Systemic Ceroid-Lipofuscinosis in a Japanese Domestic Cat

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ABSTRACT. An 11-month-old castrated male Japanese domestic cat was euthanized because of neurological symptoms such as shivering and difficulty of walking. Histopathological examination showed glial proliferation and marked deposition of ceroid-lipofuscin in the neuronal and glial cells of the brain. Ceroid-lipofuscin was deposited also in reticuloendothelial cells of the liver, spleen and some lymph nodes.—Key words: ceroid-lipofuscinosis, feline.

Ceroid and lipofuscin had been thought to be complexed lipid compounds resulting from hyperoxidation of unsaturated fatty acid [16, 21]. The former is seen in the macrophages infiltrated into the lesions of yellow fat steatitis in the cat [14] or brown gut disease in the dog [14]. The latter is often found in neuronal cells, myocardial cells or hepatocytes of aged or wasted animals [14]. These compounds, however, show very similar histopathological characteristics. It is difficult to distinguish them, so they are often called together as ‘ceroid-lipofuscin’. Recent studies on ovine ceroid-lipofuscinosis, however, revealed that the stored material was the lipid-binding protein of mitochondrial ATP synthase [12].

The inherited type of a ceroid-lipofuscin storage disorder has been reported in human [26] and various animal species including dogs [1, 4, 10, 15, 19, 22-25], cats [7], horses [9, 12, 13], goats [6], cattle [8, 20] and non-human primates [11]. In dogs, several reports are available in order to analyze the feature of the disease. There are two types of the canine ceroid-lipofuscinosis; systemic type observed in juvenile dogs less than 2 years old [15, 19, 25] and aural type in older dogs [4, 10, 24]. In cats, however, only 2 cases were reported, both of which were juvenile type seen in 22 months and 2 years old Siamese cats and the lesions were restricted to the neural tissue [7]. The present report describes systemic ceroid-lipofuscinosis observed in a 11 months old Japanese domestic cat.

A 7-month-old castrated male Japanese domestic cat presented shivering and difficulty of walking. By computed tomograph (CT) examination, lateral and fourth ventricles of the brain were dilated. Although glycerol, prednisolone, physiolsol and acetazolamide treatment was performed, the symptom was not improved. The cat was euthanized 4 months after the onset of the disease and autopsied shortly after the death. The familial history of the cat was unknown.

Gross examination revealed that both the cerebrum and cerebellum were moderately atrophied, being yellowish brown, and showed prominent sulci on the surface (Fig. 1). On cut surface, lateral and fourth ventricles were dilated and the cerebral cortex was atrophied. Skull bone was thickened and osseous cerebellar tent was deeply protruded into the fissura transversa cerebri. The liver was brown in color and small yellowish white nodules less than 1 mm in diameter were scattered on the surface and cut surface of the liver. Other organs showed no gross lesions.

Tissues were fixed in 10% neutral buffered formalin solution and embedded in paraffin after dehydration in an ethanol series. Four micrometer sections were stained with hematoxylin and eosin (HE). Sections from the brain, liver, spleen and lymph nodes were also applied for periodic acid Schiff (PAS), Nile blue, Sudan black B, acid fast, luxol fast blue (LFB) and Masson’s trichrome stainings. Unstained sections were observed with a fluorescent microscope using blue or ultraviolet excitation. Immunohistochemical staining was performed on the brain sections using rabbit anti-glial fibrillary acidic protein (GFAP) serum (Dako, Carpinteria, CA, U.S.A.) as a first antibody. Ultrathin sections were made by a routine procedure and observed under a JEM 1200 EX electron microscope.

In the whole of cerebral cortex, higher cellularity was observed, compared with that of a normal cat of the same age (Fig. 2). Two types of glial cells proliferated in the lesion; one was astrocytes showing pleomorphic shape and long processes and identified by the immunohistochemical method using anti-GFAP serum, and the other was microglia which were filled with semi-transparent light-yellowish substance (Fig. 3). The same substance was also seen in neurons which were decreased in number compared with a normal control. Histochemical nature of the substance was reddish purple with PAS reaction, dark blue with Nile blue, black with Sudan black B, light blue with Masson’s trichrome, partly blue with LFB and light red with acid fast stain. This substance showed yellowish green autofluorescence under a fluorescent microscope. Ultrastructurally, the substance was aggregates of electron-dense pleomorphic granular materials which consisted of much finer dot-like granules (Fig. 4). Together with the results of histopathological nature of the substance, it should be ceroid-lipofuscin. In some regions of the cerebral cortex, unrelated to the ceroid-lipofuscin accumulation, spongy degeneration of neuropil, perivascular cuffing and small glial nodules were observed.

In the cerebellum of the cat, Purkinje cells and nerve cells of granular layer were markedly decreased, and the remaining cells were atrophic. Nerve cells and proliferated microglial cells in the granular layer also contained ceroid-lipofuscin granules (Fig. 5). Deposition of ceroid-lipofuscin was detected in the Kupffer cells of the liver and certain reticuloendothelial...
Fig. 1. Gross appearance of the brain. Both the cerebrum and cerebellum are atrophied. Sulci of the cerebrum are prominent.

Fig. 2. High cellularity of the cerebral cortex due to glial proliferation. HE. × 130.

Fig. 3. Glial proliferation in the cerebral cortex. Astroglia are stained black (arrows). Many microglia containing ceroid-lipofuscin (arrow heads) are also seen. Immunostain for GFAP. × 400.

Fig. 4. An electron micrograph of a cerebral microglial cell. Pleomorphic electron-dense granules are seen in the cytoplasm.

N: Nucleus. bar = 1 μm.

Fig. 5. Border between the granular and molecular layers of the cerebellum. Loss of Purkinje cells and ceroid-lipofuscin-containing microglia (arrow heads) are observed. HE. × 400.

Fig. 6. A cervical lymph node. Ceroid-lipofuscin-containing macrophages are gathered in the lymphatic sinus (arrow heads). PAS. × 400.

cells of the spleen. In cervical superficial lymph nodes, many macrophages containing ceroid-lipofuscin aggregated in the sinuses (Fig. 6). Histochemical features of the ceroid-lipofuscin granules in these reticuloendothelial cells were the same as those in the brain. No other organs and cells showed ceroid-lipofuscin deposition.
According to the findings, the present case was diagnosed as ‘feline systemic ceroid-lipofuscinosis’. Ceroid-lipofuscinosis has been reported in human [26] and a variety of mammalian species [1, 4, 6–13, 15, 19, 20, 22–25] as described before. The lesions of the 2 Siamese cats which are the only reported cases of feline ceroid-lipofuscinosis, were limited to the brain [7]. The present case was the first case of feline systemic ceroid-lipofuscinosis. The authors of the previous report [7] said that the disorder might be inherited and that the extensive inbreeding in pure bred cats might cause the condition or other types of feline lipid storage diseases such as Niemann-Pick-like disease [3, 17] and GM1 gangliosidosis [2, 5]. The present case is inconsistent with those cases because of systemic involvement of the lesion and onset in a Japanese domestic cat that is highly mixed population in Japan. Although genetic background of the patient cat could not be traced, it is possible that this cat was born in a closed colony.

Acquired type of ceroid deposition is well known in cats, that is yellow fat steatosis caused by vitamin E deficiency [14]. Ceroid deposition followed by lipodisis in the liver and related lymph nodes was also observed in four dogs and one cat [18]. These conditions might be caused by acquired malfunction of lipid metabolism and were not inherited. As the present case did not show any steatitic lesion and fatty change in the liver, it is not involved in the acquired conditions.

REFERENCES