Optic Neuritis Complicating West Nile Virus Meningitis in a Young Adult

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Abstract

A case of West Nile virus (WNV) infection with meningitis and optic neuritis in a 28-year-old man is presented. The patient had a number of unusual clinical and laboratory findings that broadened the differential diagnosis. The emergence of WNV infection in southern Europe and North America calls for increased awareness of physicians to this clinical entity.

Infection 2003; 31: 55–56
DOI 10.1007/s15010-002-3039-4

Introduction

The West Nile virus (WNV) is the most widespread of the flaviviruses, with geographic distribution in Africa, West Asia, the Middle East and Europe. Birds are the natural hosts for the virus; it can be transmitted to humans and other animals through bites of infected mosquitoes (mainly the *Culex* species) [1]. Since discovery of the virus in the West Nile province of Uganda in 1937, many epidemics have been recorded, including the 1951 to 1954, 1980 and 1999–2000 epidemics in Israel [2, 3] and the large outbreak of 1974 in South Africa [1]. In 1996, the first major epidemic in Europe was reported in southeastern Romania, consisting of 393 cases of serologically confirmed WNV infection [4]. A similar epidemic occurred in Russia in 1999.

Case Report

A 28-year-old man was admitted in October 2000 with a 1-week history of fever up to 39 °C, headache and diffuse muscle pain. He was initially seen by his primary care practitioner who diagnosed a viral infection and prescribed amoxicillin-clavulanate. Three days before admission, the patient noted pain and blurred vision in the right eye. His medical history consisted of migraines and a family member with familial Mediterranean fever. He used to take care of cats and kittens and had contact with a pet dog owned by his mother. On admission, he was alert, oral temperature was 38 °C and his neck was stiff. Fundoscopic examination revealed a swollen, slightly pale disc on the right and a less swollen disc on the left. A concentric constriction of the visual field was noted on the right and non-specific changes on the left. A fluorescein angiography of the eyes was consistent with the diagnosis of optic neuritis. There was no evidence of lymphadenopathy or skin rash and the rest of the examination was unremarkable. Blood cell count and routine blood chemistry were normal. Examination of the CSF disclosed a normal opening pressure, 430 white blood cells with 90% lymphocytes, a low sugar of 36 mg/dl (101 mg/dl in the serum) and raised proteins at 182 mg/dl. Electroencephalography and a brain computed tomography were normal. Therapy was initiated with ceftriaxone (4 g daily) and doxycycline (200 mg daily).

The association of lymphocytic meningitis and hypoglycorrhachia suggested an "atypical" bacterial or fungal meningitis. The close contact with cats and a dog suggested *Bartonella henselae* infection or rickettsiosis, although other infections, such as leptospirosis, Q fever and cryptococcosis, had to be excluded. The presence of optic neuritis increased the likelihood of *Bartonella* infection [5], although it can be associated with a variety of other conditions, such as cryptococcosis, syphilis, tuberculosis, Q fever, toxoplasmosis, cytomegalovirus (CMV), Epstein-Barr virus (EBV) and lymphocytic choriomeningitis virus infection. Autoimmune diseases (Behcet's disease, lupus erythematosus, sarcoidosis and multiple sclerosis) should also be considered.

The results of an extensive laboratory work up were negative for *B. henselae* (serology and PCR in CSF) and *Mycobacterium tuberculosis* (PCR and culture of CSF). Cryptococcal antigen was not detected in CSF. Serologic tests for leptospirosis, brucellosis, rickettsiosis, syphilis, toxoplasmosis, HIV, CMV and EBV were negative or showed no evidence of recent disease. Antinuclear and rheumatoid factors were not detected and the angiotensin converting enzyme level was within the normal range. However, IgM against WNV was detected by IgM-capture ELISA in both serum and CSF. The assay was developed in the Israeli Central Virology Laboratory using an antigen prepared from Vero cells infected with a local isolate of WNV [2].

The patient's condition improved gradually: his temperature returned to normal (≤ 37.5 °C) on the 7th day of hospitalization, at which time the right optic disc was less swollen but paler and the left optic disc was no longer swollen and minimally pale. Repeat CSF examination on day 9 of hospitalization showed 249

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Received: February 21, 2002 • Revision accepted: September 12, 2002

white blood cells, 90% of which were lymphocytes, a glucose of 43 mg/dl and proteins of 109 mg/dl. One month later, there were signs of right optic atrophy and mild temporal pallor of the left optic disc. Visual acuity was 6/6.

Discussion

Our patient did not display many of the findings commonly seen in WNV infection [1]: he had no lymphadenopathy, maculopapular rash, sore throat, conjunctivitis, gastrointestinal symptoms or arthralgia. CNS involvement is uncommon in patients below the age of 40 years [4] and optic neuritis has been previously described in association with WNF only once [6]. Moreover, the presence of hypoglycorrhachia was suggestive of a nonviral infection. WNV infection was nevertheless considered in the differential diagnosis only because the patient's illness coincided with an outbreak of the disease in Israel [2]. It is unlikely that the positive serology was due to cross-reaction to other flaviviruses, such as yellow fever, Japanese encephalitis or tick-borne encephalitis, because the patient did not travel to endemic areas, nor did he receive any previous flavivirus vaccinations.

In endemic areas, WNV most often causes an asymptomatic infection or a mild disease, usually in children [3]. However, all the recent epidemics of WNV infection were associated with a high prevalence of neurologic involvement, mostly in the form of meningitis and meningoencephalitis, and a high mortality rate [2–4, 7, 8]. Other rare forms of neurological involvement in WNV infection include myelitis, polyradiculitis, Guillain-Barré syndrome and peripheral neuropathy. A Medline search revealed a single case of optic neuritis in a 30-year-old woman who presented with fever, a maculopapular skin rash, headache and somnolence. CSF examination showed slightly elevated levels of protein and cells. The case was documented during the 1980 epidemic in Israel [6].

The present case illustrates the importance of considering epidemiologic events in the work up of patients with possible infection. Because WNV infection is spreading over Europe [4] and has recently reached the North American continent [7, 8], physicians in these areas should be aware of this emerging disease and consider including WNV infection in the differential diagnosis of acute neurologic manifestations, including optic neuritis.

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