West Nile virus — Canada's index case

Norman L. Epstein, MD

Introduction

The first Canadian case of West Nile virus (WNV) in a human was diagnosed in Southern Ontario in the summer of 2002. WNV was first reported in New York state in 1999, with additional cases reported in 2000 and 2001, encompassing large areas of the northeastern part of the US. Public health surveillance identified the first positive case in a bird in Canada in August 2001 in Southern Ontario. As of October 2002, birds testing positive for WNV had been identified in all provinces except British Columbia.[1] There have been 66 confirmed human cases of WNV in Canada, with an additional 62 probable cases.[1] Clinicians need to be aware of the existence of WNV and be familiar with its presentation, as part of the differential diagnosis of febrile illness during the summer months. This index case illustrates the difficulty in making the diagnosis, particularly when there are distracting elements.

Case report

In mid-August 2002, a 70-year-old male came to the emergency department with complaints of fever and tremulousness. He reported consuming 4 to 5 ounces of alcohol per day, but had stopped drinking 5 days previously. He was taking ciprofloxacin for an infected stasis ulcer on his right leg. Non-bloody diarrhea began 2 days earlierl. Fever, accompanied by rigors and chills, and left lower quadrant pain started 1 day prior to presentation. He denied any recent travel. Functional inquiry was essentially negative for cough, dyspnea, dysuria, urgency, frequency, nausea, vomiting or headaches.

According to family members, he had been intermittently confused over the previous 24 hours. His medical history revealed ethanol abuse and non-insulin dependent diabetes, for which he was taking glyburide. He was a retired executive and spent most of his time golfing.

Examination revealed an older gentleman who was tremulous but had no asterixis or jaundice. His initial vital signs were: temperature 39ºC, heart rate 96 beats/min, respiratory rate 24 breaths/min, blood pressure 114/78 mm Hg, and oxygen saturation 96% on room air. He was alert, oriented to person, place and year, but unable to recall the precise date. His neck was supple, and on examination the ear, nose and throat appeared normal. Cardiovascular examination yielded normal heart sounds with a grade 2/6 systolic murmur, heard best at the left sternal border. His abdomen was distended, bowel sounds increased and he had minimal tenderness in the left lower quadrant but no costovertebral tenderness. Rectal examination revealed no blood and a slightly enlarged but non-tender prostate. There was a 2-cm stasis ulcer on his lower right leg with erythematous borders.

Laboratory results included a hemoglobin of 140 g/L, leukocyte count (WBC) 4.4×10^9/L, platelets 67×10^9/L, INR 1.4, and blood sugar level 14 mmol/L. Blood urea nitrogen, creatine and electrolyte values were normal, but amylase and lipase were slightly elevated at 120 IU/L (normal, 23–110 IU/L) and 500 IU/L (normal, 30–300 IU/L) respectively. Liver function tests revealed a γ-glutamyltransferase level of 1094 U/L, aspartate aminotransferase 117 U/L, alanine aminotransferase 95 U/L, and normal conjugated and unconjugated bilirubin levels. His urinalysis showed trace amounts of ketones, glucose and protein. Chest and abdominal x-rays were normal. Blood cultures and stool cultures (including a search for *Clostridium difficile*) were ordered. The patient was referred to the medical service with a provisional diagnosis of sepsis possibly sec-

University of Toronto, Toronto, Ont.; Credit Valley Hospital, MIssissauga, Ont.

Received: Oct. 28, 2002; final submission: Nov. 28, 2002; accepted: Dec. 2, 2002

This article has been peer reviewed.

ondary to pseudomembranous colitis or an infected stasis ulcer. The admitting internist also considered epididymitis as a source, due to a perceived tenderness of the left epididymis. Broad-spectrum antibiotics were initiated.

Preliminary 24-hour blood cultures grew *Streptococcus viridans*. Although there were no stigmata of endocarditis other than a systolic murmur, a diagnosis of endocarditis was entertained. A two-dimensional echocardiogram was unremarkable, and the positive blood culture was ultimately attributed to skin contamination.

On day 3 the patient became obtunded and bilateral myoclonic jerks developed in his upper limbs. CT of the head was normal. Lumbar puncture (LP) revealed a clear cerebrospinal fluid (CSF) with a protein level of 2.02 g/L (normal, 0.12–0.6 g/L), glucose of 5.2 mmol/L (normal, 2.2–3.9 mmol/L) and a WBC of 244×10^6/L (normal, 0–5 $\times 10^6$/L), predominantly lymphocytes. Tests for tuberculosis and *Cryptococcus* were negative, but WNV titres, ordered 2 weeks after admission because of a local cluster of human cases, returned positive.

The patient eventually developed axonal polyneuropathy, similar to Guillain–Barré syndrome (GBS), and required tracheostomy for respiratory failure. He died one month after admission after a difficult course in intensive care that involved multi-system organ failure. Autopsy confirmed that the cause of death was respiratory failure secondary to WNV.

Discussion

Epidemiology

WNV was first isolated and identified in 1937 from an infected person in the West Nile district of Uganda.[2–5] The virus is endemic in parts of Africa, Europe and the Middle East. Notable outbreaks have occurred in Israel (in 1957 and 2000), Romania (1996) and Russia (2000).[6] The first western hemisphere outbreaks occurred in New York state in 1999, 2000 and 2001, with 62, 21 and 66 confirmed cases respectively. Attacks peak from mid-August to late September, but the true disease incidence is unknown because most people suffer a mild illness and do not seek medical attention.[3–7] As of Nov. 27, 2002, there were 66 confirmed cases in Canada, 65 in Ontario and 1 in Alberta.[1]

Virology

WNV is a single-stranded RNA virus of the flavivirus family that includes dengue, hepatitis C, Japanese encephalitis, and St. Louis encephalitis, which is endemic to Missouri and Mississippi. This accounts for the cross-reactions observed in diagnostic tests.[4] The New York virus has genetically close association with the one circulating in Israel, suggesting its importation came from a bird, mosquito or human from the Middle East during an airplane flight.[8]

Ecology

Several bird species provide a reservoir for the virus during the winter months. Birds usually become infected from the bite of an infected mosquito and thus, this cycle of bird–mosquito–bird becomes apparent in spring.[7] Mosquitoes harbour the virus in their gut and transmit it to humans through bites. WNV is an arbovirus that has been detected in 29 species of North American mosquitoes.[7–9] Although most birds develop a subclinical viremia, it has 100% mortality in a few species, most notably the blue jay, raven and the American crow. Local public health agencies will usually track these deaths.[1] It is to be expected that a significant number of these birds will die concurrently with a human outbreak. These avian deaths are a public health warning that should alert physicians of risk to humans. There have also been rare reports of transmission of WNV through blood transfusions, organ transplants and breast milk.[10,11] One patient with cancer in Canada died from WNV thought to have been contracted through a blood transfusion.[1]

Clinical presentation

The incubation period is not precisely known, but it ranges from 3 to 14 days.[3,6] Most affected individuals have an acute febrile illness, often accompanied by malaise, anorexia, nausea, vomiting, headache, myalgias, morbilliform rash and lymphadenopathy. This generally lasts 3 to 6 days.[2–9] Those who develop severe neurologic disease generally present with fever, confusion, headache and profound muscle weakness.[8] Serosurveys (random tests in affected areas) conducted in New York City after an outbreak estimated that 1/157 people developed meningoencephalitis requiring hospitalization.[9] Patients suffering from hypertension, cardiac disease, vasculitis or diabetes seem particularly vulnerable, but virtually any illness can exacerbate the risk.[5–9] In the case presented, age, diabetes and alcoholism were risk factors for serious disease.

Previous cases have reported severe muscle weakness culminating in flaccid paralysis. It was first thought to be similar to the GBS, but there was sparing of the sensory network.[5,6,8] Nerve conduction studies and electromyographic studies confirmed axonal polyneuropathies. In the case presented here the patient required a tracheostomy and ventilatory support. Rare clinical manifestations of WVN include optic neuritis, myocarditis, pancreatitis and fulminant hepatitis.[5]

Diagnostics

IgM antibodies are detectable in serum and in CSF within a week of infection. Since most patients suffer a mild or subclinical illness, only those with more severe symptoms should undergo an LP.[12] CSF usually shows a pleocytosis/lymphocytosis with elevated protein. In the US, the initial IgM antibody assays are done by ELISA (enzyme-linked immunosorbent assay);[2–9] in Canada, the initial test is the hemagglutin inhibition test. Acute and convalescent sera should be taken with a minimum of 2 weeks' separation. Unfortunately, this test is non-specific because there may cross-reactivity with other arboviruses such as St. Louis encephalitis.[5–9] If preliminary testing is positive, the diagnosis is confirmed by a plaque reduction neutralization test, available at the National Microbiology Laboratory in Winnipeg. This test also requires acute and convalescent sera.[8] Unfortunately, there are no diagnostic tests available for the acute setting.

Treatment

Treatment is largely supportive, directed at the specific complications. No proven antiviral therapy is currently available, although ribavirin (a nucleoside analogue), interferon alpha, and human immunoglobulin are being studied and show promise.[8,9,12] At present, mortality is approximately 10% in those with meningoencephalitis.[3,8]

Prevention

Widespread chemical spraying for mosquitoes to eliminate the virus has to be weighed against the potential toxicity of the pesticide. Larval control in the spring through an integrated program of water management and chemical spraying should be a strong consideration.[2–9]

Public education is vital. The elderly especially should avoid areas where mosquitoes are prevalent. Limiting outside activity during peak periods and wearing long-sleeved shirts and long trousers are of paramount importance. Mosquito repellants containing DEET (N,N-diethyl-meta-toluamide) are most effective.[5–9] The patient in the case report spent a significant amount of time golfing during peak periods without appropriate protection.

Conclusion

WNV has arrived in Canada. Most victims experience mild symptoms and recover uneventfully. A small minority, particularly the elderly and those with co-morbidity, may suffer neurological illness that can result in death. Emergency physicians should be vigilant for this disease, particularly in late summer and especially if public health authorities have reported suspicious avian deaths.

Competing interests: None declared.

References

1. West Nile Virus Surveillance Information. Health Canada Online. Available: www.hc-sc.gc.ca/pphb-dgspsp/wnv-vwn/index.html (accessed 2002 Dec 2).
2. Petersen LR, Roehrig JT. West Nile Virus: a reemerging global pathogen. Emerg Infect Dis 2001;7:611-4.
3. Meek J. West Nile virus in the United States. Curr Opin Pediatr 2002;14:72-7.
4. Bernard K, Kramer L. West Nile virus activity in the United States, 2001. Viral Immunol 2001;14:319-38.
5. Roehrig JT, Layton M, Smith P, Campbell GL, Nasci, R, Lanciotti RS. The emergence of West Nile virus in North America. Curr Top Microbiol Immunol 2002;267:223-40.
6. Petersen LR, Marfin AA. West Nile virus: a primer for the clinician. Ann Intern Med 2002;137:173-9.
7. Garmendia AE, Van Kruiningen HJ, French RA. The West Nile virus: its recent emergence in North America. Microbes Infect 2001;3:223-9.
8. Campbell GL, Marfin AA, Lanciotti RS, Gubler DJ. West Nile virus. Lancet Infect Dis 2002;2:519-29.
9. Martin AA, Gubler DJ. West Nile encephalitis: an emerging disease in the United States. Clin Infect Dis 2001;33:1713-9.
10. Possible West Nile virus transmission to an infant through breast-feeding — Michigan, 2002. MMWR Morb Mortal Wkly Rep 2002;51:877-8.
11. From the Centers for Disease Control and Prevention. West Nile virus activity — United States, September 26–October 2, 2002, and investigations of West Nile virus infections in recipients of blood transfusion and organ transplantation. JAMA 2002;288:1975-6.
12. Fact sheet. West Nile virus (WNV) infection: information for clinicians. Atlanta (GA): Centers for Disease Control and Prevention (CDC). Available: www.cdc.gov/ncidod/dvbid/westnile (accessed 2003 Jan 21).

Correspondence to: Dr. Norman L. Epstein, The Credit Valley Hospital, Department of Emergency Medicine, 2200 Eglinton Ave. W, Mississauga ON L5M 2N1; 905 813-4530, 905 813-4548, norman.epstein@rogers.com.