Enzyme kinetic analysis of leukocyte β-galactosidase in Shiba dogs with GM_1 gangliosidosis

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GM_1 gangliosidosis is a lysosomal disease due to a deficiency of acid β-galactosidase. The substrates of the enzyme such as GM_1 ganglioside and glycoconjugates with terminal β-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. In human beings, GM_1 gangliosidosis is classified into type 1 (infantile form), type 2 (juvenile form), and type 3 (adult form) on the basis of clinical signs and symptoms. For studies on therapeutics of the disease, animal models that are suitable for each type of the human disease are highly desirable. However, it has been impossible to classify the canine disease on the basis of clinical signs and symptoms. In the present study, enzymatic characteristics of leukocyte β-galactosidase in Shiba dogs with GM_1 gangliosidosis were investigated, and the results obtained were compared with the human disease in order to evaluate the significance of the disease as animal model of the disease.

The leukocyte β-galactosidase in affected and normal dogs was examined using 4-methylumbelliferyl-β-D-galactoside (4-MU-β-gal) and *p*-nitrophenyl-β-D-galactoside (PNP-β-gal) as artificial substrates. The Km of the enzyme in the affected dogs (4-MU-β-gal : 1.07 mM and PNP-β-gal : 2.43 mM) was markedly higher than the value in the normal dogs (4-MU-β-gal : 0.16 mM and PNP-β-gal : 0.05 mM), showing that the affinity of the enzyme to these substrates in the affected dogs was markedly lower than that in the normal dogs. The optimum pH (pH 3.2) in the affected dogs was lower than in the normal dogs (pH 3.8) when 4-MU-β-gal was used as a substrate. Higher residual enzyme activity was found in the affected dogs than in the normal dogs, suggesting greater resistance of the enzyme in the affected dogs to heat inactivation at 42℃ than that in the normal dogs. The enzymologic characteristics found in the affected Shiba dogs were similar to those of the infantile form of the human disease.

In conclusion, the results suggest that Shiba dogs with GM_1 gangliosidosis are a suitable animal model for the study of the human infantile form of the disease on the basis of the enzymologic characteristics.