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A HUMAN CASE OF ENCEPHALITIS ASSOCIATED WITH VESICULAR STOMATITIS VIRUS (INDIANA SEROTYPE) INFECTION

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Abstract. This paper describes a case of severe encephalitis in a 3-year-old Panamanian boy infected with the Indiana serotype of vesicular stomatitis virus. The virus was recovered from the child's throat on the fifth day of illness and a rise in neutralizing antibody titer was demonstrated in paired serum specimens. This is the second report of childhood encephalitis associated with vesicular stomatitis virus infection. These suggest that infection with vesicular stomatitis viruses may cause severe disease. Human infection with vesicular stomatitis viruses is common throughout the tropical Americas.

Numerous cases of human disease due to infection with the Indiana or New Jersey serotypes of vesicular stomatitis virus (VSV) have been described.[1] These cases have followed accidental laboratory infections or occurred in individuals, such as veterinarians or livestock handlers, in direct contact with cows or horses manifesting vesicular stomatitis. In most of these cases, VSV infection has resulted in an acute, self-limited illness of 3–5 days duration characterized by fever, headache, myalgia, weakness, and occasionally vesicular lesions of the mouth or at the site of inoculation.

Serologic surveys among rural populations in the southeastern United States and in Latin America have demonstrated VSV neutralizing antibodies.[1,2] Antibody prevalence increases with age, indicating that the longer one resides in an endemic area of VSV activity, the greater the probability of infection.[3,4] It has been assumed that naturally occurring infections are either subclinical or produce a mild febrile illness.[5]

We observed a child who developed a severe meningoencephalitis associated with natural VSV-Indiana infection.

CASE STUDY

The patient, a 3-year-old male, was admitted to a regional hospital on 12 February 1984 with fever, chills, vomiting, and a generalized clonic-tonic seizure of 3–5 min duration. These symptoms had begun suddenly about 7 hr prior to his admission.

Past medical history revealed that the child was the product of a normal pregnancy and weighed 2.7 kg at birth; psychomotor development was appropriate for his age. He had been hospitalized in June 1983 with probable febrile convulsions and in November 1983 with possible nephrosis. He lived with his parents and 3 older siblings in a rural area about 55 km east of Panama City, Panama. Their home was made of thatched palm leaves, had a dirt floor, and lacked running water or sanitary facilities. The family had chickens and a horse but no other domestic animals. The adjacent farm kept dairy cows, but no recent illness had been noted in these animals. Rats, opossums, squirrels, rabbits, and armadillos were abundant in the surrounding countryside and the family was bitten regularly by arthropods.

The child had a temperature of 37.4°C, and was somnolent and dehydrated upon admission. Physical examination was normal except for tonsillitis. No nuchal rigidity or neurologic abnormalities were noted. The white blood count was 13,800/mm^3. The child was placed on a liquid diet, a mixture of 600,000 units of procaine penicillin and penicillin G and phenobarbital (32 mg orally every 12 hr).

During the first 48 hr of hospitalization, the

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patient's temperature fluctuated between 37.2–38.8°C; thereafter it remained normal, and the child appeared to be improving. By day 3, phenobarbital was discontinued. On day 4, he suddenly became disoriented, developed generalized muscle spasticity and abnormal movement of the four extremities and was transferred to the Children's Hospital in Panama City.

Upon arrival at this hospital the patient was afebrile, disoriented and lethargic. Neurological examination revealed nuchal rigidity and massive, spontaneous choreoathetoid movements. Muscle tone was slightly increased in the upper left arm but normal in the other extremities. His patellar reflexes were hyperactive.

A complete blood count showed hemoglobin 11.8 gm%, hematocrit 35%, total white blood cells 7,600/mm^3 with 41% neutrophils, 58% lymphocytes, and 1% eosinophils. Urinalysis was normal. A lumbar puncture revealed clear cerebrospinal fluid (CSF) with 44 mg% protein, 45 mg% glucose and 3 leukocytes/mm^3. The CSF pressure was not determined, but no papilledema was observed. Bacterial cultures of blood and CSF were negative. Bacterial cultures from the throat and fecal specimen yielded normal flora. Test for C-reactive protein and antistreptolysin-O were negative. Neither an EEG nor a CAT scan was done. The clinical diagnosis was viral meningoencephalitis. Isolation attempts on the patient's serum, CSF, and fecal specimen (obtained on admission to Children's Hospital) were negative in standard systems (suckling mice and/or Vero and fetal tonsil cells). However, the throat specimen produced a cytopathic effect in both cell cultures. The Vero isolate was identified as VSV-Indiana serotype by plaque reduction neutralization test.[6]

Acute (16 February) and convalescent (13 March) serum specimens were examined by plaque reduction neutralization test against VSV-New Jersey and -Indiana, herpes simplex types 1 and 2, Venezuelan equine encephalitis subtype I-D, Eastern equine encephalitis, St. Louis encephalitis, and yellow fever viruses. Antibody titers to all except VSV-Indiana were $<1{:}8$ in both specimens. VSV-Indiana neutralizing antibody titers were 1:8 in the acute serum and 1:4,096 in the convalescent specimen. Cerebrospinal fluid obtained on 17 February was negative for VSV-Indiana IgM antibody.[7] The patient's father and mother had VSV-Indiana antibody titers of 1:128 and 1:256, respectively.

The patient was treated aggressively with dexamethasone, mannitol and phenobarbital. After several days haloperidol was prescribed. Mannitol was discontinued as signs of cerebral edema improved. Later hydroxyzine was used as a psycholeptic drug. Physiotherapy was prescribed.

The child was hospitalized for 40 days; he gradually regained consciousness but remained severely retarded. He responded to his name, smiled, and was able to pronounce a few words. He was unable to sit up but could eat when fed. Generalized muscle hypotonia and continuous choreoathetoid movements persisted. He was discharged on 26 March and was lost to follow-up.

Isolation of VSV-Indiana from the child's throat at the time of admission and demonstration of a significant rise in neutralizing antibody titer to the same agent indicated that the patient was infected with this virus. This suggests that VSV-Indiana infection may be related to the encephalitis, although dual infections are not uncommon and the encephalitis could have been caused by another agent. However, infection with herpes simplex viruses or any of 5 other arboviruses known to be intermittently active in Panama was ruled out.

Our failure to recover the virus from the patient's blood is not surprising, since he had a low level of neutralizing antibody (1:8). VSV infection in animals and in humans characteristically produces a transient, low level viremia.[1,5,8] The neuroinvasiveness of VSV for laboratory rodents is well documented;[9] however, this is the first report of encephalitis associated with VSV-Indiana infection in a human. The clinical history and laboratory findings in this case are similar to those reported in other acute viral encephalopathies of childhood.[10] This case is also similar to a recent report[11] of fatal acute viral encephalopathy in an Indian child, associated with Chandipura virus infection. Chandipura virus belongs to the VSV serogroup (Rhabdoviridae: *Vesiculovirus*).[12] These observations suggest that human infection with VSV is capable of producing severe central nervous system disease.

The source of VSV-Indiana infection in this patient is unknown. However, since there was no evidence of direct contact with an infected animal, insect transmission seems likely. The patient lived with his family under primitive rural conditions, without protection against biting ar-

thropods. His parents were also found to have antibodies to VSV-Indiana. Recoveries of this virus have been made from naturally infected phlebotomine sand flies in Panama,[13] and experimental transmission by sand flies has also been demonstrated.[14] Previous serologic studies[1,4] have demonstrated widespread occurrence of VSV-Indiana and -New Jersey antibodies, with prevalence as high as 90% in rural, but not in urban, populations of Panama.

Note added in proof: Four months after discharge on 26 March the child in the case study showed some improvement. He was able to sit up with assistance. Speech was monosyllabic, choreiform movements had disappeared, but generalized hypotonia persisted. He was subsequently lost to follow-up.

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