Clinicopathologic findings of GM_1 gangliosidosis in Shiba dogs

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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-galactose accumulate in the brain and visceral organs. This disease is manifestated as progressive motor dysfunction and is inherited as an autosomal recessive trait. Only conservative therapy has been performed for the human disease. For testing various therapeutic programs, spontaneous animal models are expected to provide a versatile *in vivo* system. In veterinary medicine, it is difficult to diagnose the disease of affected dogs as GM_1 gangliosidosis because there are few clinicopathologic markers to support the diagnosis of the canine disease. The present study describes the clinicopathologic and neurochemical characteristics of GM_1 gangliosidosis observed in Shiba dogs in order to clarify the scientific characteristics as an animal model and to define useful markers for supporting the diagnosis of the canine disease.

In blood examinations, some lymphocytes with large vacuoles in their cytoplasm were found on blood smears of affected dogs. The abnormal vacuolation was observed in approximately 40% of lymphocytes and the rate of appearance did not correlate with the ages of the dogs. In cerebrospinal fluid (CSF) examinations, aspartate aminotransferase (AST) and lactate dehydrogenase (LDH) activities in CSF were significantly higher in affected dogs than in normal dogs. In general, the central nervous system possessed relatively high activities of these enzymes. The increases of AST and LDH activities in CSF were thought to be responsible for release from the central nervous system tissues. In addition, there was a significant positive correlation between AST activity in CSF and the ages of the affected dogs, suggesting that the degree of AST activity in CSF reflects the severity of central nervous system degeneration.

GM_1 ganglioside increased in the cerebellum, cerebrum and spinal cord according to the age of the affected dog. The extent of the accumulation of GM_1 ganglioside in the following order: cerebellum>cerebrum>spinal cord. The degree and localization of the substrate accumulation were correlated with the characteristics and severity of the clinical manifestations. On the other hand, GD_{1a} ganglioside increased in the cerebellum and cerebrum in the affected dogs until 3-6 months after birth and then rapidly decreased. The change of GD_{1a} ganglioside may be associated with the onset of the disease (5-6 months old).

In conclusion, the vacuolation of peripheral lymphocytes and the significant increase of AST and LDH activities in CSF were useful clinicopathological findings for the diagnosis of GM_1 gangliosidosis in Shiba dogs.