

Bull Yamaguchi Med Sch 39(3-4) : 71-74, 1992

Magnetic resonance imaging in probable Alexander's disease

Kiyoshi Yamamoto¹, Mitsunori Morimatsu¹, Takeshi Ukita² and Michio Yamada²

Departments of ¹Neurology and ²Neuropsychiatry, Yamaguchi University School of Medicine, Ube, Yamaguchi 755, Japan (Received June 5, revised July 23, 1992)

Abstract We report the case of a 14-year-old girl with suspected Alexander's disease. Magnetic resonance imaging of the brain showed a decreased intensity in the frontal white matter on T1-weighted sequences, and an increased intensity on T2-weighted images. T1-weighted sequences demonstrated an increased attenuation of the basal ganglia, occipital lobes, cerebellum and brainstem. T2-weighted images showed a decreased intensity of the basal ganglia and brainstem. Magnetic resonance imaging is a useful adjunct in establishing a premortal diagnosis of Alexander's disease without brain biopsy.

Key Words : Alexander's disease, Magnetic resonance imaging, Single photon emission computed tomography(SPECT)

Introduction

Alexander's disease is a progressive degenerative neurological disorder of unknown etiology which is characterized by the early onset of megalencephaly, psychomotor retardation, spasticity and convulsions [1]. Because there is no definitive biochemical test for this condition, diagnosis relies on brain biopsy findings [2].

However, recent reports suggest that, in a child with megalencephaly and progressive retardation, changes in white matter, mainly in both frontal regions, in conjunction with the exclusion of other similar leukodystrophies by biochemical testing may lead to a precise diagnosis of Alexander's disease without brain biopsy [3,4].

We report the case of a 14-year-old girl who presented with mild megalencephaly and psychomotor retardation. The characteristic brain findings by computed tomography (CT), magnetic resonance imaging (MRI) and single photon emission computed tomography (SPECT) of the brain led to the diagnosis of

probable Alexander's disease without brain biopsy.

Case report

This 14-year-old girl was born after an uneventful full-term pregnancy. Her birth weight was 3,050g, the circumference of her head was 33 cm at birth. The parents were not consanguineous, and there were no family history of neurological disease. At 6 months of age, a delay in motor development was noted. At the age of 12 months, she developed generalized convulsions and received treatment with sodium valproate. At the age of 3 years she began to walk, and thereafter developed fairly well. When she was 7 years old, CT revealed low density lesions mainly in the frontal white matter and a dilatation of the lateral ventricles bilaterally. When she was 9 years old, her intelligence quotient (IQ) was 32 (Wechsler Intelligence Scale for Children). At 13 years she developed a gait disturbance.

She was admitted to our hospital at the age

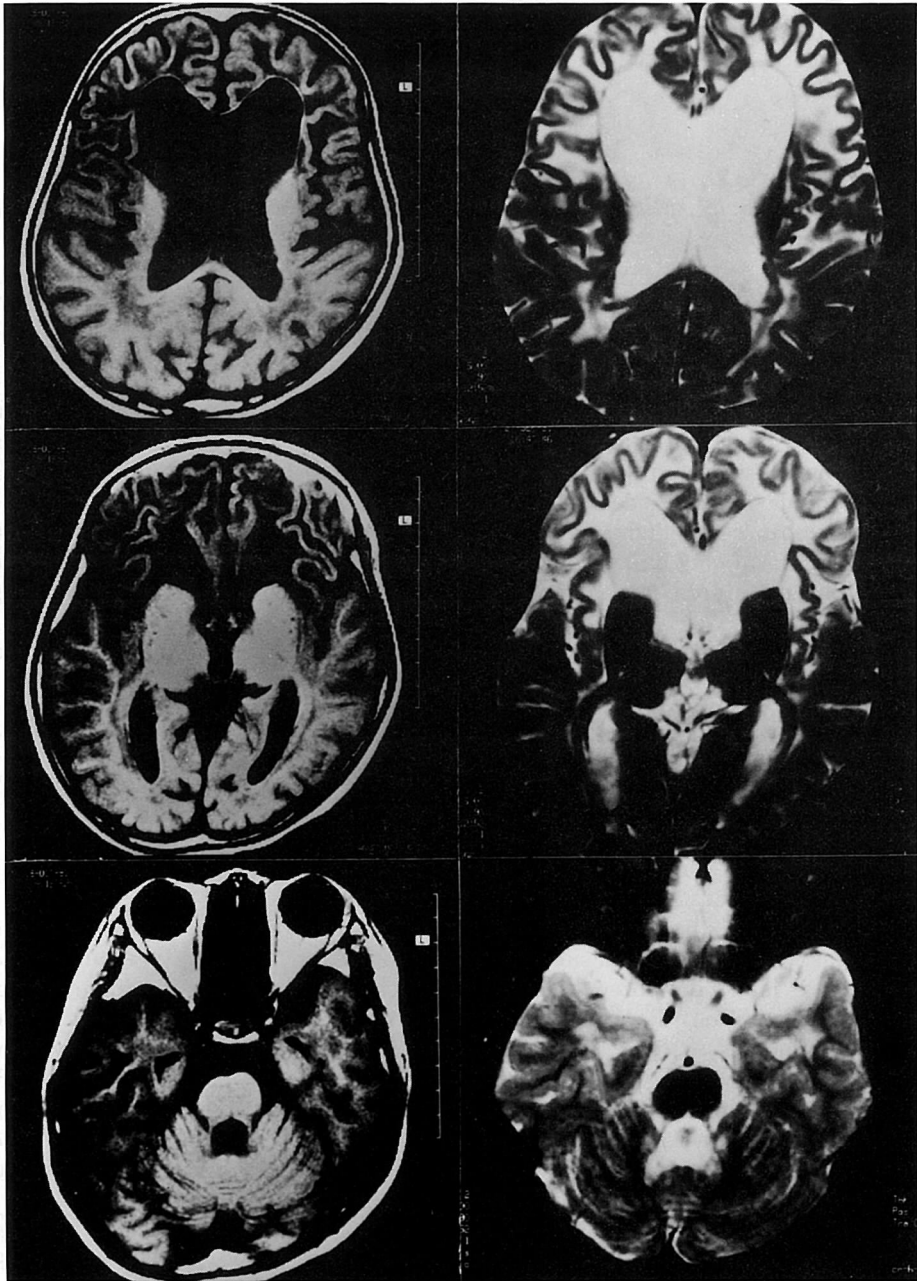


Fig 1. MRI(1.5T, Magnetom, Siemens-Asahi Medical) revealed a decreased intensity of the frontal white matter on T1-weighted sequences(TR 550msec, TE 15msec) and an increased intensity on T2-weighted images(TR 3000msec, TE 90msec). T1-weighted sequences demonstrated an increased attenuation of the basal ganglia, occipital lobes, cerebellum and brainstem. T2-weighted images showed a decreased intensity of the basal ganglia and brainstem.

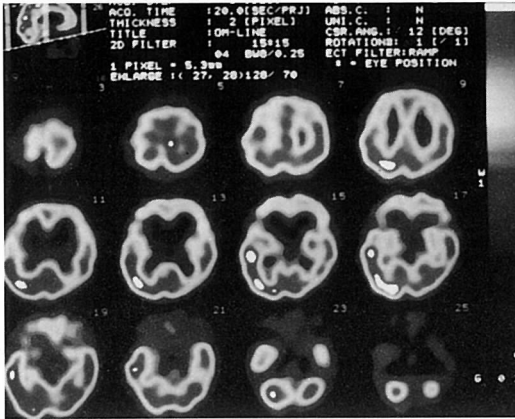


Fig 2. ^{123}I -IMP SPECT revealed a reduction of activity in both frontal regions.

of 14 years for evaluation of the gait disturbance. Physical examination revealed no abnormalities except for mild macrocephaly. The circumference of her head was 56 cm. Neurological examination showed hyperreflexia in both lower limbs without pathological reflexes. Funduscopic examination showed no abnormality. Although her gait was wide-based and unsteady, she was able to walk unaided. Nerve conduction studies were normal.

The following laboratory examinations gave normal results: hemoglobin, white blood cells, acid-base status, serum and urinary amino acids, and liver and renal function testing. Leukocyte lysosomal enzymes were normal, including α -glucosidase, α -galactosidase, α -mannosidase, β -glucosidase, α -fucosidase, β -glucuronidase, β -galactosidase, N-acetyl- β -glucosaminidase and arylsulfatase A. Plasma very long chain fatty acids were normal. Chromosome analysis revealed a 46,XX karyotype.

CT revealed low density lesions that were more extensive in the frontal lobes and dilated ventricles. MRI revealed a decreased intensity of the frontal white matter on T1-weighted sequences and an increased intensity on T2-weighted images. T1-weighted sequences demonstrated an increased attenuation of the basal ganglia, occipital lobes, cerebellum and brainstem. T2-weighted images showed a decreased intensity of the basal ganglia and brainstem

(Figure 1). ^{123}I -IMP SPECT revealed a reduction in activity of both frontal regions (Figure 2).

Discussion

The clinical features of this patient included mild megalencephaly, delayed motor development followed by a slowly progressive psychomotor retardation, seizures, and a progressive gait disturbance. In the differential diagnosis we considered includes Tay-Sachs disease, GM₁ gangliosidosis, mucopolysaccharidoses, Alexander's disease and Canavan's disease [3,5]. By means of laboratory testing we ruled out Tay-Sachs disease, GM₁ gangliosidosis, and mucopolysaccharidoses [6]. Although a definitive diagnosis of Alexander's disease or Canavan's disease can be made only by brain biopsy [2], recent reports suggest that CT or MRI can be useful for the premortem diagnosis of these diseases [3,4]. Typically, the CT of a patient with Alexander's disease shows a lesion of the white matter that is more extensive in the frontal lobe [7], and MRI demonstrates the increased attenuation of the basal ganglia or cerebellum representing the Rosenthal fibers on T1-weighted images [7,8]. In contrast in Canavan's disease, abnormal signals are always found diffusely in the white matter [9]. We believe that the characteristic CT and MRI findings in this patient support the diagnosis of Alexander's disease. The diffuse, confluent high signal on T2-weighted images and low signal on T1-weighted images are thought to indicate the dysmyelination or demyelination that has been reported in Alexander's disease [3,10]. However, the increased signals of the basal ganglia, occipital lobes, cerebellum and brainstem on T1-weighted images, and the decreased intensity of the basal ganglia and brainstem on T2-weighted images, may indicate the distribution of the Rosenthal fibers without a marked demyelination or a defective myelin formation [7], although we did not have pathological findings. ^{123}I -IMP SPECT demonstrated a reduced activity dominantly in both frontal regions, suggesting a dysfunction mainly in the frontal lobes due to lesions in the white matter [11].

Alexander's disease is an invariably fatal degenerative disease of the nervous system with three clinical subgroups: infantile, juvenile, and adult, [1,10,11]. The infantile group is characterized by a slow enlargement of the head due to an increase in brain substance (megalencephaly), progressive retardation, spasticity and seizures. The average age of onset is 6 months, but symptoms may develop at birth. The average duration of illness is 28 months. In the juvenile group, symptoms appear between the age of 7 and 14 years. Seizures are less prominent, and progressive bulbar symptoms and spasticity are common. The average life span is 8 years. In the adult group, onset occurs between the second and seventh decades, the disease may exhibit a course consistent with classical multiple sclerosis, or the patient may be asymptomatic. Although our patient is now 14 years old, we believe that she belongs to the infantile group of Alexander's disease because the symptoms appeared at 6 months of age. Some patients with Alexander's disease have survived more than 10 years [12].

In conclusion, MRI is a useful adjunct in the diagnosis of Alexander's disease. It may be a useful tool for evaluating the lesions of the white matter and the distribution of the Rosenthal fibers. SPECT can help to understand the dysfunction of the brain in Alexander's disease.

References

- 1) Russo, L. S., Aron, A. and Anderson, P. J.: Alexander's disease: a report and reappraisal. *Neurology*, **26**:607-614, 1976.
- 2) McGregor, D. L., Humphrey, R. P. and Becker, L. E.: Brain biopsies for neurodegenerative disease in children. *J. Pediatr.*, **92**:903-905, 1978.
- 3) Hess, D. C., Fisher, A. Q., Yaghami, F., Figueroa, R. and Akamatsu, Y.: Comparative neuroimaging with pathologic correlates in Alexander's disease. *J. Child Neurol.*, **5**:248-252, 1990.
- 4) Schuster, V., Horwitz, A. E. and Kreth, H. W.: Alexander's disease: cranial MRI and ultrasound findings. *Pediatr. Radiol.*, **21**:133-134, 1991.
- 5) Harbord, M. G. and LeQuesne, G. W.: Alexander's disease: cranial ultrasound findings. *Pediatr. Radiol.*, **18**:227-228, 1988.
- 6) Rios, E., Mutoh, K., Okuno, T., Itoh, M., Fujii, T. and Mikawa, H.: A case of probable Alexander's disease: neuroradiological and evoked potentials findings. *Ann. Pediatr. Japon.*, **35**:22-29, 1989.
- 7) Weinstein, M. and Chuang, S.: Diseases of the white matter. In: Latchaw, R. E. (ed.). MR and CT imaging of the head, neck, and spine. St Louis, Mosby Year Book, 1991, p.382-388.
- 8) Nowell, M. A., Grossman, R. I., Hackney, D. B., Zimmerman, R. A., Goldberg, H. I. and Bilaniuk, L. T.: MR imaging of white matter disease in children. *A. J. N. R.*, **9**:503-509, 1988.
- 9) Altman, N.: Neuroimaging of macrocephaly. *Int. Pediatr.*, **6**:135-139, 1991.
- 10) Arend, A. O., Leary, P. M. and Rutherford, G. S.: Alexander's disease: a case report with brain biopsy, ultrasound, CT scan and MRI findings. *Clin. Neuropathol.*, **10**:122-126, 1991.
- 11) Bobele, G. B., Garnica, A., Schaefer, G. B., Leonard, J. C., Wilson, D., Marks, W. A., Leech, R. W. and Brumback, R. A.: Neuroimaging findings in Alexander's disease. *J. Child Neurol.*, **5**:253-258, 1990.
- 12) Rankin, W. E., Hart, M. N. and Weisenburger, D. D.: Thrombotic, thrombocytopenic purpura in a child with Alexander's disease. *Arch. Pathol. Lab. Med.*, **101**:655-656, 1977.