Jpn. J. Trop. Med. Hyg., Vol. 21, No. 1, 1993, pp. 21-24

ALTERATIONS OF SPINAL CORD IN JAPANESE B ENCEPHALITIS

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Abstract: The cytopathologic changes of Japanese B encephalitis (JBE) are basically similar to those of other forms of arbovirus encephalitis. Because the entire central nervous system including the spinal cord is involved to varying degrees, the nomenclature of JBE should actually be Japanese B panencephalomyelitis.

INTRODUCTION

Japanese B encephalitis (JBE) is a tropical neurological disease found in the countries of east and south Asia, such as Japan, Korea, China, Taiwan, Malaysia, Indonesia, Thailand, Nepal and India. Since the isolation of the pathogenic virus by a Japanese neuropsychiatrist in 1934, the disease has been called Japanese B encephalitis (Hayashi, 1937). As a result of the geographical distribution, very few neuropathological details of JBE can be found in European and American textbooks. Descriptions of the spinal cord lesions are also rare in the textbooks.

MATERIALS AND METHODS

Spinal cord and brain specimens of nine JBE cases were available from two children, two middle-aged and five aged patients who underwent autopsies (Table 1). The duration to death was 4 days to 307 days. All of these JBE cases were confirmed serologically. Neuropathological investigations were performed histopathologically and immunohistopathologically.

RESULTS

The surfaces of the brains usually showed congestive and sometimes edematous changes. But no suppurative alterations were observed. The thalamus, corpus striatum and substantia nigra were always affected prominently. Hemorrhagic lesions were frequently found in the thalamus. Petechiae and small foci of necrosis were also detected not only in the thalamus but also in other parts of the cortex and centrum semiovale. Histologically, focal and small necroses of the cerebral cortex were frequently observed. Vacuolar changes of

Table 1 The cases of spinal cord studies on Japanese B encephalitis

No.	Age	Sex	Antibody	Duration	Brain	Others
1	4 mos.	M	↑ ↑	4 days	935 g	Brain edema
2	5 yrs.	M	↑	8	1,300	Brain edema
3	47	M	↑ ↑	18	1,370	
4	51	F	↑ ↑	307	—	Only spinal cord
5	65	M	↑ ↑	14	1,250	
6	65	F	↑ ↑	68	1,140	Cervical cord
7	69	M	↑ ↑	4	1,300	
8	72	M	↑ ↑	18	1,360	Brain edema
9	82	M	↑	12	1,100	

Duration: course from onset to death (days)

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A part of this paper was presented at XIth International Congress of Neuropathology, Kyoto, September, 1990.
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the cerebral cortex and white matter were also occasionally found. Glial nodules were one of the most conspicuous alterations. The reactive cells were astrocytes and microglias. Neutrophils were also mixed in the glial nodules in the cases lasting only 4 days. Perivascular lymphoid cell cuffing was easily detected. Relatively well circumscribed demyelinated lesions were also commonly observed. The axons of these foci were almost completely preserved. Cases of long duration, however, showed a few axonal swellings. Immunohistochemical staining for anti-JBE virus antibody (courtesy of Dr. Sata, JNIH: Tokyo) showed positive findings in the neurons of the thalamus (Fig. 1a). The substantia nigra was another one of the most severely affected sites. Marked gliosis and neuronal degeneration with dropping out of neuromelanin were easily observed. Although the entire cortex was involved mildly to severely, the thalamus, midbrain and corpus striatum were mainly and severely affected in all cases. The cerebellum, pons and medulla oblongata were also involved to varying degrees.

With regard to the spinal cord, macroscopically, moderate to marked congestion was found in almost all JBE spinal cords. Microscopically, the spinal lesions of JBE displayed basically the same appearance as those in the brains. Perivascular lymphoid cell cuffing, glial reactions such as glial nodules and neuronophagia (Fig. 1b), petechiae and myelin loss were detected. Of all the spinal levels, the lumbar portion was affected most severely. Neuronal loss of the anterior horn and rarefaction were detected occasionally. Perivascular lymphoid cell cuffing was clearly evident, while thickening of the vascular wall was not observed in JBE. Central chromatolysis was found frequently in the motor neurons of the anterior horn. Three of the nine cases showed some degree of alterations in the lateral pyramidal tract, but with indistinct circumsription. Two cases showed mild demyelination and/or myelin pallor (Fig. 2a), and the other case showed moderate vacuolar changes in the pyramidal tract. The pyramidal lesion was more prominent at the thoracic level. The patient who died after only four hospital days also showed vacuolar changes in lateral pyramidal tract. A few cases showed intracytoplasmic vacuolar changes in the large neurons of the anterior horn. There was no confirmation of the existence of neutral fat in these vacuolar lesions. Perivascular lymphoid cell cuffing and chronic inflammatory cell infiltration were also observed in both the motor and sensory nerves of the cauda equina. Demyelinating foci were occasionally detected in the peripheral nerves (Fig. 2b).

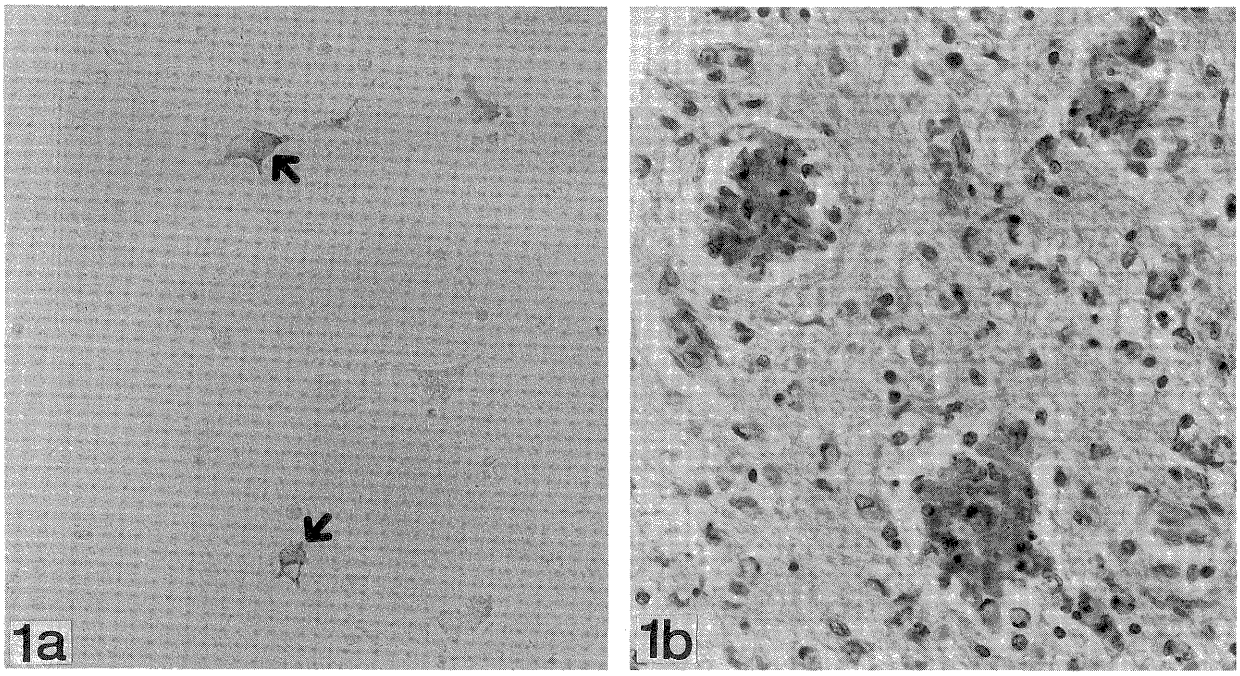

Figure 1 a. Immunohistochemical staining for anti-JBE virus antibody. Neurons positive for anti-JBE virus are detected (arrows). Thalamus of case No. 3. ABC method, ×300. b. Neuronophagia of the spinal motor neurons. Marked glial reactions are observed in the spinal anterior horn of case No. 1. HE stain, ×300.

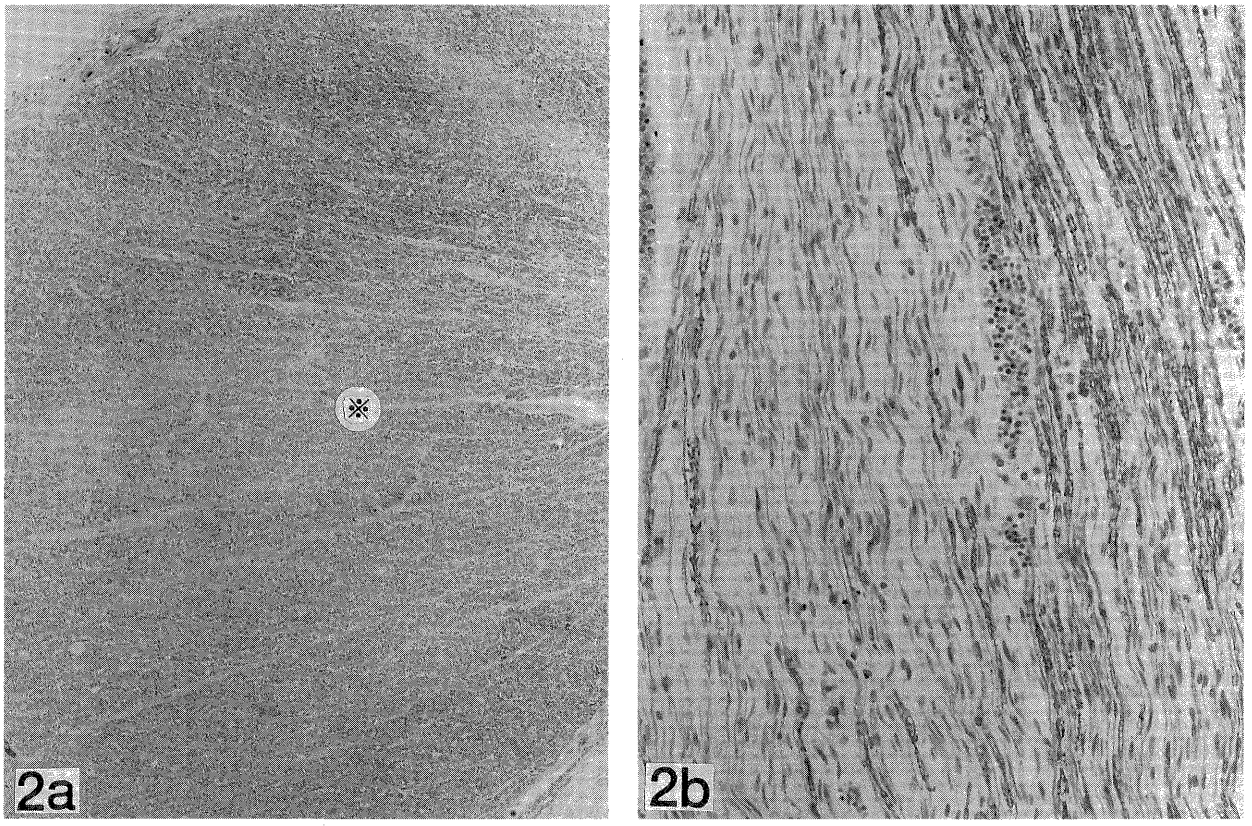

Figure 2 a. Alteration of the lateral pyramidal tract. Mild demyelination and/or myelin pallor is seen at the lateral pyramidal tract(*) of case No. 7. KB stain, ×30. b. Sensory nerve of the cauda equina of case No. 5. Demyelinating lesion (left side) and preservation of myelin (right side) are mixed. KB stain, ×150.

DISCUSSION

As a result of the geographical distribution of the disease, very few neuropathological details of JBE can be found in European and American textbooks. Before discussing the neuropathological features, it will be useful to present a brief epidemiological introduction of JBE in Japan.

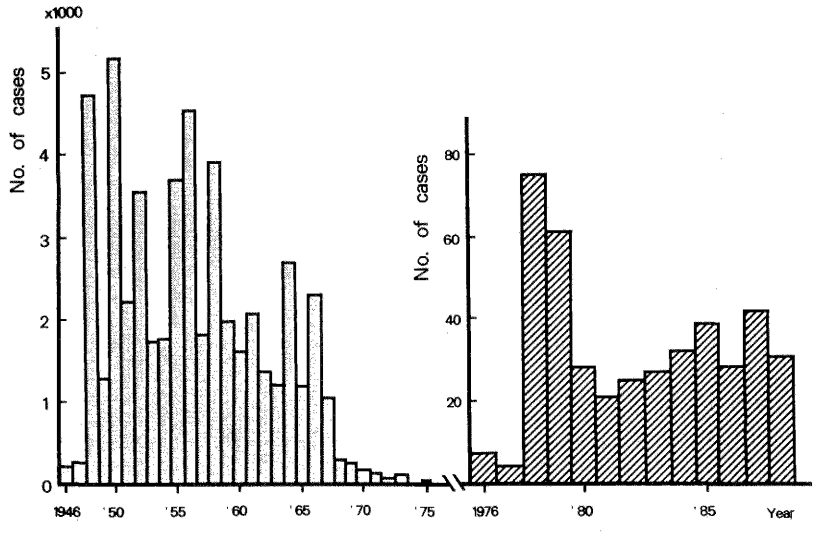

Figure 3 The number of cases of Japanese B encephalitis in Japan: 1948—1988.

JBE has been the subject of a nation-wide statistical surveillance in Japan since 1946 and has been designated as a legal epidemic disease since 1954. The number of cases peaked in 1950, with 5,196 patients and a morbidity of 6.2. From 1948 to 1967, more than one-thousand patients were detected each year. In recent years, however, a total of less than 50 patients (Fig. 3) and 0.0 morbidity are observed. JBE was seen predominantly in children and in aged groups. But in recent years, very few cases are detected among children because of vaccinations for JBE. The southwestern part of Japan, especially the island Kyushu, shows the highest incidence, while most of the northern island Hokkaido, located above a latitude of 41°N, has no JBE patients.

The morphological aspects of JBE are basically similar to those of other forms of arbovirus encephalitis, with the exception of Eastern equine encephalitis (Heffner, 1976). Macroscopically, brain edema and congestive changes are the most prominent features in the early phase. Although the inflammatory reactive cells are mainly neutrophils rather than lymphoid cells in Eastern equine encephalitis, the reactive cells of other forms of arbovirus encephalitis including JBE are mainly lymphocytes and glial cells (Heffner, 1976).

Very few details of the spinal changes can be found in the English literature. The spinal changes of JBE display basically the same features as those of other forms of arbovirus encephalitis, such as glial nodule, neuronophagia (Fig. 1b), petechiae and myelin loss. Perivascular lymphoid cell cuffing is also prominent, while thickening of the vascular wall such as that seen in HTLV-I associated myelopathy (HAM/TSP) (Akizuki *et al.*, 1989) is not observed in the spinal cord of JBE. Mild demyelination and/or myelin pallor (Fig. 2a) and moderate vacuolar alterations in the lateral pyramidal tract were detected in three cases in this spinal study. Some aspects of the alterations in the lateral pyramidal tract, which show indistinct circumscription of the lesion, might be secondary to proximal lesions such as those in the cerebral cortex and white matter. In the acute phase, however, edematous changes might play the role of vacuolar changes, because one case with lesions in the lateral pyramidal tract did not show lesions in the related cerebral areas and this patient died after only four hospital days.

Because the entire central nervous system including the spinal cord is involved to varying degrees, the nomenclature of JBE should actually be Japanese B panencephalomyelitis.

ACKNOWLEDGEMENTS

The author expresses his appreciation to Dr. S. Era (National Beppu Hospital), Dr. Y. Otsuka (Kumamoto Chuo Hospital), Dr. H. Miyayama (Kumamoto Municipal Hospital), Dr. M. Takeya (Kumamoto University), Dr. O. Nakashima (Kurume University), Dr. H. Fujii (National Nagasaki Chuo Hospital), who provided the specimens of JBE. Thanks are also extended to Dr. T. Sata (National Institute of Health, Japan) for his immunohistochemical staining with anti-JBE virus antibody.

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