Experimental Transmission of Human Subacute Spongiform Encephalopathy to Small Rodents

IV. Positive Transmission from a Typical Case of Gerstmann-Sträussler-Scheinker's Disease

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Summary. Spongiform encephalopathy was transmitted to mice from a patient belonging to the “Sch” family with Gerstmann-Sträussler-Scheinker's disease (GSS). Incubation periods in the first passage were much shorter than those in mice infected with Creutzfeldt-Jakob disease. Clinical and pathologic findings of mice infected with both diseases were almost identical. This is the first successful transmission from a typical GSS case without severe spongiform change which suggests the possible transmissible nature of this disorder.

Key words: Gerstmann-Sträussler-Scheinker's disease - Spongiform encephalopathy - Slow virus - Experimental transmission - Small rodents

Introduction

A rare familial disease first reported by Gerstmann et al. (1936) is known as Sträussler's disease (Seitelberger 1981 a), “spinocerebellar ataxia with dementia and plaque-like deposits” (Seitelberger 1981 b), Gerstmann-Sträussler-Scheinker's disease (Schlote et al. 1980), and Gerstmann-Sträussler syndrome (Masters et al. 1981). The disease or syndrome (GSS) is characterized by familial occurrence, chronic progressive dysfunction of the CNS, with predominant cerebellar symptoms and occasional involvement of the brainstem, cerebrum, and spinal cord. Pathologically, degenerative changes often appeared systematically in the above mentioned areas, and there were numerous amyloid plaques either accompanied or unaccompanied by spongiform changes. Seitelberger (1962) pointed out the resemblance of the clinicopathologic features with kuru seen in New Guinea. Masters et al. (1981) reported the successful transmission of spongiform encephalopathy from four patients with similar clinicopathologic features of GSS to nonhuman primates and suggested similarities between GSS and Creutzfeldt-Jakob disease (CJD). These four patients showed severe spongiform change or other unusual pathologic features and transmission from a typical case without spongiform change has not been achieved. We now report the positive transmission from a patient who lacks evidence of severe spongiform change and is one of 13 affected members of the “Sch” family reported by Boellaard and Schlote (1980) and Schumm et al. (1981).

Materials and Methods

Inoculation material taken from the brain of the patient Sch., E., case no. 14 of the “Sch” family reported by Boellaard and Schlote (1980) and Schumm et al. (1981) was sent to Japan in a state of deep freeze. Thawed material was homogenized with a glass homogenizer in normal saline 15 % (W/V). Twenty microliters of the suspension were inoculated intracerebrally into closed-colony CF 1 mice which were supplied and kept in the Institute for Animal Experimentation at Kyushu University. The first passage from the patient’s brain to mice was done twice by inoculating newly homogenized material into 18 and 10 mice, respectively. The second passage was into five mice each from two diseased mice of the first passage. The same was done with the same number of control animals inoculated with brain homogenate from a patient who died of cerebrovascular disease and from a normal mouse, respectively. All animals which survived for more than 2 months were studied histologically. A few mice were perfused with 2% glutaraldehyde and 2% paraformaldehyde and processed for electron-microscopic study.

Results

Among 28 mice in the test groups in the first passage, 20 developed spongiform encephalopathy and eight did
Table 1. Experimental transmission of GSS to mice

<table>
<thead>
<tr>
<th>Passage</th>
<th>No. of mice</th>
<th>Days after inoculation (mean ± SD)</th>
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<tbody>
<tr>
<td></td>
<td>inoculated</td>
<td>infected</td>
</tr>
<tr>
<td>I</td>
<td>18</td>
<td>13</td>
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<tr>
<td>I</td>
<td>10</td>
<td>7</td>
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<tr>
<td>II</td>
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<td>II</td>
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* Inoculations with separately prepared brain homogenates from the patient (I) or homogenates from different mice (II)

not show any particular change in the CNS (Table 1). Three mice in group IIb in the second passage died within 2 months of inoculation. Ten to 20 days prior to the date of killing or death listed in Table 1, diseased mice began to isolate themselves from the group, sit with an arched back, and impulsively run around when touched. Increased rigidity in the body and tail, and decreased body weight due to reduced food uptake appeared at a later stage, as was seen in mice infected with CJD in our previous experiment (Tateishi et al. 1980).

The pathologic findings of diseased mice were identical with those of mice inoculated with CJD: a spongiform change and astroglial proliferation were commonly seen in the cerebral cortex, especially in the parietal lobe and hippocampus, thalamus, and basal ganglia (Figs. 1, 2). Changes in the cerebral white matter, brainstem, and cerebellum were less prominent than those in mice inoculated with CJD Fukuoka-1 strain. The same lesion was confirmed in all diseased mice in the first and second passages but was not found in any mouse of the control group. Inflammatory reaction in the lesions was absent, except for perivascular cuffing of lymphocytes of a mild degree in the leptomeninges of some animals in both the test and the control groups.

Ultrastructural findings in the brains of the diseased mice were identical with those seen in the CJD mice, as reported previously (Sato et al. 1980). Spongiform change seen light-microscopically in the gray matter corresponded to the numerous vacuoles located in the neuropil observed electron-microscopically (Fig. 3). Some vacuoles were identified as intra-dendritic or axonal by the presence of synapses. The neuronal perikarya were free from the vacuole. In the white matter, vacuoles were often located within myelin sheaths, splitting the major dense lines and expanding the inner loops. A few vacuoles were also found in the axons. There were numerous reactive astrocytes and macrophages.

Discussion

Clinicopathologic features of the mice in this experiment were almost identical with those of mice infected with CJD. Some mice infected with CJD showed amyloid plaques which were similar to those seen often in patients with GSS and kuru, but rarely in CJD patients (Tateishi et al. 1984). Lack of plaques in the mice of this experiment may be due to the far shorter incubation period than in CJD mice in which plaques were induced more than 400 days after intracerebral inoculations (Tateishi et al. 1984). The short incubation period in the first passage confirmed in repeated experiments may be due to specific features of the patient with this peculiar disease. The sparse lympho-