Mumps virus encephalitis can mimic herpes simplex encephalitis

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ABSTRACT
We describe an 18 month old Saudi girl who presented with fever, acute coma, hyperreflexia and seizures. Cerebrospinal fluid examination revealed 115 WBC, 4902 RBC, with normal protein and glucose. Computed tomography (CT) of the brain suggested right frontotemporal brain edema. Electroencephalogram showed right temporal periodic lateralized epileptiform discharges. Despite treatment with high dose acyclovir, the patient sustained left sixth cranial nerve and pseudobulbar palsy, and spastic double hemiparesis. Magnetic resonance imaging was suggestive of postinfectious encephalomyelitis. Serum mumps antibody titer was 1:16 384 and Herpes simplex serology was negative. Mumps virus infection, although uncommon, should be included in the differential diagnosis of viral encephalitides in Saudi Arabia.

Keywords: Mumps, postinfectious encephalomyelitis, herpes simplex encephalitis, viral encephalitis, Saudi Arabia.

Although mumps was a common cause of viral encephalitis in the pre-mumps-vaccination era,1 effective national mumps immunization programs have contributed to a decline in the incidence of encephalitis to one in 6000 cases of mumps.2 In contrast, Herpes simplex virus continues to be the most common cause of acute, sporadic, focal encephalitis in temperate countries with frequent mortality and neurologic sequelae.3 We describe an 18 month old child who was initially diagnosed as herpes simplex encephalitis due to characteristic clinical, cerebrospinal fluid, radiologic, and neurophysiologic features. Subsequent serologic testing suggested mumps virus as the etiology, and magnetic resonance imaging revealed widespread demyelination compatible with a diagnosis of postinfectious encephalomyelitis. Recognizing that mumps virus encephalitis may mimic herpes simplex encephalitis in an era of national mumps vaccination programs is important for subsequent prognosis and management.

Case Report. A previously healthy 18-month old child was transferred to our hospital because of coma and seizures. Her immunizations were up to date including mumps, measles, and rubella vaccination at age one year. One week prior to admission she developed fever and gingival swelling, and was seen at a clinic where she was prescribed oral cefuroxime and an antipyretic for upper respiratory tract infection. Twelve hours later, she developed high grade fever, wheezing, and tachypnea that did not respond to bronchodilator medication. She became progressively lethargic and hypotonic, and was admitted to another hospital. Initial investigations showed WBC 8.6 x 10^9/l (80% neutrophils, 17% lymphocytes, 3% monocytes), hemoglobin 11.2 g/dl, and platelets 276 x 10^9/l. Electrolytes and chemistry profile were normal. Lumbar puncture revealed cerebrospinal fluid (CSF) WBC 115, RBC 4902, and normal protein and glucose. CSF gram stain and latex agglutination were negative. Urine, blood, and CSF culture showed no growth after three days. She was treated with intravenous ampicillin and chloramphenicol. She deteriorated the next day with new onset seizures and respiratory failure requiring intubation. Computed tomography (CT) of the brain was interpreted as showing right frontotemporal edema. She was given intravenous diazepam, mannitol, ceftriaxone, and acyclovir before transfer to our institution.

Physical exam revealed a well-nourished girl who

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was intubated, sedated, and unresponsive except to painful stimulation. She had no meningismus or cutaneous lesions. Cranial nerves were normal except for depressed gag response. There was no evidence of papilloedema. She was hypertonic with grade 3+ deep tendon reflexes throughout. Plantar responses were equivocal. She withdrew symmetrically to painful stimulation of her extremities. The remaining examination was normal. Shortly after arrival to our hospital, the patient developed left eye and facial twitching following by generalized tonic-clonic movements of her body. Electroencephalogram recording during her seizures revealed diffuse background slowing, right temporal periodic lateralized epileptiform discharges, and frequently recurring runs of high amplitude generalized spike and slow wave discharges. She required intravenous phenytoin loading dose following by midazolam bolus and continuous infusion before cessation of seizure activity 30 minutes later. Ceftriaxone was continued and the patient also received high dose intravenous acyclovir (30mg/kg/day) for three weeks for suspected herpes simplex encephalitis. Gradually she regained consciousness and was extubated on the third day. Follow-up neurologic evaluation revealed a left sixth cranial nerve and pseudobulbar palsy. She developed double hemiparesis (worse on the left side) with spasticity, hyperreflexia, and sustained ankle clonus. She required nasogastric feeding and her seizures were controlled with carbamazepine. Repeat CT of the brain two weeks later showed no abnormalities. Magnetic resonance imaging (MRI) of the brain showed multiple periventricular and brainstem demyelinating lesions suggestive of postinfectious encephalomyelitis. **Herpes simplex** virus serology performed four and nine days after disease onset was negative for IgM and IgG antibodies. Serology for influenza A and B, and mycoplasma were also negative. Measles virus antibody titers were 1:8 at 16 and 23 days after disease onset. Her serum mumps virus IgG titer as determined by immunofluorescence (Virago® IFA) was 1:2048 at 16 days after disease onset and rose to 1:16 384 at 23 days onset. Mumps isolation and IgM testing were not available at our institution. Rubella IgG was greater than 10 IU/ML.

**Discussion.** In this report, we describe a case of mumps encephalitis mimicking herpes simplex encephalitis (HSE). Of interest, a case of HSE mimicking mumps encephalitis has been reported.4 Our patient was diagnosed as presumptive HSE for several reasons. The clinical presentation of a febrile illness with seizures and the CSF picture of mild pleocytosis with a large number of RBCs was suggestive of the diagnosis, as was the presence of right frontotemporal edema on CT of the brain with corresponding right temporal periodic lateralized epileptiform discharges on EEG.4 Although the incidence of HSE is not known in Saudi Arabia, its occurrence has been well documented4,6 and it has also been shown in one study that infection with **Herpes simplex** virus type 1 - by far the most common cause of HSE in children and adults—in Saudi Arabian children may not be uncommon.9 It should be noted that the presence of diffuse cerebral and brainstem demyelination on MRI did not include the possibility HSE because recent studies have documented the potentially diffuse involvement of the brain in HSE as opposed to classic temporal or frontal lobe localization.10-12 Furthermore, postinfectious encephalomyelitis has been described as a complication of HSE.13

In contrast, mumps infection was not considered a probable diagnosis based on the absence of parotitis and the relative infrequency of encephalitis complicating mumps infection. Furthermore, the history of previous mumps vaccination (corroborated by the positive rubella serology suggestive of previous measles-mumps-rubella vaccination) made mumps less probable because immunization produces protective levels of neutralizing antibodies in 95% of vaccines.14 Nonetheless, it was concluded that our patient had mumps-associated postinfectious encephalomyelitis as suggested by the greater than four fold rise in titer of mumps-specific IgG antibodies, the negative acute and convalescent herpes simplex antibody tests, and MRI findings. Testing of the cerebrospinal fluid for herpes DNA by polymerase chain reaction would have been diagnostically helpful, but was not readily available.

Our patient's clinical presentation was certainly compatible with mumps encephalitis which is generally a nonfocal encephalitis with two different presentations. Early-onset encephalitis involves direct viral invasion with neuronolysis and absence of demyelination, whereas late-onset disease begins seven to ten days after infection and is a postinfectious demyelinating process characterized by perivenous demyelination, perivascular mononuclear cuffing, and increase in microglia with sparing of the neurons.15 Not all patients with mumps infection of the central nervous system have parotitis,1 so absence of parotitis did not rule out the diagnosis. It is unclear why this patient developed mumps encephalitis. Encephalitis can be rarely associated with mumps immunization but the etiologic role of immunization is not definitive.16 Furthermore, the high and rising titers of mumps antibodies in our patient suggest recent mumps infection presumably due to vaccine failure with late-onset demyelination.

Suspecting a diagnosis of mumps encephalitis has important implications for diagnosis and treatment. Some case reports have documented the higher sensitivity of MRI as compared to CT scan in
detecting clinically silent brain lesions in mumps, and thus MRI, if available, should be obtained when mumps is a possibility. Although the treatment of mumps encephalitis is supportive, a report from Japan describes the possible benefit of inosine pranobex in treating a case of chronic mumps virus encephalitis. Early recognition and diagnosis of mumps virus as a cause of encephalitis may lead to a better understanding of the prognosis and treatment of this uncommon but potentially devastating condition.

References