Postinfectious Myeloradiculoneuropathy With Cranial Nerve Involvements Associated With Human Herpesvirus 7 Infection

Takateru Mihara, MD; Tatsuro Mutoh, MD, PhD; Tetsusi Yoshikawa, MD, PhD; Shigeaki Yano, MD; Yoshizo Asano, MD, PhD; Hirono Yamamoto, MD, PhD

Background: Infection with human herpesvirus 7 (HHV-7) generally results in a febrile illness with accompanying exanthema subitum.

Objectives: To ascertain and describe the role of HHV-7 in a case of acute myeloradiculoneuropathy.

Patient: A previously healthy young man with complaints of motor weakness, dysphasia, and nasal voice.

Methods: Serological examinations were performed with the patient’s serum. We also examined virus genome DNA in cerebrospinal fluid by regular and real-time polymerase chain reaction. Moreover, we checked the antiganglioside antibody level in the patient’s serum samples by the immunoblot analysis.

Results: Serological studies revealed significant change in titers of antibodies against cytomegalovirus, Epstein-Barr virus, and HHV-7, but only HHV-7 genome was detected in the cerebrospinal fluid, with its disappearance after therapy. No antiganglioside antibody was detected in the patient’s serum.

Conclusion: The unique clinical picture of the present patient might be closely related to the reactivation of HHV-7 in the nervous system.

Arch Neurol. 2005;62:1755-1757

Guillain-Barré syndrome (GBS) has been recognized as a postinfectious autoimmune disorder against the peripheral nervous system, characterized by acute muscle weakness and areflexia. Many GBS cases have antiglycosphingolipid antibodies such as GM1 ganglioside in patients with Campylobacter jejuni infection and GM2 ganglioside, which shares common epitopes between the infectious agents and peripheral nerves, in patients with cytomegalovirus (CMV) infection.

Previous studies have shown that one of the most common classes of viral infection that precedes GBS is the family of herpesviruses. Of GBS cases with respiratory insufficiency and cranial nerve involvement, roughly 10% to 13% and 8% to 10% demonstrate serological evidence of recent exposure to CMV and Epstein-Barr virus, respectively. Another group of the herpesvirus family includes human herpesvirus (HHV) 6 and HHV-7. Primary infections with either HHV-6 or HHV-7 generally occur in children and are characterized by exanthema subitum and febrile illness. Human herpesvirus 6 is recognized as an opportunistic pathogen that causes limbic encephalitis in persons infected with human immunodeficiency virus. Human herpesvirus 7 has recently been described as a cause of encephalitis and myelitis in immunologically competent adults.

We report a case of acute myeloradiculoneuropathy mimicking GBS, with genetic evidence documenting the presence of HHV-7 in the cerebrospinal fluid (CSF).

Report of a Case

A 26-year-old man was admitted to the hospital with a 2-day history of progressive motor weakness, tingling in the extremities, dysphasia, and nasal voice. He had preceding flu-like symptoms 2 weeks before admission. Initial neurological examination revealed moderate motor weakness in the extremities (score of 3 to 4 of 5 on the Medical Research Council scale), with mild hyperreflexia except for the absence of an Achilles tendon reflex. The plantar response was initially flexor and then temporarily extensor. There was evidence of cranial nerve involvement including the facial, glossopharyngeal, and hypoglossal nerves, and autonomic dysfunctions were manifested as a heart conduction block. Examination results of CSF samples taken at admission were normal, but successive examinations demonstrated an increase in protein (89 mg/dL).
body responses to CMV and Epstein-Barr virus. We further investigated HHV-6 and HHV-7 DNA in the CSF on day 1 and day 20 (after treatment) by real-time polymerase chain reaction, and we found a significant decrease in the amount of HHV-7 DNA (2800 copies/mL to 0 copies/mL), although no HHV-6 or HHV-7 genomes were detected in the serum sample. Fluorescent antibody testing of serum samples on day 1 and day 20 demonstrated an increase in anti–HHV-7 titers from 1:16 to 1:64 (Table).

**ANTIGANGLIOSIDE ANTIBODY**

To evaluate the patient’s serum for the presence of anti-ganglioside antibodies, mixtures of gangliosides (GM1, GM2, GM3, GD1a, GD1b, GT1b, GQ1b, and asialo GM1) processed by thin-layer chromatography (using a solvent of chloroform, methanol, and 0.02% calcium chloride in a 55:45:10 vol/vol/vol ratio) were blotted onto a polyvinylidene difluoride membrane by an electrotherm blotter (ATTO Co Ltd, Tokyo, Japan). This polyvinylidene difluoride membrane was probed using patient sera taken on day 1 and day 20 (×1000 dilution) in blocking buffer (2% nonfat milk in the wash buffer, which was phosphate-buffered saline containing 0.5% Nonidet P-40 [Nakarai Tesque Inc, Kyoto, Japan]). After treatment with the second antibody, a positive band was sought using an enhanced chemiluminescence reagent (New England Nuclear, Boston, Mass). A band was present in the positive control (anti-GM1–antibody positive), but no band was detected using the patient’s serum samples (Figure).

Human herpesvirus 6 can be silently harbored in the human brain following primary infection. Detection of vi-

### Table. Changes in Serum Virus Titer and Virus DNA in Cerebrospinal Fluid Before and After Treatment

<table>
<thead>
<tr>
<th>Serum virus titer</th>
<th>Before Treatment (Day 1)</th>
<th>After Treatment (Day 20)</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mumps virus</td>
<td>&lt;4</td>
<td>4</td>
<td>&lt;4*</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>&lt;4</td>
<td>16</td>
<td>&lt;4*</td>
</tr>
<tr>
<td>Coxsackie B1 virus</td>
<td>&lt;4</td>
<td>4</td>
<td>&lt;4*</td>
</tr>
<tr>
<td>Coxsackie B2 virus</td>
<td>&lt;4</td>
<td>&lt;4</td>
<td>&lt;4*</td>
</tr>
<tr>
<td>Coxsackie B3 virus</td>
<td>&lt;4</td>
<td>&lt;4</td>
<td>&lt;4*</td>
</tr>
<tr>
<td>Coxsackie B4 virus</td>
<td>&lt;4</td>
<td>&lt;4</td>
<td>&lt;4*</td>
</tr>
<tr>
<td>Herpes simplex virus</td>
<td>&lt;4</td>
<td>&lt;4</td>
<td>&lt;4*</td>
</tr>
<tr>
<td>Varicella-zoster virus</td>
<td>&lt;4</td>
<td>&lt;4</td>
<td>&lt;4*</td>
</tr>
<tr>
<td>EBNA IgM†</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>EBNA IgG†</td>
<td>−</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td>Human herpesvirus 6 (IgG)</td>
<td>&lt;4</td>
<td>&lt;4</td>
<td>&lt;4*</td>
</tr>
<tr>
<td>Human herpesvirus 7 (IgG)</td>
<td>16</td>
<td>64</td>
<td>&lt;4*</td>
</tr>
<tr>
<td>Virus DNA amplification by PCR in CSF, copies/mL§</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human herpesvirus 6</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Human herpesvirus 7</td>
<td>2800</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Epstein-Barr virus</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*The values were obtained with the complement fixation test.
†The values were obtained with the enzyme-linked immunosorbent assay method.
‡The values were obtained with immunofluorescence method.
§The PCR amplification was performed on the supernatant of CSF samples after centrifugation.

Abbreviations: CSF, cerebrospinal fluid; EBNA, Epstein-Barr nuclear antigen; PCR, polymerase chain reaction; + sign, positive for; − sign, negative for.
This case supports the contention that HHV-7 may be a pathological factor in the development of acute myeloradiculoneuropathy.

Accepted for Publication: February 22, 2005.

Correspondence: Tatsuro Mutoh, MD, PhD, Department of Neurology, Fujita Health University School of Medicine, 1-98 Dengakugakubo, Kutsukake-cho, Toyoake, Aichi 470-1192, Japan (mutoh@fujita-hu.ac.jp).

Author Contributions: Study concept and design: Mutoh. Acquisition of data: Mihara, Yoshikawa, and Yano. Analysis and interpretation of data: Asano and Yamamoto. Drafting of the manuscript: Mihara and Mutoh. Critical revision of the manuscript for important intellectual content: Yoshikawa, Yano, Asano, and Yamamoto. Obtained funding: Mutoh. Administrative, technical, and material support: Mutoh. Study supervision: Asano.

Funding/Support: This work was supported in part by the grant-in-aid for the Center of Excellence program, High-Tech Research Project, and Scientific Research of Priority Area (functional glycomics) from the Ministry of Education, Culture, Sports, Science, and Technology of Japan, Tokyo (Dr Mutoh).

REFERENCES


Figure. Electrothermale blotting of gangliosides following immunoblot analysis with serum. Various ganglioside subspecies (GM3, GM2, GM1, GD1a, GD1b, GT1b, GT1c, and asialo GM1) were electrothermally blotted onto a polyvinylidene difluoride membrane. The membrane was probed with serum from the present patient obtained before (at day 1; lane 1) and after (at day 20; lane 2) intravenous immunoglobulin treatment, and with serum samples from positive controls who have anti-GM1 antibody in the serum (lane 3). The positions of each ganglioside were determined on a thin-layer chromatography plate developed simultaneously without electrothermal blotting. Gangliosides were visualized with the resorcinol reagent.10 These experiments were performed at least 3 times using different serum samples, with essentially identical results. The arrow indicates the position of GM1 ganglioside.