Neuroacanthocytosis in Japan – Review of the Literature and Cases

G. Hirose

Abstract Since the first case report of this disease in 1974, a total of 71 cases of probable chorea-acanthocytosis (ChAc) were collected in Japan up to the end of 2006. These reports were reviewed for their clinical features and to document research achievements in Japan in this field. Whilst the clinical phenotype of these patients was typical of ChAc, most of these cases were diagnosed clinically without molecular diagnosis, so the diagnosis of McLeod syndrome cannot be completely excluded.

The mean age of onset was 30.5 (range 18–42) years and the male:female ratio was 18:7. Involuntary movements consisting of oro-lingual-facial dyskinesias and choreiform limb movements were seen in over 90% of cases. Self-mutilation of the lower lip was also seen with the same incidence. Depression or absence of deep tendon reflexes was noted in almost all cases. Cognitive impairment with or without psychiatric symptoms was noted in 40% of cases. The degree of acanthocytosis of peripheral red blood cells varied from 6 to 80% (mean value 24%). Serum creatine phosphokinase activity was increased in 86%. Computed tomography of the brain revealed symmetrical atrophy of the caudate nuclei in almost all cases examined. Forty percent of patients had seizures. The mode of transmission was predominantly autosomal recessive, but four families have been reported with apparent dominant inheritance. Sural nerve biopsy showed evidence of chronic denervation with axonopathy. Grouped atrophy of muscle fibers was also reported, but recent studies suggest a primary disorder of the muscle membrane or muscle fibers as a...
cause of elevated creatine kinase. *Post mortem* examination of the brain revealed marked neuronal loss and gliosis affecting the caudate nucleus and pallidum. The cerebral cortex and substantia nigra seemed to be spared. 15 cases of McLeod syndrome were identified in Japan between 1994 and 2006.

Many scientific advances were made in Japan with respect to ChAc. The red cell membrane pathology was studied morphologically as well as biochemically. Abnormal conformation of the red cell membrane was found, with an increase of palmitic and docosahexaenoic acids and a decrease of stearic acid. A mutation in the gene coding for a protein designated “chorein” was found and reported in a Japanese family with autosomal recessive inheritance, and a new single heterozygous frame shift mutation was also found from a family with apparent autosomal dominant inheritance. In addition, a gene-targeted mouse model of ChAc was reported from our country. The future of research in the area of ChAc in Japan is very promising.

1 Introduction and Historical Review

Levine and his colleagues [19] and Critchley and his associates [5] independently published a new syndrome of hereditary neurological disease with acanthocytosis in two different families, the Goode family from New England and the Stevens family from Eastern Kentucky in 1968. Thereafter another three families were reported, two from England and one family from the United States. However, recognition of the disease in Japan was delayed for about 10 years.

The first case of probable ChAc was reported in a local medical journal of Hiroshima Prefecture, the Journal of the Hiroshima Medical Association, in 1978 by Professor Kito and colleagues [11] of Hiroshima University Medical School. Clinical studies were reported, in addition to scanning microscopic findings of acanthocytes, neurogenic atrophy of muscle fibers, and caudate nucleus atrophy, in a 50-year-old man with a family history of a similar neurological disease in his younger brother and paternal uncle. The authors published a detailed family pedigree with apparent autosomal dominant inheritance in 1980 [16]. The authors claimed that their family was the first with this disorder in Japan and the sixth family in the world. However, looking back at previous reports of this disorder in our country, there is an earlier case report by Shimizu et al. [32] in 1974. These authors described an adult patient with self-mutilation, choreoathetosis, hypotonia, areflexia and normouricemia. They considered this patient to have a new disease, distinct from Lesch–Nyhan syndrome, without recognising acanthocytosis. In 1978 [33], however, they found acanthocytes in the patient’s younger brother in addition to the patient. The authors subsequently reported the family in more clinical detail, and also found a reduced ratio of C24:1/C24:0 fatty acids in sphingomyelin from red cell membranes [14].