

Magnetic resonance imaging of G_{M2} -gangliosidosis in a golden retriever

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G $_{M2}$ -gangliosidoses are a rare group of lysosomal storage diseases caused by excessive accumulation of G_{M2} -ganglioside (G_{M2}) in neurons. They are manifested by progressive neurological disorders involving motor and psychointellectual dysfunctions and visual defects (1). There are 3 main forms of G_{M2} -gangliosidosis: B variant (Tay-Sachs disease), resulting from deficient activity of lysosomal β -hexosaminidase (Hex) A, but normal Hex B; variant 0 (Sandhoff disease) with deficient activities of both Hex A and Hex B; and AB variant, resulting from the G_{M2} -activator protein deficiency instead of normal Hex A and Hex B. Briefly, the deficiency of either Hex A activity or G_{M2} -activator protein results in the accumulation of G_{M2} and the onset of similar neurologic deterioration.

In domestic animals, naturally occurring G_{M2} -gangliosidosis has not been investigated to the point of determining a definitive diagnosis because of difficulties with the differential diagnosis based on clinical symptoms and the biochemical diagnosis with specimens from living individuals (2). Thus, until now, the disease has been reported in only 3 canine breeds (3–6), 3 feline breeds (7–9), Yorkshire pigs (10), and Muntjak deer (11).

In this report, findings on magnetic resonance imaging (MRI) of a golden retriever with Sandhoff disease are described, previously identified as the 1st canine case with deficiencies of both Hex A and Hex B (6). It also describes clinical and clinicopathologic features of the dog, which were not reported in the initial paper.

A 15-month-old, neutered male, golden retriever was referred to the Veterinary Medical Center at the University of Tokyo for evaluation of progressive neurologic abnormalities, including depression, dementia, ataxia, and blindness, which were first observed at 11 mo of age. Upon admission, the dog had fallen into a stupor. On physical examination, bilaterally, the pupils were miotic and pupillary light reflexes were absent. The dog did not respond to auditory stimuli. Palpebral reflexes and thoracic and pelvic limb reflexes were weak; however, flexor reflexes seemed normal. All data from a

complete blood cell count and serum chemical analysis were within normal ranges.

Since serious abnormalities in the central nervous system were suspected, the dog was submitted for an MRI examination on a 0.3 Tesla unit (AIRIS; Hitachi, Tokyo, Japan) without sedation. The nucleus caudatus displayed bilateral T2 hyperintensity and T1 hypointensity (Figure 1A). This lesion was not enhanced by administration of gadolinium-diethylenetriamine penta-acetic acid (DTPA), IV. In addition, mild atrophy of the cerebral cortex was observed, especially in the temporal lobe (Figure 1B). No obvious abnormality was detected in other regions.

Analyses of cerebrospinal fluid (CSF) revealed a normal number of leukocytes ($< 2/\mu\text{L}$), normal glucose (4.5 mmol/L; reference range, 1.9 to 7.8 mmol/L), and total protein concentrations (290 mg/L; reference range, 100 to 400 mg/L). The immunoglobulin-G titer against canine distemper virus was below the detection limit ($< 1:3$). Glucocorticoids and supportive therapy were not beneficial, and the dog died 1 wk after being admitted. A necropsy was not permitted by the owner. Consequently, tentative diagnosis was established by demonstrating the deficient activities of Hex A and Hex B in peripheral leukocytes, and by determining the level of G_{M2} in the CSF (2,6).

Clinical symptoms of human cases of Sandhoff disease have been reported to be spasticity, dystonia, rigidity, choreiform movements, and blindness (1,12), most of which were observed in the present case. On the other hand, although tonic-clonic or myoclonic seizures are frequently observed in human cases (1), there was no history of seizures in this case.

This is the first MRI report of canine G_{M2} -gangliosidosis. While there have been few MRI reports in cases of human G_{M2} -gangliosidoses, abnormal signal intensities in the thalamus and basal ganglion, and cerebral atrophy seem to be the most common findings (12,13). In the early stages of the disease, the thalamus and basal ganglion are reported to exhibit focal T2 hyperintensity and T1 hypointensity, which presumably represent loss of axon and myelin, gliosis, and intralysosomal storage (12). In the later stages, these regions were found to change to hypointense on T2-weighted images due to local calcification (13). On the other hand, an MRI study on feline cases of Sandhoff disease demonstrated the broad hyperintensity of white matter on T2-weighted images (14). The MRI changes observed in this case may be specific to the disease in dogs. An MRI abnormality specific to

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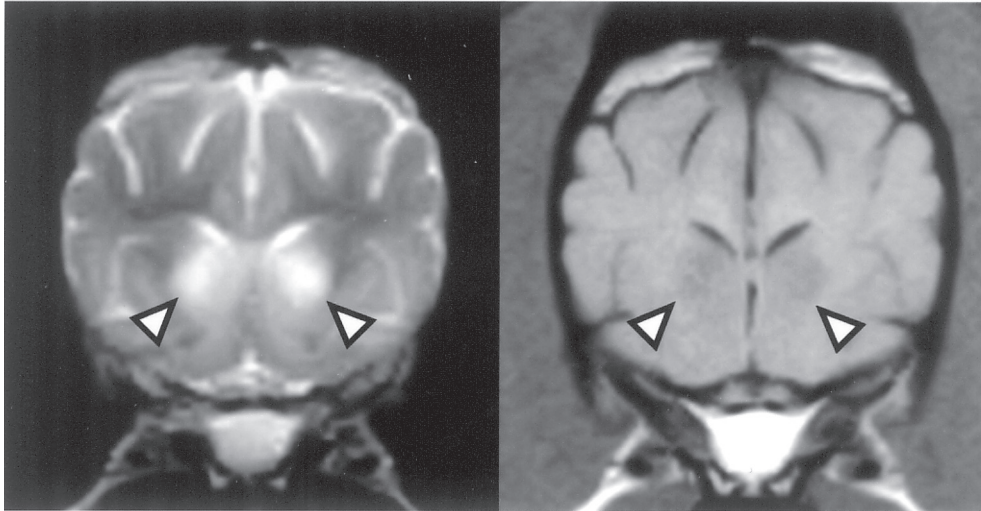
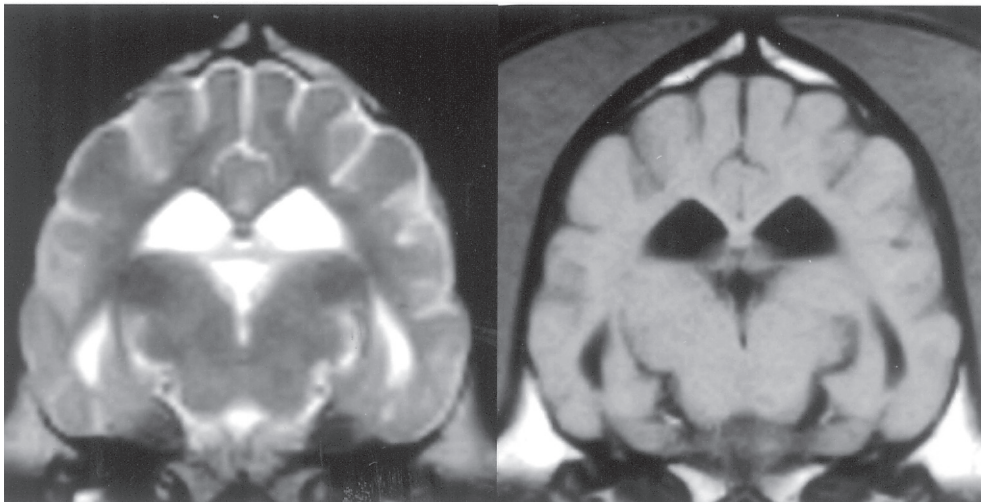
A**B**

Figure 1. (A) Transverse T2-weighted image at the level of nucleus caudatus (left: TR/TE = 4500/119 ms). There are symmetrical hyperintense areas in nucleus caudatus (arrows) that display mild hypointensity on the T1-weighted image (right: TR/TE = 700/20 ms). (B) Transverse T2 (left: TR/TE = 4500/119 ms)- and T1 (right: TR/TE = 700/20 ms)-weighted images at the level of hippocampus. Mild atrophy of the cerebral cortex is observed.

the basal ganglion is very rare in canine brain diseases, and such a change could be characteristic of canine Sandhoff disease. However, data on more affected dogs will be needed to specify the MRI findings of the disease.

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BOOK REVIEW



COMPTE RENDU DE LIVRE

Melo EC, Gerster F. *Veterinary Services: Organization, Quality Assurance, Evaluation*. Office International des Épizooties, Paris, France, 2003. 414 pp. ISBN 92-9044-596-3. 45€.

The roles of veterinarians and the contributions of veterinary medicine to today's society are varied and vast. One such role, often unnoticed and undervalued, is that of international animal health.

This compendium of 31 papers presents a comprehensive picture with examples from multiple countries of the approaches and perspectives taken in different areas of the world. The broad subject areas fall into the challenges facing veterinary services in the currently changing international environment, the organizational design of veterinary services, approaches taken to assure the quality of products and performance, and finally examples of systems and tools to evaluate the adequacy and competence of the Veterinary Services.

No one system or approach is universally effective. However, this volume offers an opportunity to understand and compare the rationale of a number of countries in attempting to respond to the massive challenges of international animal health in a rapidly evolving international milieu.

To exemplify these concepts, the compendium identifies that the Veterinary Services must apply the skills, knowledge, and resources of the veterinary profession to the protection and improvement of human and animal health. But the official Veterinary Services must also play the role of "guarantor," and it needs a verifiable credibility to do so. There is no single organizational scheme for the Veterinary Services, only an evaluation of its effectiveness.

To perform this role, risk analysis becomes an indispensable instrument for justifying protective measures and for ensuring access to international markets.

Particularly in developing countries, cooperation of the public and private sectors in animal health programs is essential. There is a new role for private sector professionals in the evolution of the Veterinary Services for future sustainability. This role must be included in international guidelines, especially since developing countries often do not have the range of skills required for risk analysis, which is of strategic importance to trade.

Similarly, the role of laboratories is integral to the success of animal health systems, be it as a network of laboratories, as a central reference laboratory, or as regional laboratories.

Also of importance is a method with criteria for the optimal distribution of available human resources.

At the base of global efforts to achieve fair international trade is the World Trade Organization (WTO) Agreement on the Application of Sanitary and Phytosanitary Measures. This Agreement seeks to balance the rights and obligations of trading countries. The WTO recognizes the Office International des Épizooties (OIE; World Organization for Animal Health) as the scientific reference for animal health and zoonoses.

To meet its responsibilities in this regard, the OIE produces standards and guidelines for safe international trade in the OIE Terrestrial Animal Health Code. As well, it recommends fundamental principles for the Veterinary Services and guidelines for their evaluation.

An evaluation of the Veterinary Services of an exporting country is a key element in risk analysis. Actually, the evaluation of the quality assurance systems in the delivery of veterinary services, in surveillance and monitoring and in a coregulatory approach in meat inspection, will reinforce international confidence in the reliability of the Veterinary Services performance.

As a tool for such an evaluation, the development of an extensive questionnaire is presented.

In the failure of 2 trading countries to reach an agreement, various options are offered for the resolution of such trade disputes.

Of the 31 papers included in this compendium, 15 are presented in English, 8 in French, 4 in Spanish, 3 in both English and French, and 1 in both English and Spanish. However, all summaries are offered in the 3 official OIE languages (English, French, Spanish).

Since a number of authors are involved in these papers, there are significant differences in style, which tend to make a direct reading a little more difficult. The volume does, however, offer itself as an unique and very valuable reference to the many aspects of the delivery of the Veterinary Services, particularly in the international milieu. The strong endorsement of the OIE, recognized as the most prominent international organization for animal health, contributes significantly to its credibility.

This, therefore, is an important source of information on the current and evolving international thinking on the role of the Veterinary Services.

Thus, as clearly identified in this volume, this area of veterinary medicine plays a fundamental role in promoting the well-being of society, the security of the food supply, and the economic vitality of the agro-food industries.

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