A First Clinical Case Report of West-Nile Viral Meningoencephalitis Complicated with Acute Pancreatitis in North America

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Abstract

Most affected humans with west-nile virus (WNV), a mosquito-borne virus of the flaviviridae family, remain asymptomatic, while a minority may develop neurological manifestation such as meningitis, encephalitis or a flaccid paralysis. Gastro-intestinal symptoms such as anorexia and abdominal pain are less common, whereas full blown symptomatic acute pancreatitis has only been described twice in the literature. These cases occurred in the Netherlands and in Israel where WNV is fairly endemic. We report the first clinical case in North America of a previously healthy 52 year old man who developed full blown WNV meningo-encephalitis with concurrent acute pancreatitis. Acute WN viral meningo-encephalitis was confirmed by a lumbar puncture, while other causes of meningitis/encephalitis were excluded. Acute WNV pancreatitis was diagnosed clinically as well as by abnormal serological markers including elevated amylase and lipase levels. The patient was treated conservatively, and his symptoms gradually improved until full recovery, requiring a total of three weeks from onset. WNV and its complications are reviewed, in addition to a description of prior cases of pancreatitis associated with WNV infection.

Keywords: West Nile virus; Infection; Meningitis; Encephalitis; Meningoencephalitis; Acute pancreatitis; Mosquitos

Abbreviations WNV: West-Nile Virus; CSF: Cerebrospinal Fluid; CBC: Complete Blood Count; NPO: Nothing Per Month; CT: Computed Tomography

Introduction

WNV is a mosquito-borne virus of the flaviviridae family. It is indigenous to Africa, Asia, Europe and Australia [1], and has been associated with several outbreaks in Israel [2,3]. WNV was virtually unknown to North America until 1999, when it made a first appearance during an epidemic of meningo-encephalitis in Queens, New York, NY [1]. From the period between 1999 and 2004, there have then been over 7,000 reported cases of neuro-invasive WNV induced encephalitis in the United States [4]. The neurological manifestations of WNV infection can range from meningitis, encephalitis and cranial nerve dysfunction to acute flaccid paralysis and motor neuron disease [5-10]. Most cases of WNV infections are asymptomatic. The incubation period is typically 2 to 14 days [11,12]. There are no specific symptoms that typify WNV infections. Clinically, they may present with symptoms similar to aseptic viral meningitis, usually with fever, headache, and other non-specific symptoms. These typically carry a low associated mortality [13]. Some patients may present with a more abrupt onset of encephalitis with altered mental status, vomiting, severe headaches, accompanied by a high grade fever. In about 15% of cases, cerebral dysfunction may progress to coma, with accompanying abnormalities such as diffuse muscle weakness, flaccid paralysis, and respiratory failure [13-15].

The diagnosis of WNV infection is made by obtaining serum and CSF antibodies. False positive serological results may occur in patients who have recently been vaccinated against yellow fever, Japanese encephalitis, or those who had recently been affected with dengue or St-Louis encephalitis. Rarely, WNV has been isolated from other solid organs such as the liver, spleen, lungs and pancreas [16]. Clinical management of WNV infections is generally supportive. All patients with suspected WNV meningitis or meningo-encephalitis should be admitted to an inpatient hospital setting for further observation and supportive care, while ruling out other CNS infection that may be subject to more directed therapy [1]. In this report, we describe a previously healthy man with WNV meningoencephalitis and concurrent acute pancreatitis. To the best of our knowledge, this is the first described case of WNV meningo-encephalitis with concurrent acute clinical and chemical pancreatitis in North America.

Case Report

A 52 year old man with no prior medical history presented to our center with headache, fever, lethargy and general malaise of about a one-week duration. He denied recent contact with sick individuals, had not sought medical attention, and was not on any home medications. He denied alcohol consumption, smoking and illicit drug use. He also denied any awareness of being recently bitten by arthropods, ticks or animals.

On admission, he was noted to be febrile, lethargic and in moderate distress secondary to abdominal pain (Table 1). His head, eyes, ears, nose, throat, neck, pulmonary and cardiac examinations were unremarkable. His abdominal exam was significant for moderate yet poorly localized tenderness throughout his abdomen, which he rated as 7/10, along with hypoactive bowel sounds and mild guarding without evidence of rebound. His liver and spleen were not palpable.

Date:	Day 1	Day 6

WBC	4.21 k (range: 3.2 K-10K)	4.45
Platelet	327 k(range: 150 K-450 K)	190
Total bilirubin	0.8 (range 0.4 mg/dL -1.5 mg/dL)	0.5
AST	38 (range 15 U/L -41 U/L)	55
ALT	20 (range 14 U/L -54 U/L)	58
Alkaline Phosphatase	65 (range 24 U/L -110 U/L)	59
Lipase	693 (range 17 U/L -50 U/L)	560
Amylase	499 (range 15 U/L -50 U/L)	227
Triglyceride	161 (range < 150 mg/dL)	66
HDL	44	
	Range: < 40 mg/dL LOW	
	≥60 mg/dL High (Negative Risk Factor)	
LDL	61	
	Range: <100 mg/dL Optimal	
	100 mg/dL -129 mg/dL Near Optimal/Above Optimal	
	130 mg/dL -159 mg/dL Borderline High	
	160 mg/dL -189 mg/dL High	
	≥190 mg/dL Very high)	
Calcium (calculated)	10 (range: 8.7 mg/dL -10.2 mg/dL)	10.1
Glucose	110 (range: 70 mg/dL -140 mg/dL)	102

Table 1: Laboratory results of the Patient.

On neurological examination, he was oriented to place, person and time, but required constant stimulation to remain awake and was notable for mild photophobia No nuchal rigidity, Kernig or Brudzinski's signs were noted. His strength was intact and sensory examination was unremarkable. His gait examination was deferred given general weakness, and lethargy. The remainder of his neurological examination was unremarkable.

After a normal head CT without contrast and subsequent MRI of the brain with and without gadolinium, lumbar puncture findings including cerebrospinal fluid pleocytosis, elevated protein and positive WNV IgM antibody confirmed the diagnosis of WNV meningo-encephalitis. The results of the cerebrospinal fluid (CSF) analysis and microbial work-up are detailed in table 2 and table 3 respectively.

Additional extensive infectious work-up including work up for mosquito borne viruses and other potential infectious etiologies was negative (Tables 3 and 4 respectively). Serum laboratory work-up included CBC, liver function tests, pancreatic function tests, lipid profile, electrolytes, and urinalysis. This revealed elevated levels of amylase and lipase. Ultrasound of the pancreas, liver, and gallbladder revealed mild dilation of the common bile duct without evidence of choledolithiasis, pancreatic ductal dilatation or peripancreatic fluid. No pancreatic calcifications or pseudocysts were noted. The liver appeared of normal echogenicity without intrahepatic lesions. Based upon our work-up, the patient was diagnosed with WNV meningo-encephalitis with concurrent pancreatitis.

In the hospital, he received aggressive intravenous hydration with normal saline, made NPO, and treated with Ondansetron for nausea, oxycodone for abdominal pain, and pantoprazole for gastrointestinal prophylaxis.

This patient's hospitalization course significant for persistent debilitating headaches, associated with nausea, vertigo and dizziness. His abdominal pain persisted for the first 6 days following his admission, with several failed attempts at advancing his diet from clear liquids to regular texture. After one week of hospitalization, the patient began to gradually improve, with decreased requirement for narcotics and anti-emetics. By day 9 post-admission, he was able to tolerate a regular diet. He was evaluated by physical therapy the following day, who noted that he had made a remarkable recovery and may be safe to be discharged home. He was eventually discharged home approximately 2 weeks following his admission. This patient's symptoms fully resolved approximately 3 weeks from their onset.

CSF analysis (Day1)	
WBC	1243 (range 0 cubic mm-5 cubic mm)
Neutrophils	0.74
Lymphocytes	0.21
Monocytes	0.05
Glucose	50 mg/dL (range 45 mg/dL-80 mg/dL)
RBC	0 (range: negative)
Total protein	196.2 mg/dL (range: 20 mg/dL-40 mg/dL)
Apparence	Hazy
Microscopy	No bacteria seen, polymorpho. Neutrophils, and mononuclear cells present

Table 2: Cerebrospinal fluid analysis

Discussion

The primary vector for the transmission of WNV is the Culex mosquitos' genus, but other genera have also been implicated [6]. In Europe, the principal vectors are *C. pipiens, C. univittatus., and C. antennatus, and in India, C. vishnui* [7,8]. In Northern America, more than 59 different mosquito species with diverse ecology and behavior have been implicated, but only approximately 10 of these are considered to be the principal WNV vectors (CDC, unpublished data) [6,8,9]. In 2001, 57% of these positive mosquito pools in the Northeastern US were *C.pipiens* or the Northern house mosquito, which feeds primarily on birds and mammals' blood [4,6]. Although infected mosquito bites are the primary form of transmission, non-mosquito borne WNV transmission has also been documented in the literature [4]. By 2002, four novel routes of WNV transmission to human had been identified: blood transfusion, organ-transplant recipient, trans-placental infection, and breast-feeding [28]. The patient described in this case lived in Northern New England, an area not known to be endemic for WNV. This case illustrates the first clinical presentation of WNV meningo-encephalitis with concomitant pancreatitis in North America. In our patient, this was confirmed by history, physical examination, and serological markers.

Since IgM does not cross the blood-brain barrier, detection of CSF WNV IgM strongly suggests CNS involvement with WNV [25]. IgG titers usually become detectable within 7-21 days in patient presenting with acute WNV infections [26]. We excluded other mosquito-borne virus and other causes of pancreatitis, such as alcohol, gallstone, medication, hyperkalemia, and spider bites by history, physical examination, imaging and laboratory investigations.

It is important to note that acute pancreatitis was not detected by abdominal imaging. Trans abdominal ultrasonography has only a limited role when diagnosing acute pancreatitis due to operator dependence, difficulty with pancreatic necrosis detection, and restricted visualization secondary to abdominal pain or intra-abdominal gas.

Test:	Source	Result
Ehrlichia chaffeensis Antibody	CSF	IgG Antibody < 1:64 (Ref:<1:64)
Anaplasma phagocytophilum	CSF	Antibody titer < 1:64 (Ref: < 1:64)
Rickettsia	CSF	Antibody panel
		< 1:64 IgG (Ref: < 1.64)
Typhus fever group	CSF	Antibody Panel: < 1:64 IgG
		Antibody Panel: < 1:64 IgM
		(Ref < 1.64)
Enterovirus	CSF	No RNA detected by PCR
West-Nile virus antibody	CSF	Negative for WNV IgG
		Positive for WNV Ab IgM (Ref: Negative)
Bacterial culture	CSF	Negative after 72 hr
Herpes simplex type I, or type II	CSF	Negative by PCR detection

Bacterial culture	Blood	No growth
Bacterial culture	Urine	< 10,000 CFU/ml mixed gram positive organisms
HIV antibody	Blood	Negative
Lyme antibody	Blood	Negative
Tuberculosis quantiferon B	Blood	Negative TB by QuantiFERON, B
		TB Antigen value: 0.02I U/mL (Ref: < 0.3I U/mL)
West Nile virus, Serum	Blood	Positive for IgG antibody
		Positive for IgM antibody
Brucella Antibody	Blood	< 1:20 (negative reference)
Syphilis serology	Blood	Nonreactive (ref: non-reactive)

Table 3: Microbiology work-up during admission

This case illustrates a very rare complication of WNV infection. The association of fever, headache, lethargy, persistent vertigo, dizziness and the CSF findings, along with abdominal pain, nausea, anorexia and elevated serum lipase/amylase levels in our patient's suggest that the etiology of pancreatitis was induced by WNV. This emulates the neural-infection with enterovirus or mumps complicated by acute pancreatitis.

Test:	Source	Result:
California/Lacrosse Encephalitis Profile	Blood	Negative
St-Louis Encephalitis	Blood	Negative
Western Equine Encephalitis	Blood	Negative
West Nile virus, Serum	Blood	Positive for IgG antibody
		Positive for IgM antibody
Eastern Equine Encephalitis	Blood	Negative

Table 4: Mosquito-Borne Panel

Due to the paucity of reports of patients with acute WNV pancreatitis, it is difficult to identify patients at risk of developing WNV pancreatitis during the acute phase of WNV neural infection. Our case illustrates that, in WNV encephalitis patients presenting with abdominal pain and vomiting, pancreatitis related to their infection, rather than just a separate entity, should be considered. Although treatment remains supportive at this point, the patient may benefit from a multidisciplinary approach.

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