Lafora Disease Diagnosed by Liver Biopsy

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A patient with progressive myoclonus epilepsy and Lafora bodies in the central nervous system also has a material with staining properties similar to polyglucosans in other organs. This suggests that Lafora disease is a glycometabolic disorder (Harriman et al. 1955).

Liver biopsy (Inoue et al. 1974; Nishimura et al. 1980), muscle biopsy (Carpenter et al. 1974) and skin biopsy (Carpenter et al. 1981) are useful in the diagnosis of Lafora disease. Familial cases of Lafora disease diagnosed by liver biopsy have been reported (Inoue et al. 1974).

More recently, we again made the diagnosis of Lafora disease by liver biopsy in a sporadic case study with myoclonus epilepsy. This report includes a description of the case.

Case

K. T., male, died at the age of 21.

The family and past histories revealed nothing of note. He was considered to be a normal boy until the first convulsive seizure occurred at the age of 6. Treatment with anticonvulsant medications was initiated when he was 11, and the seizures became infrequent for a short time. However, generalized convulsions became progressively more severe after the age of 14. And myoclonus of the upper extremities and oral region, associated with a slowing of behavior and response time became prominent. Intelligence disturbances and personality changes, such as childishness and viscosity were noted.

When he was admitted to Kurume University Hospital at the age of 15, mental symptoms such as circumstantiality of thought, memory disturbances, acalculia and the personality changes mentioned above were seen. Neurological abnormalities, such as cerebellar and extrapyramidal signs except myoclonic jerks in the upper extremities and oral region, were not found. The spleen and liver were not palpable.

Laboratory Findings — The blood and urine were normal. No vacuolation of lymphocytes was observed. There were no abnormal findings in the fundus either. An EEG recorded on July 5, 1978 (at the age of 15) during treatment with phenytoin, phenobarbital and sodium valproate was dominated by high amplitude (100 μV), irregular slow waves at 3-7 Hz, showing high amplitude atypical spike and wave complex or polyspike and wave complex increased by stimulation (Fig. 1). The EEG findings improved transiently after the administration of clonazepam. X-rays and CT scans showed a slight dilatation of the cerebral ventricles and gyri. Gradually, aggravation of the myoclonic jerks, the generalized convulsions and the ataxic
Gait became apparent. Lipidosis, mucolipidosis and mucopolysaccharidosis could be differentiated from findings on lysosomal enzyme activity in white blood cells and cultured skin fibroblasts.

Liver Biopsy — A section of the liver biopsy specimen had a pale basophilic material that stained with Hematoxylin-Eosin (H-E). A PAS-positive substance that resisted diastase digestion was clearly identified in the cytoplasm of liver cells, these observations made the diagnosis of Lafora disease possible (Fig. 2).

15 years after the onset of symptoms, the patient died of pneumonia.

Finding at Autopsy — Only the brain and liver were observed. The brain, macroscopically, was normal except for a slight edema. It was, however, noticed with histological examination that Lafora bodies were diffusely found in many regions of the brain, although the distribution density was different. Only the internal portions of Lafora bodies were basophilic. It contained a strongly PAS-positive substance, whereas the external portion was weakly PAS-positive (Fig. 3). As shown in (Fig. 4), the histological findings of the liver were similar to the result of biopsy. The substance appeared like ground glass, which is somewhat consistent with the PAS-positive reaction that was observed in the section stained with H-E. Although both the Lafora bodies and the degenerated substances in the liver cells were PAS-positive, they were histochemically somewhat different.

The concentrations of the glycosaminoglycan and glycoprotein in the urine obtained before death were not significantly different from normal (Inoue, 1983).

References


Fig. 1. EEG with an atypical spike and wave complex or polyspike and wave complex.

Fig. 2. A section of liver biopsy showing the PAS-positive substance in hepatocytes (PAS staining ×400).

Fig. 3. A section of an autopsy specimen showing Lafora bodies containing PAS-positive material observed in the neurons of nucl. dentatus (PAS staining ×400).

Fig. 4. A section of an autopsy specimen showing a ground glass-like substance in the hepatocytes (H-E staining ×400).