West Nile virus disease also affects children

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Summary

Background: West Nile virus (WNV) is one of the most widely distributed arboviruses in the world. WNV disease is now an established infection in the western hemisphere. Severe disease usually occurs in the elderly and immuno-compromised individuals, but it can also affect healthy adults and children. Although WNV encephalitis has been reported in children, such reports are rare. No specific drug treatment is available at present, and vaccines are still experimental. Active bird and mosquito surveillance, and mosquito control are the most effective ways to prevent transmission of WNV.

Case report: We describe here a four-year-old boy from the Washington, D.C. area who presented with high fever, severe headache, cough, lethargy, irritability, vomiting and a stiff neck. The diagnosis of WNV was confirmed by a very strongly positive serum WNV IgM performed at the Center for Disease Control in Atlanta. He had complete recovery.

Conclusions: Pediatricians and practicing physicians in the United States should consider the diagnosis of West Nile virus disease when evaluating febrile patients in the summer months, particularly those with associated neurological and gastrointestinal symptoms. Physicians are reminded that WNV disease does affect healthy children.

Key words: West Nile virus • Encephalitis

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BACKGROUND

West Nile virus (WNV) is one of the most widely distributed arboviruses in the world. The virus was first recognized in the United States in 1999 when it caused an epidemic of encephalitis in New York City. Although WNV encephalitis has been reported in children, such reports are rare. We describe here a four-year-old boy from the Washington, D.C. area with WNV encephalitis, to serve as a reminder to pediatricians and practicing physicians that this disease does affect healthy children.

CASE REPORT

A 4-year-old, previously healthy Caucasian male, presented with fever reaching 104 degrees, severe headache, cough, lethargy, irritability, and vomiting of two days duration. He had loose stools for four days, and also developed a rash on the day of admission. While his parents did not recall any bites, his two-year-old sister was noted to have many mosquito bites. The family lives in Northern Virginia (Washington, D.C. area), but had visited South Carolina in the previous month.

Physical examination revealed a temperature of 104 degrees, weight 17 kg (75th percentile), height 107.5 cm (90th percentile), blood pressure 100/60, pulse 117 per minute, and respiratory rate 22 per minute. He was lethargic and irritable. He also had a stiff neck and an erythematous, blanching macular rash on his abdomen, lower extremities and buttocks. The rest of his physical examination was normal.

White blood cell count was 9200 with normal differential count, hemoglobin 12.2 gm/dL, hematocrit 35.5%, sedimentation rate 68 mm/hour, and serum electrolytes were normal. Urinalysis was normal with a specific gravity of 1.020. Cerebrospinal fluid revealed 603 white blood cells with 81% neutrophils and 19% lymphocytes, 9 red blood cells, protein 98 mg/dL, and glucose 67 mg/dL. Blood, cerebrospinal fluid and urine cultures were all negative. Serum and CSF Lyme and enterovirus titers / PCR were negative. Rectal swab for enteroviral culture was also negative. The diagnosis of WNV was confirmed by a very strongly positive serum WNV IgM performed at the Center for Disease Control in Atlanta; no further tests were deemed necessary for the diagnosis of WNV disease.

The patient had high fever for five days with symptoms of encephalitis including lethargy, delirium, and severe headache. He had no muscle weakness or neuropathy. He received supportive therapy and was discharged on the seventh hospital day with a normal physical examination and no evidence of neurological deficit.

DISCUSSION

West Nile virus (WNV) is a human neuropathogen, mosquito-borne flavivirus [1-3]. It is one of the most widely distributed arboviruses in the world. In Madagascar, 29% of 3177 children between the ages of five and 20 years had positive IgG antibodies to WNV, with increase in prevalence with age [4]. The virus was first isolated in 1937 in Uganda [5], and was first recognized in the US in New York City in 1999, most likely introduced from the Mediterranean region [1,2]. WNV was confirmed in 62 cases, including seven fatalities, and was subsequently isolated from mosquitoes and dead birds in New York, Connecticut, New Jersey and Maryland [6]. In 2002, 4156 cases of WNV infections including 284 fatalities were confirmed from 40 states. Nebraska (1108), Illinois (884), and Michigan (614) had the most cases. The state of Virginia reported only 29 cases with two deaths. During the first ten months of 2003, 6657 human cases were reported from 45 states including 139 deaths. Colorado had the most cases (2171) followed by Ohio (441 cases), suggesting changes in the epidemiology of WNV within the US from one summer to the next. Only 12 cases with one death were reported in Virginia [7]. Encephalitis from WNV has been reported only from India, Israel, Pakistan, Romania, Russia and the US [8].

The enzootic WNV cycle is maintained predominantly by virus transmission between ornithophilic mosquitoes of the genus Culex and wild birds, although the virus can infect a variety of vertebrates [9]. In the US mosquitoes of the C. pipiens variety are the major vectors, although WNV has been also isolated from the Aedes vexans and Anopheles mosquitoes. A total of 2,642 WNV-positive mosquito pools have been so far reported in 32 states and New York City [10]. Extrinsic and intrinsic factors, including a high density of avian hosts in proximity to mosquito vectors and favorable environmental factors help circulate WNV [8]. Virus transmission in the US has been limited exclusively to the summer and early autumn months when mosquitoes are active suggesting that alternative vectors probably do not play a major role in the transmission of the virus. Birds are the predominant vertebrate host worldwide. Mammals are incidental hosts.

In addition to humans, WNV may affect horses, dogs, and other unidentified animal species.

The most common route of human infection is through the bite of an infected mosquito. The virus can also spread through blood transfusions, organ transplantation, breast feeding and transplacentally [3]. The incubation period for WNV infection is 5 to 15 days,
the viremia peaks between days 4 and 8, and the mortality is about 5-10%, usually in elderly patients [11,12]. Most human infections are unapparent. About 20% of people infected with the virus develop WNV disease with symptoms including fever, headache, and body aches lasting three to six days [13]. One in 150 individuals infected with the virus will develop severe infection with encephalitis or meningitis presenting with headache, high fever, neck stiffness, stupor, disorientation, coma, tremors, convulsions, arthralgias, muscle weakness and paralysis [13]. About half of patients develop a non-pruritic, maculopapular rash on the trunk and arms lasting one week. Lymphadenopathy is also common, and myoclonus and rhabdomyolysis may also occur. Severe disease with encephalitis, coma and possibly death usually occurs in the elderly and immunocompromised individuals. Most of these patients present with a febrile illness associated with meningeal signs, altered mental status or both. Neurological and gastrointestinal symptoms usually predominate, occurring in 84% and 58%, respectively. The most common clinical findings include fever in 90% of cases, fatigue 63%, altered mental status 58%, headache 58%, vomiting 42%, nausea 42%, myalgia 42%, stiff neck 32%, photophobia 32%, abdominal pain 21%, motor weakness, cough, diarrhea, seizures 16% each, arthralgia, cranial nerve palsy and shortness of breath 11% each [14]. Healthy individuals are at lower risk of getting seriously sick from WNV, although they probably have the same risk of acquiring the virus. A small number of people may have flu-like symptoms but they usually recover quickly.

Although WNV encephalitis has been reported in children, such reports are rare. Among the 4,156 cases reported by CDC in the US in 2002, six cases were below the age of one year, five cases between the ages of two and five, and 22 cases between the ages of six and 12. The ages of affected patients were from three months to 97 years, with a median age of 48 years [10]. In one study, WNV was isolated from the brains of three children, age four, six and 14 years that died of encephalitis [14]. Most infants and young children infected with WNV are asymptomatic or develop mild disease as well; serious neurological disease is uncommon [11,15]. The child in this report, who is probably the youngest patient reported in the state of Virginia, had an illness consistent with viral encephalitis with complete recovery.

Transplacental transmission in humans has been reported in one infant [13]. The infant was born with chorioretinitis and cerebral abnormalities, but causal relationship with WNV is not definite. Screening of asymptomatic pregnant women or newborns is not indicated, since there is no treatment for this condition at the present time. The Center for Disease Control has initiated a voluntary registry to monitor birth outcomes among WNV-infected women. WNV has also been reported in one instance to pass from an infected mother to her infant through breast milk [16]. The infant had the virus, but did not have symptoms of the disease. The degree to which the virus is transmitted in the milk and the extent to which breast-fed infants become infected are unknown. The CDC and American Academy of Pediatrics advise no change in the current breast-feeding recommendations.

Routine laboratory studies for WNV are non-specific, or may show leukopenia. With CNS involvement, cerebrospinal fluid findings are consistent with a non-bacterial inflammatory process namely, pleocytosis and elevated protein. Diagnosis is established by IgM and IgG enzyme-linked immunosorbent assays (ELISAs) for WNV, and/or by virus isolation and identification. Viral RNA may also be detected by transcriptase polymerase chain reaction (RT-PCR). WNV is confirmed by either: 1) a four-fold rise in serum antibody titer in paired CSF or serum samples; 2) isolation of virus from blood or any body tissue or fluid, or demonstration of viral antigen or genomic sequences in those sites; 3) presence of both WNV-specific IgM and IgG antibodies in a single serum specimen; 4) IgM antibody in the CSF [15]. Specific IgM in the serum of our patient was so elevated that CDC confirmed the diagnosis without further tests.

At present, there is no specific drug treatment or vaccination against the disease. In vitro studies have shown activity of ribavirin, interferon alfa, and pyrazidine nucleosides against WNV, but clinical data does not support their use at present [3]. Prophylactic and therapeutic efficacy of intravenous human immunoglobulin was shown in mice, but efficacy in humans is only anecdotal [17]. Two candidate vaccines against WNV are ready to be tested in phase 1 human trials [3]. One vaccine (Acambis, Cambridge, Mass) is based on the yellow fever vaccine; the other vaccine which was developed by the National Institute of Allergy and Infectious Diseases uses the dengue virus.

**Conclusions**

WNV is now an established infection in the western hemisphere. The disease may also affect healthy children. Pediatricians and practicing physicians in the US should consider the diagnosis of WNV disease when evaluating febrile patients in the summer months, particularly those with associated neurological and gastrointestinal symptoms. Active bird and
mosquito surveillance to detect the presence and monitor WNV activity and mosquito control by larval source reduction are the most effective ways to prevent transmission of WNV [18]. In addition to vector control, personal protection including the use of insect repellents is also important. Public education about modes of transmission and reducing risk for exposure is critical in any prevention and control program.

REFERENCES


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