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# A 64-year-old man presenting MRIs of expansive multiple high intensity areas in the cerebral white matter, cerebellum and brainstem

**Shigeki Takeda,[1] Kazunori Yamazaki,[2] Teruo Miyakawa,[2] Hitoshi Takahashi,[3] Fusahiro Ikuta[4] and Hiroyuki Arai[2]**

Department of [1]Pathology and [2]Neurosurgery and [4]Brain Research Center, Niigata Neurosurgical Hospital, and [3]Department of Pathology, Brain Research Institute, Niigata University, Niigata, Japan

## CLINICAL COURSE

A 64-year-old man, who had been suspected as a hepatitis carrier 25 years ago and also was detected with a decrease of leukocytes and lymphocytes in the previous year, visited our hospital on 31 January, because of vertigo. Neurological status revealed normal findings. Blood cell count disclosed 4200 WBCs with a differential count of 66% segmented neutrophils, 8% non-segmented neutrophils, 10% lymphocytes, 14% monocytes, 1% eosinophiles and 1% basophiles. HBs Ag and HCV Ag were negative. T2-weighted brain MRI showed small high intensity areas (HIAs) in the left occipital white matter (Fig. 1a) and the midbrain tegmentum. He was admitted for 20 days as having cerebral infarcts. Anticoagulant therapy was effective. He was readmitted because of paralysis of the left leg 2 months after discharge. MRI showed a new HIA in the convolutional white matter of the right motor area. Anticoagulant therapy and rehabilitation were effective. He was admitted at the 3rd time on 3 July, because of worsened weakness of the left leg. On MRI examination HIA in the motor area spread and a small HIA was revealed in the right frontal white matter. Left hemiparesis was progressive. Mental retardation, visual disturbance and emotional instability developed. In September he was suspected as having vascular dementia or some degenerative condition in the cerebral white matter as well as cerebral infarcts. MRI examination revealed widespread HIAs in the brainstem, cerebellar white matter, thalamus and cerebral white matter (Fig. 1b). He died in December. The duration of the present illness was 11 months after his first visit to our hospital.

## PATHOLOGICAL FINDINGS

Postmortem examination, performed 2 h after death, revealed no malignancy, atrophy of the adrenal gland, nor thrombi on the aortic valves. Atherosclerosis was mild.

The fresh brain weighed 1150 g. Sections of the fixed brain revealed subcortical grayish discoloration of the cerebral white matter (Fig. 2a). The cerebral arteries including Willis circle were delicate. KB preparation showed extensive loss of myelin sheaths in widespread areas in the bilateral cerebral hemispheres (Fig. 2b). The lateral angle of the lateral ventricle and optic tract were relatively or well preserved. In the extensive lesions of the cerebral white matter, macrophage infiltration and astrocytic gliosis were seen in variable degrees. In the margin of the diffusely affected white matter, multiple small lesions, which stained pale in KB preparation, were seen (Fig. 2b). These small lesions were confluent in part. The arcuate fibers were mostly involved. The intracortical myelinated fibers were also affected. In fresh lesions, the axons were well preserved in contrast to the marked loss of myelin sheaths (Fig. 2c,d). In older lesions, the myelin sheaths and axons disappeared. The cortical neurons were relatively preserved. The same demyelinated lesions were seen in the basal ganglia and thalamus.

The extensive demyelinated lesions as seen in the cerebrum were also seen in the brainstem, cerebellar white matter and the spinal cord.

In the periphery of the lesions there were many cells with oval basophilic nuclei (Fig. 2e). The cells revealed negative immunoreactivity for GFAP and vimentin. These nuclei revealed positive immunostaining for a JC virus

Correspondence: Shigeki Takeda, MD, Department of Pathology, Niigata Neurosurgical Hospital, 3057 Yamada, Niigata, Niigata 950-1101, Japan. Email: s-takeda@deluxe.ocn.ne.jp

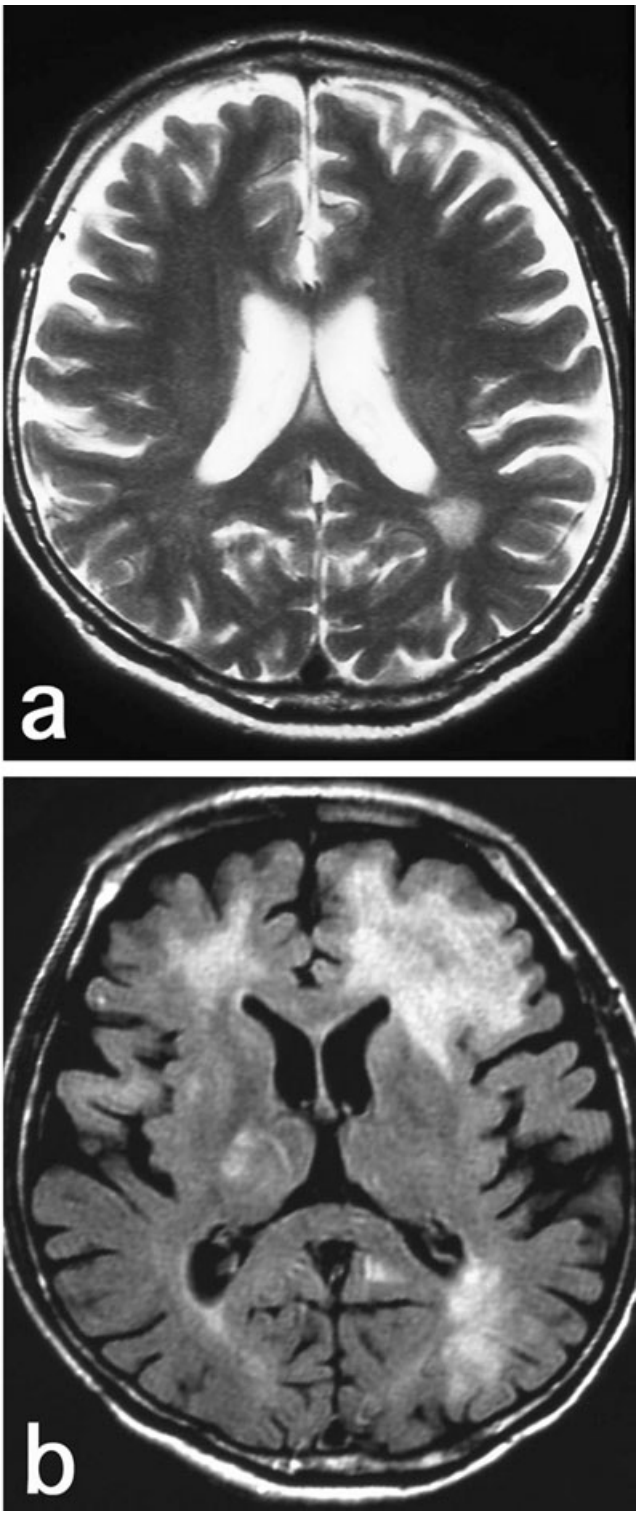


**Fig. 1** (a) T2-weighted MRI in January at the first visit to our hospital. A high intensity area (HIA) is seen at the left occipital white matter. (b) Fluid attenuated inversion recovery imaging in September reveals multiple HIAs in the cerebral white matter and thalamus.

protein, VP1 (Fig. 2f). Under electronmicroscopy the nuclei of the cells had numerous round particles of 30–40 nm in diameter resembling those of papova viruses (Fig. 2g). They sometimes showed in crystalloid arrangement. The filamentous profiles were sometimes seen among them.

## DIAGNOSIS

Progressive multifocal leukoencephalopathy.

## DISCUSSION

The patient had no neurological disorders in his family. He was diagnosed as having a rebral infarct at his first visit to our hospital. The neurological symptoms rapidly worsened. MRI examination revealed rapidly expanding HIAs in the brain, especially the cerebral white matter. Although he was suspected as having vascular dementia or some degenerative condition in the cerebral white matter as well as cerebral infarcts, the definitive clinical diagnosis was unknown. There are many diseases implicated in cerebral infarcts on MRIs. Although, PML is a rare neurological disorder in Japan, it is important to differentiate from cerebral infarct on MRIs.

Most PML patients have been reported in an immunosuppressive state accompanied with lymphoma, leukemia, carcinoma and tuberculosis, and so on. The present case had no such underlying diseases. Although blood cell count revealed a small number of lymphocytes, some outpatients in our hospital, having no blood diseases or impairment of immune responses, also showed the same number of lymphocytes. Although rare, there have been a few reported cases in which PML has occurred in patients without an immunosuppressive state. Such PML cases have been reported as 'primary PML'[1,2] or 'spontaneous PML'.[3] The present case belongs to this rare group.

The distribution of PML lesions is mainly within the cerebral white matter. On the other hand, a few cases have main PML lesions in the cerebellum and the brainstem, which have been reported as 'cerebellar form'.[4,5] Our case had extensive PML lesions in the cerebellar white matter, brainstem and spinal cord as well as the cerebral white matter.

## ACKNOWLEDGMENTS

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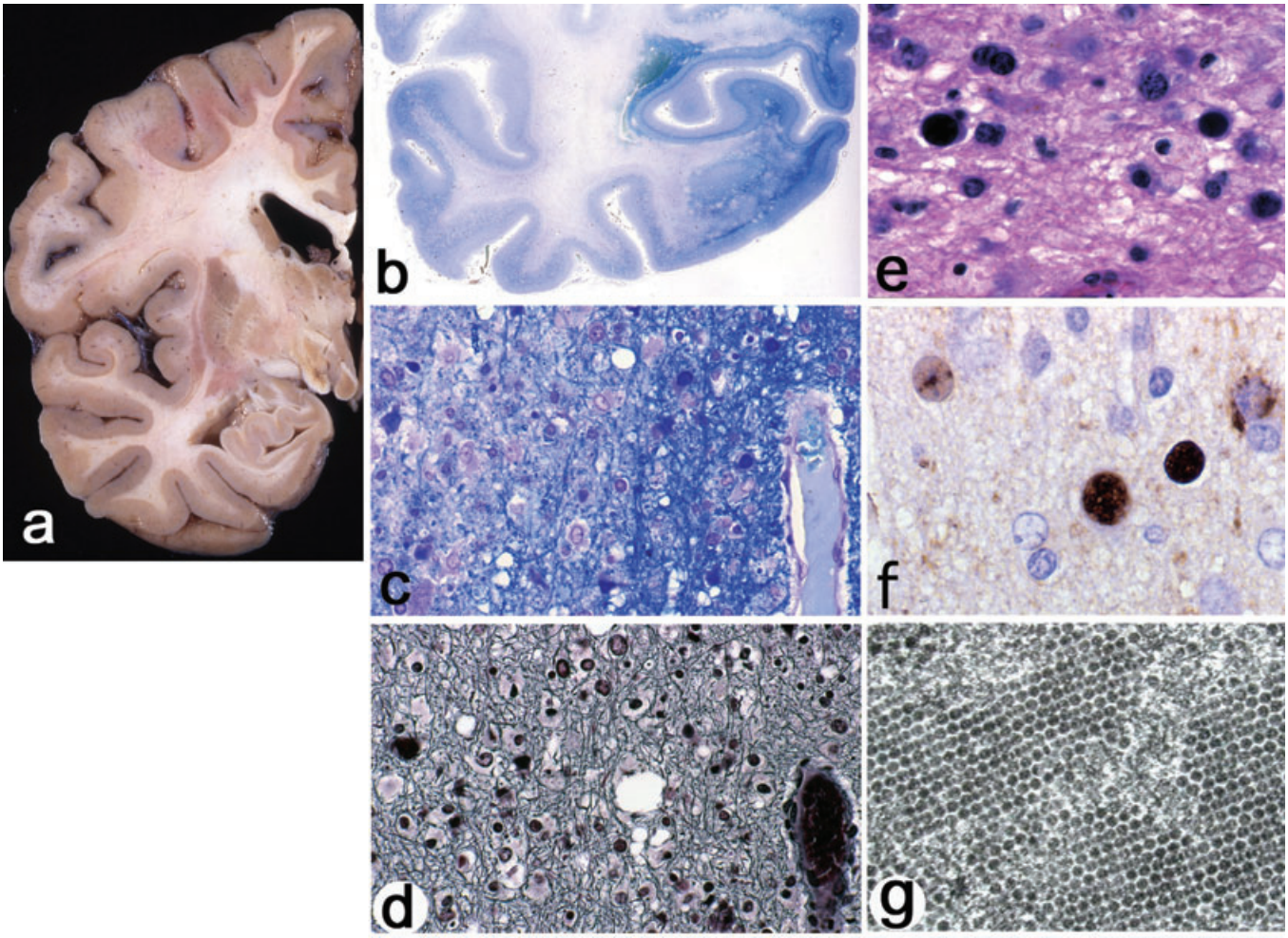


**Fig. 2** (a) The coronal section of the right cerebral hemisphere through the mammillary body. The cerebral white matter reveals grayish discoloration in part. (b) Extensive degeneration of cerebral white matter involving intracortical myelinated fibers. Multifocal spotty lesions are seen in the convolutional white matter. Occipital lobe. (c) The left half shows degeneration of the myelin sheaths. Parietal lobe. KB preparation. ×220. (d) The axons are well preserved in the same region as (c). Bodian's silver impregnation. ×220. (e) The enlarged hyperchromatic nuclei scattered in the periphery of the degenerative lesions. Frontal lobe. ×390. (f) The dens nuclei reveals positive immunoreactivity for a JC virus protein, VP1. ×540. (g) In the dens nuclei, electronmicroscopy shows numerous round particles in crystalloid arrangement resembling those of papova virus. ×38 000.

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