CASE REPORT

Altered mental status and fever

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SUMMARY

West Nile virus (WNV) is still the most common cause of neuroinvasive arboviral disease in the USA with a case death of 10–30%. We are reporting a case of a 61-year-old woman with a history of Crohn's disease, fibromyalgia treated with chronic steroid therapy that presented with a day history of fever, confusion and lethargy. She had a lumbar puncture which was notable for lymphocytosis and was positive for WNV. She initially was treated with broad-spectrum antibiotics, which were subsequently discontinued when the diagnosis of WNV neuroinvasive disease (WNND) was made. A high index of suspicion is needed to diagnose WNND, and this should be suspected in elderly immunocompromised patient presenting with altered mental status and lumbar puncture suggestive of aseptic meningitis. Recent study has showed that there is genetic variation in the interferon response pathway which is associated with both risk for symptomatic WNV infection and disease progression.

BACKGROUND

West Nile virus (WNV) is an arthropod-borne flavivirus transmitted to humans mostly by mosquitoes. Clinical presentation can range from asymptomatic infection to neuroinvasive disease. We report the first case of WNV infection in Essex County, Massachusetts that may suggest an urban spread of the virus.

WNV infection is endemic in East Africa and the Middle East. In the USA, the first report of WNV infection appeared in 1999, when an outbreak occurred in New York. The disease has since spread across the USA and established endemicity. In 2011, the Center for Disease Control reported a cumulative total of 1021 human cases of WNV disease from 40 states and Washington, DC. Of these 62% were classified as neuroinvasive disease, which is a 62% increase from that reported in 2009.¹ This suggests an evolving nature of this disease and the need for continuous education of physicians and public about this unique flavivirus.

CASE PRESENTATION

A 60-year-old woman with a history of Crohn's disease maintained on chronic steroids presented to our emergency room (ER) in October 2011 with a 1-day history of confusion. As reported by family, 2 days prior to admission the patient had developed severe exhaustion and took to her bed for an entire day. By next day, she was unable to recognise family members. This worried them and they brought her to the hospital.

INVESTIGATIONS

A lumbar puncture revealed a white cell count of 84 cells/mm³ (reference range: 0–5/mm³) with 21% neutrophils (reference range: 0%), 53% lymphocytes (reference range: 40–80%) and 26% monocytes (reference range: 15–45%). There were 27 red blood cells/mm³. Opening pressure of 16 mm Hg, glucose and protein levels were in normal range. Gram stain of the cerebrospinal fluid (CSF) was unrevealing. Serological testing for Lyme's disease, PCR for herpes simplex virus and cryptococcal antigen was negative in the CSF. Microscopically, reactive lymphocytes were noted in the CSF. MRI of the head was normal for her age. An EEG showed no epileptiform discharges. Empiric treatment was initiated with intravenous ceftriaxone, vancomycin, ampicillin and acyclovir.

By hospital day 5, PCR for WNV was noted to be positive in the CSF at the Massachusetts State Laboratory. The patient was hence, diagnosed with WNV meningitis.

OUTCOME AND FOLLOW-UP

All antibiotics were discontinued. Full supportive care with fluid management, nutrition, glycaemic control and electrolyte repletion were continued. Over the course of the next 5 days, the patient's mental status cleared and she became more conversant. She was transferred to a rehabilitation facility by hospital day 6 and was successfully discharged home 3 days thereafter. The patient recovered fully from the disease and has had no neurological sequelae till 6 months postdischarge.

DISCUSSION

WNV is an arthropod-borne flavivirus which is transmitted to humans mostly from mosquitoes (*Culex* genus especially *C pipiens* in the USA) and tick bites from feeding on birds (most commonly crows, jays and house sparrows) with humans and horses as incidental host.² WNV was first isolated from a febrile Ugandan woman in 1937.³ Since its isolation, it caused an epidemic outbreak in New York, the first in North America with 62 cases and 7 deaths. Other epidemics include Romania in 1996; Russia in 1999; Israel in 1981, 1999 and 2000; Hungary and Italy in 2009 and finally Greece in 2010.^{4 5}

Infected individuals usually become symptomatic within 2–14 days after inoculation. Clinical presentation of WNV illness ranges from asymptomatic infection to mild afebrile syndrome and neuroinvasive disease, defined by an evidence of WNV infection with any combination of meningitis, encephalitis or acute flaccid paralysis.⁶ Neurological disease predominantly affects people between the

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age of 45 and 55 years with death being highest in those over 65.⁷ Also, immunocompromised patients have a higher tendency of developing neuroinvasive disease and have a more severe disease presentation than the immunocompetent. The infection peaks in the month of July–September.

There is still no specific treatment with proven efficacy for the treatment of WNV infection. There is, however, an approved vaccine for horses. Treatment is typically supportive in nature. Investigative agents that have been tried include ribavirin, acyclovir, interferon, immunoglobulin and monoclonal antibodies, but none of them have been shown to be useful.² WNV disease is a notifiable disease to local public health facility and this can be done via the ArboNET system.

In the case presented above, our patient's demographic fits into the age range of patients mostly affected with WNV infection. She is on chronic steroid therapy, making her immunosuppressed, which is another criterion for susceptibility of having a severe infection. Her clinical presentation is highly suggestive for meningitis with low-grade fever, confusion and lethargy. She presented to our ER in October 2011, which is close to the WNV infection peak season. She lives in an endemic area with tick bites; one of the vectors for WNV.

Our patient had a short duration of clinical course with complete resolution of symptoms without development of any sequelae. A recent research on the host genetic risk factors for infection and disease progression in WNV infection showed that single-nucleotide polymorphisms (SNPs) in *IRF3* and *MXI* were associated with symptomatic WNV infection and a single SNP in the 2'–5' oligoadenylate synthase *OAS1* was associated with increase risk of WNV encephalitis and paralysis.⁸ CCR5Δ32 or its polymorphism in 5'cis regulatory region of CCR5 did not show any significant association with WNV infection in recent studies in contrary to any previous literature. This suggests that there are genetic variations in the interferon response pathway responsible for degradation of viral ribonucleoprotein. The patient was immunosuppressed and falls in the age group associated with more severe and prolonged clinical presentation, but had a complete resolution of her symptoms also supports this.

The patient presented 2 days after the state officials confirmed that a mosquito captured in Peabody, Massachusetts was tested positive for WNV. She is the fourth case of WNV disease reported in Massachusetts for 2011. Since 2001, there have been 68 cases of WNV infection reported in the State of Massachusetts. This case also suggests the spread of WNV to urban centres. Gujral *et al*⁹ reported that personal protective practices influence the rate of infection from WNV infection in

addition to implementation of comprehensive community mosquito control measures. There is a need for ongoing surveillance in communities to guide the efforts in mosquito control based on variables of habitat type, precipitation and temperature given the changing trends.¹⁰

Learning points

- ▶ Consider West Nile virus neuroinvasive disease in the broad differential diagnosis of altered mental status and fever.
- ▶ A review of the natural history, epidemiology and clinical presentation of West Nile virus neuroinvasive disease.
- ▶ Recent studies do not corroborate the popular belief that there is a genetic risk factor involved in disease progression and severity.
- ▶ The need for ongoing surveillance in communities to guide the efforts in mosquito control as this disease can become an epidemic.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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