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Neuropathology Education

43-year-old-man presenting repeated pathologic fractures of limbs, dementia and grand mal

Naoji Amano

Department of Psychiatry, Shinshu University School of Medicine, Matsumoto, Nagano, Japan

CLINICAL HISTORY

A Japanese man had been crippled by leg pain since the age of 10. He suffered from repeated pathologic fractures of the lower limbs and became bedridden after the age of 33. Neurological examination revealed hyperreflexia of the deep tendons, sucking reflex, dysdiadochokinesis and intentional tremor. He was alert and euphoric, showing frontal lobe syndrome. Xrays revealed many polycystic translucent lesions in the bones of the fingers, toes, limbs and pelvis (Fig. 1a). CT scan showed severe diffuse atrophy, predominantly in the frontal lobes. Biopsies of bone marrow and skin revealed membranous cystic lesions in adipose tissues. His general condition went slowly downhill. Babinski reflex and ankle clonus appeared at the age of 36. He suddenly developed status epilepticus at the age of 37. He gradually became dumb, and died of bronchopneumonia at the age of 43.

NEUROPATHOLOGICAL FINDINGS

The upper and lower limbs were deformed. Histological examination revealed many classical membranocystic lesions in the long bones and adipose tissues (Fig. 1c,d). The brain weighed 680 g. Coronal sections revealed severe shrinkage and grayish discoloration of cerebral white matter. Nerve cells in the cerebral cortices were greatly decreased in number. Cerebral white matter showed diffuse sclerosis, where both axons and myelin disappeared almost completely, predominantly in the frontal and temporal lobes (Fig. 1b). Many axonal swellings and a few degraded sudanophilic granules were seen. Astrocytosis and calcospherites were seen in the putamen and globus pallidum.

DIAGNOSIS

Nasu–Hakola's disease (membranous lipodystrophy).

DISCUSSION

Nasu–Hakola's disease[1–4] is rare, and clinically it exhibits osteopathy and neuropsychiatric symptoms including frontal lobe syndrome, dementia and convulsions, and pathologically, membranocystic degeneration in adipose tissues and sudanophilic leukodystrophy or sclerosing leukoencephalopathy in the brain. Many axonal swelling or spheroids in the cerebral white matter and calcospherites in the basal ganglia were characteristic. Currently the etiopathogenesis is still unknown but genetic studies have demonstrated molecular defects by identifying some mutations in the transmembrane protein.

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Correspondence: Naoji Amano, MD, PhD, Department of Psychiatry, Shinshu University School of Medicine, 3-1-1 Asahi, Matsumoto, Nagano 390–8621, Japan. Email: n-amano@hsp.md.shinshu-u.ac.jp

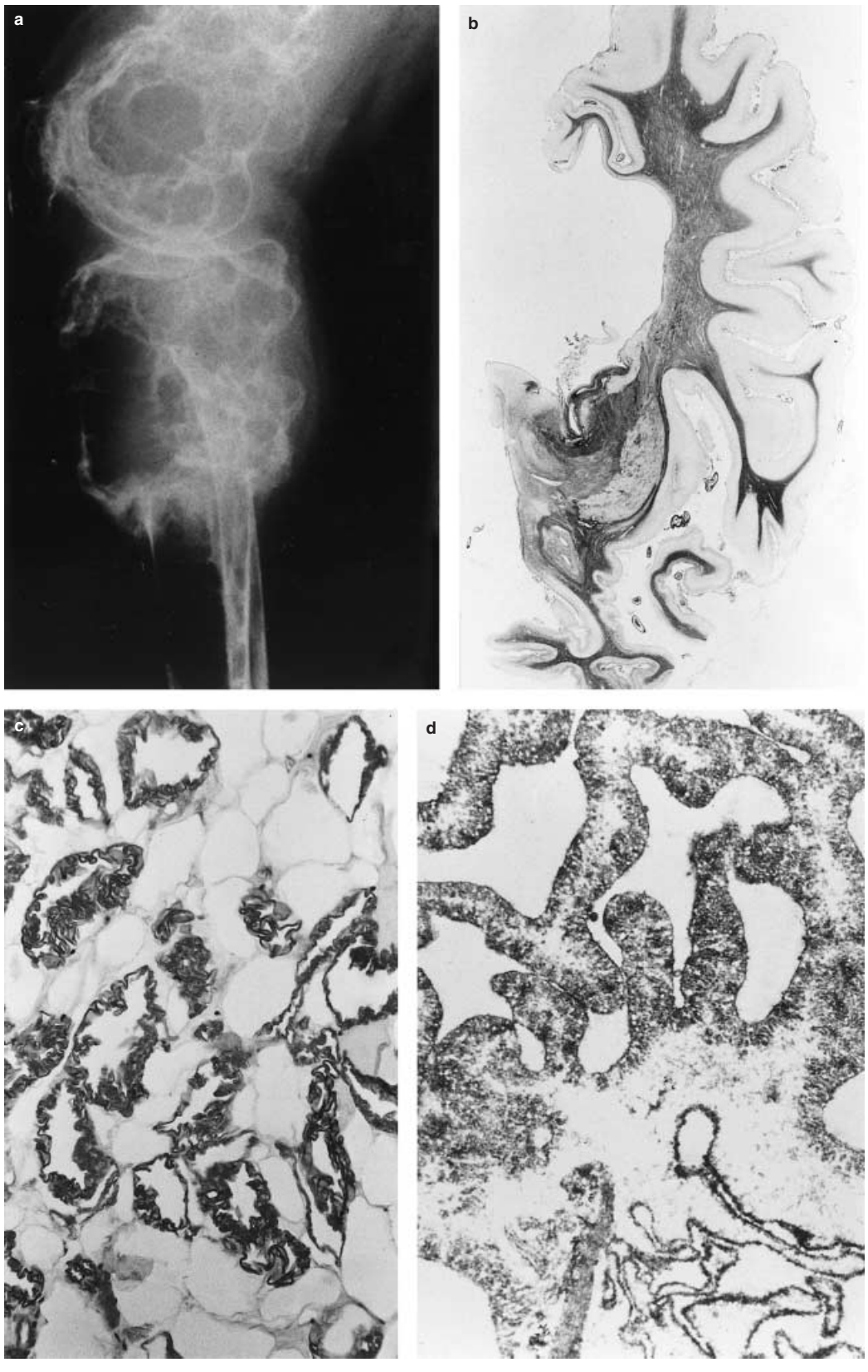

Fig. 1 **(a)** X-ray reveals many polycystic translucent lesions in the bones of femur and tibia. **(b)** The brain is sclerosing leukoencephalopathy, showing that the white matter is diffuse sclerosis and that both myelin and axons disappear almost completely. Holzer stain. **(c)** Membranocystic lesions are seen in para-aortic adipose tissues. Sudan-III stain. **(d)** The membranocystic lesion is consisted of many microcyst- or tubule-like structures arranged vertical to the lumen in ultrastructure.