West Nile virus meningitis in a patient with human immunodeficiency virus type 1 infection

D. Pilalas[1], L. Skoura[2], A. Margariti[2], D. Chatzidimitriou[2], A. Sarantopoulos[3], O. Tsachouridou[1], A. Papa[4] and S. Metallidis[1]

1) *Infectious Diseases Division, 1st Department of Internal Medicine, AHEPA University Hospital, Aristotle University Medical School, Thessaloniki, Greece,* 2) *National AIDS Reference Centre of Northern Greece—Aristotle University Medical School, Thessaloniki, Greece,* 3) *Clinical Immunology Unit, 2nd Department of Internal Medicine, Hippokration General Hospital, Aristotle University Medical School, Thessaloniki, Greece and* 4) *National Reference Laboratory for Arboviruses—Aristotle University Medical School, Thessaloniki, Greece*

Abstract

The emergence of West Nile virus lineage 2 in central Macedonia, Greece, in 2010 resulted in large outbreaks for 5 consecutive years. We report a case of viral meningitis in an individual infected with human immunodeficiency virus type 1, which preceded the recognition of the outbreak and was confirmed retrospectively as West Nile virus neuroinvasive disease.

Keywords: Case report, Greece, Human immunodeficiency virus, West Nile virus
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Corresponding author. S. Metallidis, Infectious Diseases Division, 1st Department of Internal Medicine, AHEPA University Hospital, St. Kiriakidi 1, 54636, Thessaloniki, Greece.
E-mail: metallidissimeon@yahoo.gr

West Nile virus (WNV) is a flavivirus that is transmitted in an enzootic cycle between birds and mosquitoes, while humans are dead-end hosts. Until recently, WNV lineage 1 was primarily associated with human outbreaks, whereas WNV lineage 2 was for many years restricted to Africa. Two different WNV lineage 2 strains have been detected in Europe: one, initially isolated from a goshawk in Hungary in 2004 [1] and a second one responsible for outbreaks of West Nile neuroinvasive disease (WNND) in southern Russia since 2007 [2]. WNV lineage 2 emerged in 2010 in central Macedonia, northern Greece [3], and since then outbreaks have occurred in the country for 5 consecutive years [4–6]. Most WNV-infected individuals remain asymptomatic, 25% manifest an influenza-like syndrome termed WNV fever (WNVF) and 1: 150 to 1: 250 presents as WNND [7]. Distinct patient populations are at increased risk for severe disease [8]. Immunocompromised persons, and notably transplant recipients, are of specific interest, but conclusive data are lacking [7,8]. To our knowledge, only a few cases of WNV disease in human immunodeficiency virus (HIV) -infected individuals have been reported and those are limited to the context of WNV lineage 1 epidemics [9,10]. We describe a case of WNND in an HIV-infected patient during the first year of the WNV lineage 2 epidemic in Greece.

Case report

A 35-year-old male HIV-infected patient of Greek origin was referred to the Infectious Diseases Unit with abrupt onset of severe headache and fever for 3 days before presentation. Dizziness and nausea were also present. A computed tomography scan of the head ordered by the patient's treating physician on initial outpatient evaluation was normal. Six years earlier the patient was diagnosed with asymptomatic HIV-1 disease and 1 year later he developed AIDS-related visceral Kaposi sarcoma, treated with chemotherapy. The oncological disease was in progression at the time of hospitalization. Of note, the patient had refused antiretroviral treatment. Relevant past medical history was also notable for treated asymptomatic neurosyphilis 1 year before. A recent CD4 lymphocyte count was 408 cells/μL with a viral load of 17 806 copies/mL. The patient lived in an urban area, his professional activity was indoors and he had no recent travel history nor history of exposure to animals or sick contacts.

On examination, he was afebrile and haemodynamically stable. A bilateral cervical lymphadenopathy documented in the follow up of the Kaposi sarcoma was stable. The physical examination including a detailed neurological examination was otherwise unremarkable. A lumbar puncture demonstrated a clear fluid with white blood cell count of 45 cells/μL and lymphocytic predominance, absence of red blood cells, cerebrospinal fluid

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protein concentration of 30 mg/dL and glucose of 54 mg/dL. Cerebrospinal fluid Gram, acid-fast and India ink stains were negative. The complete blood cell count was notable for mild microcytic anaemia and a depressed but within normal limits total white blood cell count (4.23×10^9/L) and lymphocyte count (1.33×10^9/L). Chest radiography was normal. On the basis of these findings, empirical treatment with ceftriaxone, acyclovir, liposomal amphotericin B and fluconazole was initiated. The clinical status of the patient improved gradually.

Laboratory tests for herpes simplex virus, varicella-zoster virus, Epstein–Barr virus, cytomegalovirus and enterovirus infection, as well as for toxoplasmosis, were performed.

Cryptococcal antigen came back negative on day 3 of hospitalization and antifungal treatment was discontinued. Syphilis serology was also negative. Blood and cerebrospinal fluid cultures were sterile and ceftriaxone was discontinued on day 4. On brain magnetic resonance imaging meningeal enhancement was present along with signs of venous sinus stasis. A computed tomography venography excluded the presence of cerebral venous sinus thrombosis. The rest of the laboratory tests were negative and the patient was discharged on day 6 with complete symptom resolution.

One week later a cluster of encephalitis cases led to the recognition of the WNV emergence in Greece [3]. This fact led us to test one of the patient's serum samples (25th day of illness) for WNV IgM and IgG antibodies using a commercial kit (WNV IgM and IgG DxSelect ELISA kit; Focus Diagnostics Inc, Cypress, CA, USA). High titres of WNV IgM and IgG antibodies were detected (indices 3.7 and 3.8, respectively, cut-off level $\geq$ 1.10); the result was confirmed by neutralization test.

Discussion

To our knowledge, 11 cases of West Nile disease in HIV-infected individuals have been reported [9,10]. All of these were reported in the USA, so were associated with WNV lineage 1 [7]. Most of the patients were male (10/11) and rather young (median 41 years, interquartile range 38–47). Two cases presented as WNV fever and were identified through an active surveillance programme [9], whereas nine patients presented WNND of which three died [9,10]. Three of the four patients who experienced the most severe disease manifestations had <200 CD4 lymphocytes/μL (CD4 lymphocyte count was not reported for the remaining patient).

We describe a case of WNND in a young antiretroviral-naive HIV-infected patient with active AIDS-related malignancy in whom the laboratory diagnosis was established after the recognition of the emergence of WNV in Greece, which was active at the time of WNV infection. The patient was diagnosed with viral meningitis and was discharged with complete symptom resolution. WNND was established retrospectively on the basis of positive cerebrospinal fluid serology results. Although WNV RNA was not detected, we consider WNV lineage 2 as the probable pathogen because the first cases of WNV disease were described in Greece in 2010 and all WNV strains isolated in the region in recurrent epidemics up to 2014 cluster with WNV lineage 2 [11].

Older patients have been associated with more severe WNV disease outcomes [8]. Nevertheless, the group of HIV patients described in the literature is rather young, providing indications that HIV disease may be an aggravating factor. Although immunosuppression has been described as a risk factor for WNND and death [8], the limited number of HIV-infected patients included in the studies precluded further analyses [12]. CD4 lymphocytes have a crucial role in the clearance of WNV infection in the central nervous system and their depletion in HIV infection may provide a plausible explanation for increased severity of the disease in HIV-infected patients, although additional factors may be in play [13].

Transparency declaration

The authors declare no conflicts of interest.

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