Clinical and biochemical findings of GM1 gangliosidosis in Shiba dogs

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GM1 gangliosidosis is a lysosomal disease due to a deficiency of acid b-galactosidase. The substrates of the enzyme, such as GM1 ganglioside and glycoconjugates with terminal b-D-galactoside accumulate in the brain and the other visceral organs. This disease is manifested as progressive motor dysfunction and is inherited as an autosomal recessive trait. There have been very few reports about animals affected with GM1 gangliosidosis. The canine disease has been described only in four European breeds. The present study described the clinical and biochemical characteristics of GM1 gangliosidosis observed in Shiba dogs, and compared it with human and other canine GM1 gangliosidosis. In addition, several lysosomal enzyme activities were measured in normal dogs and cats to evaluate the efficacy for the diagnosis of lysosomal diseases in animals.

Shiba dogs with GM1 gangliosidosis manifested signs of progressive neurologic disorders. At 5 to 6 month after the birth, the affected dogs showed mainly ataxia. The dogs were not able to stand at 8 to10 months and became mentally alert and showed a visual deficit at 9 to10 months. In blood examination, some lymphocytes with large vacuoles in their cytoplasm were found on blood smear. In the brain of the affected dogs, the amount of GM1 ganglioside was 10 to 20 times the normal level and the activities of b-galactosidase in leukocytes and tissues in those dogs were greatly reduced. The GM1 ganglioside, however, was not accumulated in the brain of a newborn dog affected with b-galactosidase deficiency. This result suggested that the degree of substrate storage is correlated with the severity of the clinical manifestations. In addition, the activities of the other lysosomal enzymes in the affected dogs were elevated when compared with normal dogs, suggesting a compensatory function against a b-galactosidase deficiency. Analysis of the pedigree of the Shiba dogs affected with GM1 gangliosidosis revealed that heterozygous carriers possess leukocytes with approximately 50% of normal enzyme activity, suggesting that this disease in Shiba dogs was transmitted through an autosomal recessive pattern of inheritance. There were some significant differences in the clinical and biochemical characteristics between the present cases of Shiba dogs and other canine GM1 gangliosidosis reported. These discrepancies may due to the different mutations of the b-galactosidase gene. The clinical features in the present Shiba dogs with GM1 gangliosidosis were similar to those in the human juvenile form, but the biochemical features to those of the human infantile form.

There were significant differences between normal canine and feline lysosomal enzyme activities. These results suggested that establishment of the reference values of the lysosomal enzyme activities in each species was needed for the diagnosis of lysosomal diseases.