elderly patients with several comorbidities, there are many confounding factors that can contribute to complicate and delay the diagnosis. We described a clinical case of WNND, the diagnosis of which was complicated by concomitant urological problems that could explain fever and, consequently, the altered neurological status. Additionally, no other cases of WNV infections were reported in the same geographical area. The persistence of neurological symptoms in a patient that was well-oriented and independent before the hospitalization, and the slight increase in inflammation indices, prompted investigations for WNV infection. We described this case to increase awareness among clinicians to include WNV in the differential diagnosis of encephalitis with fever of unknown origin, particularly in endemic areas. The reporting of this case was therefore also important for the human surveillance of WNV cases, carried out by the Istituto Superiore di Sanità and the Ministry of Health, aimed to apply specific preventive measures. At the moment, there is no vaccine for WNV infection, so prevention is essential. It is useful to reduce exposure to mosquito bites, by using repellent products or by covering the most exposed parts of the body, especially outdoors, at dawn and dusk.

Conflict of interest statement

The authors declare no conflict of interest.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contributions

FF, AM, DC, LM, AB, EP, MS: conceptualisation; FF, AM: writing-original draft preparation; FF, AB: writing-review and editing.

Ethical consideration

Not applicable.

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