

A genetic disease of Shiba dogs (GM1 gangliosidosis)

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Introduction

When genetic information (DNA) in a cell nucleus is copied at cell division, a **mutation** may occur at a very low probability. When mutation takes place during the process of producing generative cells (sperms and ova), it may cause genetic diseases and the mutation may be inherited to the offspring. However, as offspring inherits sets of genetic information from the father and mother, respectively, at the same amount (making pairs of genes), when a mutation occurs in only one of the pair, there is no onset of a disease but when it occurs in both of the pair, there is an onset of a disease. This kind of genetic diseases are called **recessive hereditary diseases**. In a word, recessive hereditary diseases are manifested only when the same causal mutation of a disease is inherited from both the mother and father.

When both the father and mother have only one same mutation (these individuals are called “**carrier**” and healthy like a normal individual), by crossing the two carrier dogs, one onset individual, which would have a disease, is born at a probability rate of 1/4 (25%). As you see Figure 1A, the probability is that one onset individual, two carriers and one normal individual would be born by crossing two carries (if four babies are born). The probability of having a male onset individual and that of having a female onset individual are the same. In addition, as Figure B below shows, when one parent is a carrier and the other is a normal one, no onset dog would be born but half of the baby dogs would be carriers. Obviously, as shown in Figure 1C, when both parents are normal, all the baby dogs are normal.

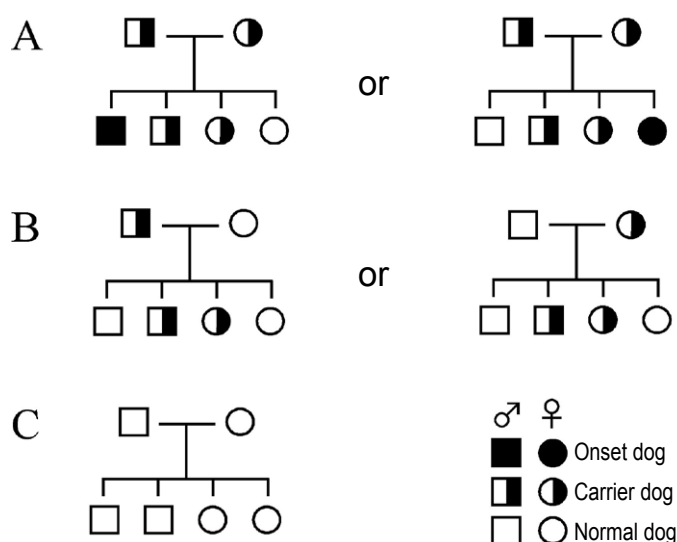


Figure 1. Crossing patterns regarding genetic diseases

In the natural probability distributions, a crossing pattern shown in 1A is rare. But, when crossing close relative individuals in the same kennel, it may happen, and an onset individual may be born incidentally. In the process of manifestation of an onset dog, crossing seen in Figure 1B would be repeated, there would be many carrier dogs in the kennel without being realized. For example, when a dog with a disease is found for the first time, immediately the dogs of the kennel may be examined, but there are already many carrier dogs into the kennel. This has happened in many cases.

[GM1 Gangliosidosis]

A genetic disease often seen in Shiba dogs is gangliosidosis. GM1 gangliosidosis is one of

50 lysosome storage diseases. Due to the mutation of GLB1 gene (c1647delC), an enzyme β -galactosidase is absent to cause this **lethal neurodegenerative disease**. An onset dog would die at the age of a little over one with the clinical development (progressive movement, visual and cognition disorders) shown in Figure 2. Unfortunately, there is no effective treatment method for the disease. Gangliosidosis is manifested when a dog is still very young and cute, and the condition is gradually aggravated regardless of intensive care. At the final stage, the dog becomes unable to recognize the owner or caretaker and dies. The dog owner is exposed to tremendous mental stress (grief, illogicality, etc.) and the stress is converted into a great rage, which may lead to a trouble involving the breeder, seller and dog registration association.

Even if a breeder has never seen dogs contracted with gangliosidosis in his kennel in the past, it can't be assured that there is no carrier dog of gangliosidosis in his kennel. The number of carriers may have increased without being noticed. Thus, when an onset dog is found, there should be quite a lot of carriers already and it is extremely difficult to take measures to prevent the disease at the time point.

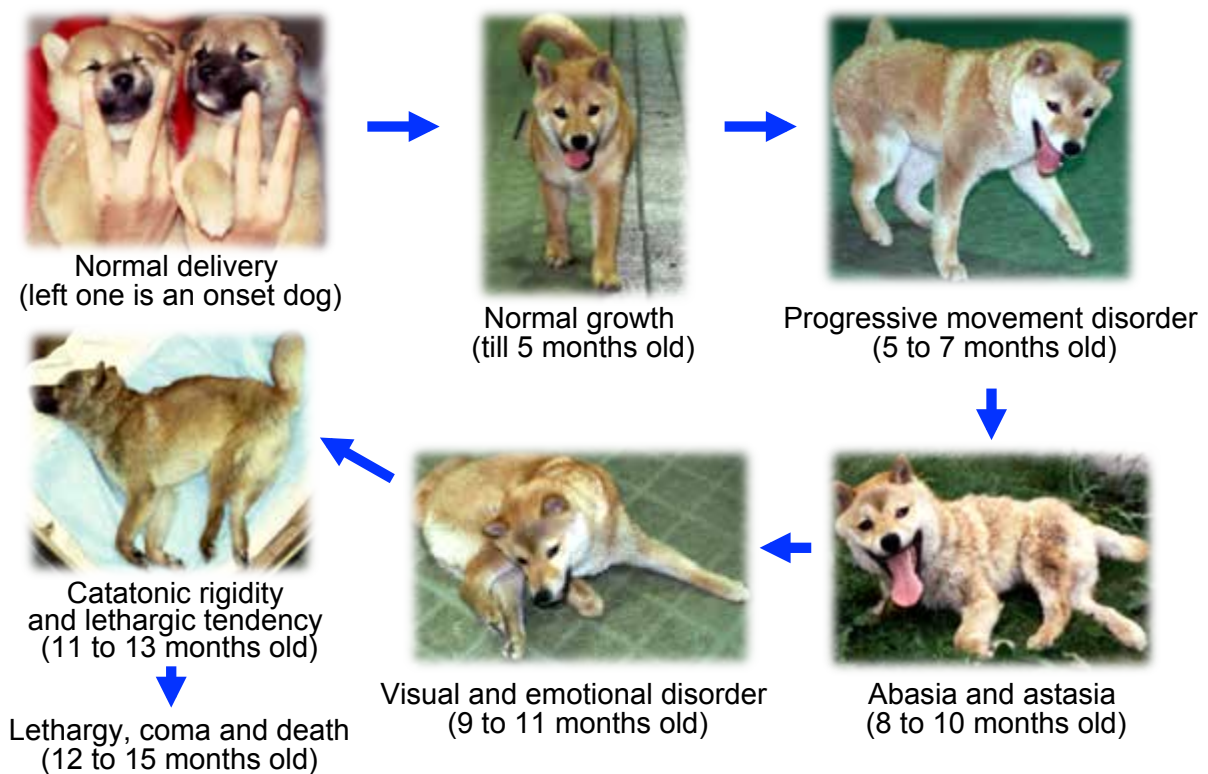


Figure 2. Clinical course of GM1 gangliosidosis in Shiba dogs

[Occurrences]

Definite diagnosis of GM1 gangliosidosis was made in about 30 cases from Hokkaido to Kyushu in Japan. However, this doesn't mean that the actual occurrences are 30 but that most of the onset cases just may have not been reported. Based on a randomly conducted survey on groups of Shiba dogs in whole Japan, the carrier rate is about 1 %. However, the carrier rate in Kinki region is about 3%, which is higher than other areas, and the rate is also expected to be higher in Chugoku and Shikoku regions.

The carrier rate of 1 to 3% means one carrier in 30 to 100 Shiba dogs. Since 30,000 to 40,000 Shiba dogs are born annually, more than several hundreds of carriers are born annually. Furthermore, by crossing the carriers, several onset dogs are born per year. Regarding gangliosidosis, in the past 10 and more years (nearly 20 years), the author's scientific literatures (for international journals) and commentaries (for veterinary magazines in Japan) have been widely published and the disease is well-known worldwide in the field of veterinary, but many veterinarians, breeders and owners in Japan are still unaware of the existence of this disease. Therefore, it is assumed that many onset dogs have not been diagnosed with gangliosidosis and died of unknown causes somewhere.

The first onset dog diagnosed by the author was a male dog born in 1997, however, it is assumed that the symptoms must have been manifested much earlier, and the dogs must have died with no clear causes found when they became a little over one year old in reality. It is also assumed that a mutation, which is the cause of this disease, happened even much earlier. It needs several or tens of years to see an onset dog since the occurrence of the mutation. In addition, excellent dogs which can be **a champion in exhibitions** may accidentally become a carrier. Because, as champion dogs are crossed with many female dogs, if a mutation happens in a champion dog, the mutation can be passed down to a lot of offspring. This is because when a carrier dog is crossed with a normal one, half of the baby dogs become carriers (refer to Figure 1). If a kennel accidentally has a champion dog which is also a carrier, dogs with the mutation to cause gangliosidosis must be prevailing in the kennel and the disease is spreading even outside of the kennel by crossing with dogs of other kennels. The phenomenon that a mutation rate suddenly increases in a certain population is called "**founder phenomenon**". Starting from a kennel where a mutation is prevailing, onset dogs are sporadically reproduced unintentionally. Therefore, if you depend only on your experience that you have not seen an onset dog in your kennel, you may have a big problem.

[Preventive measures]

As the causal mutation for GM1 gangliosidosis in Shiba dogs was already clarified by the research of the author in 2002, **genetic screening** has been available since more than ten years ago. Although the author has claimed the importance of genetic screening on many and various occasions, the information has not been spread well in Japan and preventive measures have not been implemented, which is regrettable. On the other hand, people have been well-aware of the prevention of genetic diseases overseas, and we were requested by Shiba Dog Club overseas (Czech Republic) to conduct genetic screening of stud dogs there in around 2005 (Figure 3). The difference in the awareness between Japan and overseas is very clear.

The benefit of genetic screening is to enable diagnosis of not only onset dogs but also carrier dogs in a similar way. For the exam, only a small amount of DNA sample is needed, and the DNA sample can be extracted from a small amount of not only blood but also oral mucosa and saliva.

By excluding dogs judged to be a carrier from the reproduction line, gangliosidosis can be perfectly prevented. However, if a dog is extremely excellent but is also a carrier, the dog can be crossed with normal female dogs (Figure 1B), and all the offspring is screened to choose excellent baby dogs with normal genes for reproduction to pass down the excellent nature. When the number of carriers is rather high, if all the carriers are removed from the reproduction line, the inbreeding rate would increase and

a risk that an unknown latent genetic disease might be manifested would increase as well. Therefore, a rapid increase in inbreeding rate should be avoided without failure. This is because too strict and quick measures to exterminate an existing genetic disease may cause an adverse effect to spread other multiple genetic diseases.



Figure 3. Shiba Dog Club in Czech Republic (in 2005) and DNA sampling (oral mucosa)

[Carriers and animal ethics]

Dogs judged to be a carrier by genetic screening are totally healthy and same as normal dogs as a pet. Although carriers should be avoided for the use of reproduction as much as possible (as described above, they may be crossed with normal dogs in some conditions in many cases), there is no problem to sell them as a pet (actually, they have been sold without screening). However, when carriers are sold or transferred as an inbreeding dog, it causes a very serious problem to degrade the trust in the whole association. Also, if there are some people who are against selling carrier dogs as a pet, they lack **animal ethics** and are unqualified for keeping a dog. Actually, it is considered that there are no animals including humans who are not any of genetic carriers, which means anybody has some genetic mutations. If carrier dogs are disposed of by humans, it is a big problem concerning animal ethics, and such kennels and organizations may not even be able to exist in the future. In the international society (Japan is part of the international society), breeders and organizations are required to act paying full attention to animal ethics.

[Conclusion]

I would repeat again that GM1 gangliosidosis in Shiba dogs is an internationally well-known fact now (from about 20 years ago). Highly conscious Shiba dog fans all over the world already know the content described here as common knowledge. Therefore, if a breeder, who is a specialist of Shiba dogs, or a veterinarian, who is a specialist of diseases, doesn't know about this disease, he/she can't give any excuse to the owner of a Shiba dog for the ignorance. Those breeders or veterinarians may lose people's trust in them due to their lack of knowledge.

Everybody must feel that now is the age of accountability for not taking preventive measures. I wonder that the responsibility for not having taken preventive measures for a long time is under question now. We should take some measures now, otherwise we may have no future.

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