Isolation of Parainfluenza Virus Type 3 from Cerebrospinal Fluid Associated with Aseptic Meningitis

RANDALL D. CRAVER, MD,* ROBERT S. GOHD, PhD,* DANIEL R. SUNDIN, PhD,* AND JOHN C. HIERHOLZER, PhD†

Parainfluenza virus type 3 has been isolated from the cerebrospinal fluid (CSF) from six individuals—four children and two adults—over a 10-year period. All had fever, and four had signs of meningitis. All recovered uneventfully, including one child undergoing chemotherapy for medulloblastoma. The clinical presentation of this child who developed parainfluenza virus type 3 meningitis is described, and the cases of five other individuals with parainfluenza virus type 3 isolated from the CSF are briefly reviewed. The parainfluenza virus parainfluenza type 3, in addition to mumps virus, may be considered capable of infecting the central nervous system. (Key words: Parainfluenza virus type 3; Mumps; Aseptic meningitis) Am J Clin Pathol 1993;99:705-707.

The parainfluenza and mumps viruses belong to the family Paramyxoviridae because they exhibit similar morphologic and biologic characteristics. The four serotypes of parainfluenza virus and the antigenically single mumps virus are important human pathogens. The parainfluenza viruses are commonly associated with febrile upper respiratory tract diseases, pneumonia, and croup in infants and children. Mumps virus is the main cause of epidemic parotitis in children and adults. Among children it is one of the most common causes of viral meningencephalitis.

For the past 23 years at Charity Hospital in New Orleans, all spinal fluids have been tested for hemadsorbing viruses. When hemadsorbing viruses are present, they have without exception been typed as mumps. During nonepidemic years, five to eight cases of mumps meningitis have been documented annually. More cases occur during epidemic years. When we recently isolated a parainfluenza virus from spinal fluid, the isolate was referred to the Centers for Disease Control for confirmation. The laboratory there confirmed the agent as parainfluenza virus type 3, and provided us with information on three additional cases that had been obtained from a review of CDC's laboratory files. In addition, two recent isolates from Minnesota had been confirmed as parainfluenza virus type 3 in the Centers for Disease Control laboratory. These six cases are summarized in this article to suggest, that, of the paramyxoviruses, both parainfluenza virus type 3 and mumps virus should be considered as causative agents of central nervous system infection.

CASE REPORT

A girl underwent a partial resection of a medulloblastoma at 20 months of age. She was treated with systemic cyclic monthly chemotherapy consisting of two courses of vincristine and cyclophosphamide followed the third month by a course of cisplatin and etoposide. Before her eleventh course of chemotherapy (vincristine, cyclophosphamide) at the age of 2 years and 6 months, she complained of headache and had a temperature of up to 38.7°C. Complete blood count at this time included a white blood cell count of 2.7 × 10^9/L (2700/mm^3) with a differential of 68% neutrophils, 27% lymphocytes, and 5% monocytes. The cerebrospinal fluid (CSF) from a spinal tap had a glucose level of 2.4 mmol/L (44 mg/dL) (normal, 2.5-4.4 mmol/L [45-80 mg/dL]), a protein of 1.1 g/L (113 mg/dL) (normal, 0.12-0.6 g/L [12-60 mg/dL]) and cell counts of 420 × 10^6 white blood cells per liter (420 white blood cells per cubic millimeter) and 0 × 10^6 red blood cells per liter (0 red blood cells per cubic millimeter). Differential on cytocentrifuge preparation included 42% neutrophils, 42% lymphocytes, and 16% monocytes. Cultures for bacteria and fungi were negative for disease. Cerebrospinal fluid was submitted for viral cultures at this time. The patient was treated with intravenous ceftazidime for 7 days, and her fever and symptoms resolved. After her course of antibiotics, she received her eleventh course of chemotherapy and has continued to do well. No additional neurologic sequelae were identified. One year later, she is off chemotherapy but still has residual medulloblastoma.

MATERIALS AND METHODS

Tube tissue cultures of primary rhesus monkey kidneys (MK) were inoculated with 0.2 mL of cerebrospinal fluid and incubated at 36°C. At 5 to 7 days the inoculated tissue cultures were tested for the presence of a hemadsorbing virus. The main-
Integrated natural text: 

Parainfluenza virus type 3 is a common respiratory pathogen that is rarely recognized as an agent of aseptic meningitis. In the literature, parainfluenza virus type 3 has been isolated from the CSF of eight children: five with fevers, one with muscular hypotonia, and one with convulsions. The only reported death occurred from disseminated disease in a child with severe combined immune deficiency. Parainfluenza virus type 3 has been isolated from one adult with meningitis, one adult with a demyelination syndrome, and from the CSF (without CSF pleocytosis or meningitic signs) in a 19-year-old man with the clinical diagnosis of Guillain-Barre syndrome. Isolation from pharyngeal swabs has been reported in children with seizures and Reye's syndrome.

Table 1 summarizes and compares our six individuals, in whom parainfluenza virus type 3 was isolated from the CSF. The cases covered the 10-year period between 1981 and 1991. Our isolates have come from both children and adults with evidence of meningitis. The meningitis caused by parainfluenza virus type 3 seems to be benign and self-limited in otherwise healthy individuals. Even a child who was immunosuppressed by chemotherapy recovered within 1 week and continued her systemic chemotherapy without untoward sequelae. Aseptic meningitis due to parainfluenza virus type 3 does not seem to be restricted to one locale. These isolates were collected during the summer in the warm climates of New Orleans, Kansas, and Trinidad, and through late fall in Minnesota. Two cases occurring in Minnesota within 6 weeks of one another were not geographically related. The three cases occurring in New Orleans in 1991 were probably a random event.

Finally, parainfluenza virus type 3, although a common respiratory virus pathogen, joins one other paramyxovirus—mumps—as a cause of central nervous system infection. Both of these viruses also share the propensity for causing parotitis with mumps more commonly associated with this syndrome.

Other members of this paramyxovirus group apparently do not infect the central nervous system or the parotid glands. None of us have isolated parainfluenza virus types 1, 2, 4A, or 4B from spinal fluids or from cases of parotitis, nor are there reports of such cases in the literature.

DISCUSSION

Table 1. Summary of Central Nervous System Illnesses Associated with Parainfluenza Virus Type 3 Infection

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age</th>
<th>Sex</th>
<th>Date</th>
<th>Site*</th>
<th>Specimen</th>
<th>Virus</th>
<th>Illness</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.5 yr</td>
<td>F</td>
<td>6/1/91</td>
<td>New Orleans</td>
<td>CSF</td>
<td>Para-3</td>
<td>Fever, aseptic meningitis, medulloblastoma</td>
<td>Recovered</td>
</tr>
<tr>
<td>2</td>
<td>7 mo</td>
<td>F</td>
<td>9/9/91</td>
<td>Minnesota</td>
<td>CSF</td>
<td>Para-3</td>
<td>Nonspecific febrile illness</td>
<td>Recovered</td>
</tr>
<tr>
<td>3</td>
<td>37 yr</td>
<td>F</td>
<td>10/19/91</td>
<td>Minnesota</td>
<td>CSF</td>
<td>Para-3</td>
<td>Aseptic meningitis</td>
<td>Recovered</td>
</tr>
<tr>
<td>4</td>
<td>23 mo</td>
<td>M</td>
<td>11/16/88</td>
<td>Georgia</td>
<td>CSF</td>
<td>Para-3</td>
<td>Fever, upper respiratory infection, lethargy</td>
<td>Recovered</td>
</tr>
<tr>
<td>5</td>
<td>24 yr</td>
<td>M</td>
<td>6/29/81</td>
<td>Trinidad</td>
<td>TS</td>
<td>Para-3</td>
<td>Meningitis</td>
<td>Recovered</td>
</tr>
<tr>
<td>6</td>
<td>4 mo</td>
<td>M</td>
<td>7/29/86</td>
<td>Kansas</td>
<td>CSF</td>
<td>Para-3</td>
<td>Lethargy, stiff neck, fever</td>
<td>Recovered</td>
</tr>
</tbody>
</table>

* New Orleans case, Drs. Gohd and Craver: Minnesota cases, Dr. Sundin: Trinidad, Kansas, and Georgia cases. Dr. Hierholzer.

REFERENCES