



A Diabetic Male with AMS, Fever, and Hallucinations

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In August 2001, Chicago Fire Department ALS responded to the home of a 51-year-old male with AMS. EMS reported fever and hallucinations and that the patient was hot, flushed, diaphoretic, O x 1. Pre-hospital vitals were 140/P, HR 120, RR 30, glucose 300.

The patient presented to the ED non-verbal, moaning, with a temperature of 102.2 °F. He responded to verbal stimuli, moaning “Help me.” Per family, the patient had a history of DM, HTN, and psoriasis, and no history of drugs or EtOH. Family also stated that he had had a high temp and flu-like symptoms with nausea, vomiting, and diarrhea for 2 days. The patient had been taking NSAIDs, but had refused his PMD recommendation for hospital admission.

Upon examination, the patient was agitated, confused, combative, and diaphoretic. Pupils were 2-3 mm, non-reactive. The patient’s airway was adequately contd. His neck was supple without thyromegaly. The patient was noted to be tachypnic with clear lungs. Tachycardia was noted. No abdominal tenderness was noted. On neurologic exam, there was no focal motor or sensory abnormality. A tremor and intermittent nystagmus on central gaze was noted. The skin showed old psoriasis with no new rash.

What are the next steps in the diagnosis and management of this patient?

Key Clinical Questions

How do patients with encephalitis present acutely?

What is the differential diagnosis of patients with altered mental status and fever?

What are the common etiologies of encephalitis?

What is acute disseminated encephalomyelitis?

What are the unique aspects of encephalitis caused by West Nile virus?

Key Learning Points

- The differential diagnosis of fever and altered mental status includes encephalitis or meningitis (and other related CNS infections), as well as sepsis with marked hypotension and/or dehydration.
- The three main viral encephalitis etiologies include the arboviruses, the herpes simplex viruses, and the measles virus.
- The Arboviruses are transmitted by mosquitoes, causing encephalitis, and ticks which can cause Rocky Mountain Spotted Fever and encephalitis.
- Up to one third of encephalitis are caused by Acute Disseminated Encephalomyelitis, which is an autoimmune disease that normally follows a viral illness by several weeks.
- Arbovirus encephalitis often will cause a morbilliform or maculopapular rash, as well as significant loss of muscle tone and weakness.
- Viral encephalitis is diagnosed by obtaining both acute and convalescent serum Ab titres. Direct testing of serum and CSF with viral cultures or PCR will also detect a viral cause of encephalitis. Because IgM does not cross the BBB, the presence of Ab titres in the CSF is diagnostic for West Nile Virus infection.
- Treatment of viral encephalitis includes the use of ceftriaxone for presumed bacterial meningitis and the use of acyclovir for presumed herpes encephalitis. If recent travel to endemic areas has occurred, treatment for tick borne illness such as RSMF must also occur.
- In patients who contract West Nile virus, 1 in 5 will develop a viral illness, and 1 in 150 will develop encephalitis.
- The diagnosis of West Nile virus encephalitis includes CSF pleocytosis, leukocytosis, and MRI leptomeningeal or periventricular inflammation.

- Mortality from West Nile virus encephalitis can be as high as 15% overall, and is twice as high in high-risk populations (older patients and those with immunocompromise).
- Prevention of West Nile virus is through eradication of the mosquito vector and prevention of mosquito bites. Adults should use 50% DEET, and children 10% DEET.

References

1. Rupprecht CE, Hanlon CA, Hemachudha T. Rabies re-examined. *Lancet Infect Dis.* 2002 Jun;2(6):327-43.
2. Whitley RJ, Gnann JW. Viral encephalitis: familiar infections and emerging pathogens. *Lancet.* 2002 Feb 9;359(9305):507-13.
3. Dumpis U, Crook D, Oksi J. Tick-borne encephalitis. *Clin Infect Dis.* 1999 Apr;28(4):882-90.
4. Solomon T, Mallewa M. Dengue and other emerging flaviviruses. *J Infect.* 2001 Feb;42(2):104-15.
5. Thompson MJ. Immunizations for international travel. *Prim Care.* 2002 Dec;29(4):787-814.
6. Gnann JW Jr. Varicella-zoster virus: atypical presentations and unusual complications. *J Infect Dis.* 2002 Oct 15;186 Suppl 1:S91-8.
7. Shoji H, Azuma K, Nishimura Y, Fujimoto H, Sugita Y, Eizuru Y. Acute viral encephalitis: the recent progress. *Intern Med.* 2002 Jun;41(6):420-8.
8. Bronze MS, Huycke MM, Machado LJ, Voskuhl GW, Greenfield RA. Viral agents as biological weapons and agents of bioterrorism. *Am J Med Sci.* 2002 Jun;323(6):316-25.
9. Straight TM, Lazarus AA, Decker CF. Defending against viruses in biowarfare. How to respond to smallpox, encephalitides, hemorrhagic fevers.

Patient Outcome

The patient was treated with acyclovir and ceftriaxone in the ED. The patient required ETI for airway management because of altered mental status. The LP demonstrated 20 RBCs, 20 WBCs, a glucose of 137 and a protein of 32. The CT was negative and the EEG showed diffuse slowing.

Chlamydia pneumonia, generalized seizures, and a sub-endocardial wall MI complicated the patient's hospital course. On day 10, the patient continued to spike a fever and developed a morbilliform rash. On day 11, the CSF cultures were positive for West Nile Arbovirus.

On day 26, the patient was discharged to a rehab facility. He was able to speak, walk and was functioning adequately. The patient was incidentally seen in the ED several months later for an unrelated complaint and was doing well.

Annotated Bibliography

1. Whitley RJ, Alford CA, Hirsch MS, et al. Vidarabine versus acyclovir therapy in herpes simplex encephalitis. N Engl J Med. 1986 Jan 16;314(3):144-9.

This article is a randomized trial that compares the use of vidarabine to acyclovir for the treatment of presumed herpes simplex encephalitis. Nearly 3x as many patients who received acyclovir (38 vs. 14%) were able to function normally at 6 months.

2. Schmutzhard E. Viral infections of the CNS with special emphasis on herpes simplex infections. J Neurol. 2001 Jun;248(6):469-77.

This article is a good review of viral CNS infections. It focuses on the diagnosis and treatment of Herpes Simplex viral infection of the CNS.

3. Mamidi A, DeSimone JA, Pomerantz RJ. Central nervous system infections in individuals with HIV-1 infection. J Neurovirol. 2002 Jun;8(3):158-67.

This article reviews CNS infections in patients who are HIV positive. It includes the diseases Toxoplasmosis encephalitis, Cryptococcal meningitis, CNS lymphoma, multi-focal leukoencephalopathy, and CMV infection.

4. Redington JJ, Tyler KL. Viral infections of the nervous system, 2002: update on diagnosis and treatment. Arch Neurol. 2002 May;59(5):712-8.

Much like the review article above, this article reviews all of the pertinent viral CNS infections, with a focus on current therapies. It includes a discussion of CNS both in patients without immunocompromise and those with HIV infection.

5. UC Davis Health Education Website:

www.ucdmd.ucdavis.edu/ucdhs/health/a-z/96Encephalitisviral/doc96.html

This is an excellent source of health information regarding encephalitis. It was the source of much of the information used in the slide show that accompanies this lecture.

6. Illinois Department of Public Health West Nile Virus Website:

www.idph.state.il.us/envhealth.wnv.htm

CDC West Nile Virus Website:

www.cdc.gov/ncidod/dvbib/westnile/qa/overview/html

These websites address many relevant clinical issues related to West Nile Virus and its clinical management based on the experience in Illinois and the US.

7. Petersen LR, Marfin AA. West Nile virus: a primer for the clinician.

Ann Intern Med. 2002 Aug 6;137(3):173-9.

Solomon T, Ooi MH, Beasley DW, Mallewa M. West Nile encephalitis.

BMJ. 2003 Apr 19;326(7394):865-9.

These two articles are excellent reviews of West Nile Virus epidemiology, diagnosis, treatment, and prevention.

Questions

1. All of the following can cause encephalitis except:

- a. Arboviruses
- b. Pneumococcus/meningococcus
- c. Herpes simplex virus
- d. Mycoplasma/Legionella
- e. Adenoviruses

2. All are true regarding the diagnosis of encephalitis except:

- a. CSF pleocytosis is common.
- b. IgM antibody titres should increase 4-fold at the time of a convalescent titre.
- c. Although viral cultures are low yield, PCR can increase this yield significantly.
- d. Head CT usually shows subtle signs of cerebral edema.
- e. Head MRI usually shows periventricular and leptomeningeal inflammation.

3. All are true regarding the pathophysiology of encephalitis except:

- a. Outcome is worse in patients who develop coma due to encephalitis.
- b. Motor weakness can be a significant symptom in West Nile encephalitis.
- c. Long-term sequelae are related to the site of infection in focal encephalitis.
- d. Acute disseminated encephalitis is autoimmune mediated.
- e. Outcome is related to the age and immune status of the patient.

4. All are true regarding the treatment of encephalitis except:

- a. Antivirals should be given early to all suspected viral encephalitis cases.
- b. With fever and AMS, bacterial meningitis should always be treated.
- c. Steroids should be administered in viral encephalitis.
- d. Seizures and elevated ICP should be treated only as they occur.
- e. The measles and varicella vaccines reduce the occurrence of encephalitis.

5. All are true regarding West Nile Virus encephalitis except:

- a. West Nile Virus is an arbovirus transmitted by mosquitoes.
- b. There is an expanding area in which this disease is a threat in the US.
- c. About 1 in 150 patients who are infected will develop encephalitis.
- d. Treatment of this encephalitis includes the use of acyclovir.
- e. The majority of infected WNV patients only develop a transient fever.

Answers

1. Answer b.

Bacteria such as pneumococcus and meningococcus do not cause encephalitis. Viral agents, parasites, and occasionally fungi most commonly cause encephalitis.

2. Answer d.

In patients with encephalitis, the CT most nearly always normal. Findings that suggest brain inflammation such as periventricular or leptomenigeal inflammation are usually only detectable via MRI testing.

3. Answer a.

Although the occurrence of coma suggests a more severe case of encephalitis, it does not necessarily determine outcome. Many patients who develop coma as a result of encephalitis actually will awaken with minimal to no permanent sequelae. As such, it is important to provide optimal ED therapies as quickly as is feasible.

4. Answer c.

In general, steroids are not indicated in the treatment of viral encephalitis. The only exception to this would be in the setting of ADEM, which is an encephalitis related to an autoimmune process. Steroids might also be used in the setting of cerebral edema that results from the encephalitis process.

5. Answer d.

The management of patients with West Nile Virus encephalitis is mainly supportive. Acyclovir has only been proven to be effective in the treatment of Herpes Simplex virus encephalitis. Despite the lack of efficacy in the setting of WNV encephalitis, it is reasonable to give acyclovir empirically in the ED in patients diagnosed with encephalitis.