Giant Cell Hepatitis in Two Young Cats

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ABSTRACT. A very rare case of the liver lesion characterized by formation of multinucleated giant hepatocytes with inflammatory cell infiltration were observed in two young (1.5 years and 2 years old) cats bearing thymic malignant lymphoma. Histopathological features of this liver lesion were very similar to giant cell hepatitis (GCH) in human neonates and infants. Therefore, the lesion was diagnosed as feline GCH.

KEY WORDS: feline, giant cell hepatitis, multinucleated giant hepatocyte.


In humans, the liver lesion characterized by formation of multinucleated hepatocytes is often found in neonates and infants and is called post-infantile giant cell hepatitis (PIGCH) [5], whereas it is very rare in adults. The cause of PIGCH has been considered to be viral infection [7, 8], drug intoxication [6, 8], or autoimmunity [1, 3], but it is still obscure in some cases [4, 8]. On the other hand, reports of giant cell hepatitis are strikingly few in animals [2]. We encountered two cases of such liver lesion in young cats at the Veterinary Medical Center, the University of Tokyo. In this report, we describe the histopathology of the lesion.

Case 1 was a 1-year and 6-month-old, female Japanese domestic cat. She had developed a mediastinal tumor, and had been treated with antibiotics and prednisolone. The results of blood chemical examination (glutamate pyruvate transaminase (GOT) >1000 U/L, glutamate oxaloacetate transaminase (GPT) >1000 U/L, and total bilirubin =16.4 mg/100 ml) indicated the existence of hepatic failure. Serological tests revealed that the cat was infected with feline leukemia virus (FeLV) but not with feline immunodeficiency virus (FIV). She died 1 month after the first presentation. At necropsy, severe jaundice was observed on the ocular and oral mucosa, subcutaneous tissues and omentum. Yellowish transparent pleural fluid (100 ml) and ascities (200 ml) were seen. Three yellowish-white neoplastic masses (two about 2 cm and one about 1 cm in diameter) were found at the mediastinum. The liver was congestive, and two light brown nodules, one in the right medial lobe (about 1 cm in diameter) and the other in the quadrate lobe (about 7 mm in diameter), were found (Figs. 1a and 1b). Other organs showed no significant changes.

Case 2 was a 2-year-old, spayed female Japanese domestic cat which had developed a mediastinal tumor. The results of blood chemical examination (GPT >1000 U/L and GOT >1000 U/L) indicated the existence of hepatic failure. Serological tests revealed that FeLV was positive and FIV was negative. Although treatments using prednisolone and drugs for hepatic failure had been performed, the cat died 12 months after the first presentation. Samples were obtained only from the mediastinal mass and the liver, because complete necropsy could not be done.

The tissue samples were fixed in 10% neutral buffered formalin, and 4 µm-thick sections were stained with hematoxylin and eosin (HE) and Masson’s trichrome. Immunohistochemistry was performed by avidin-biotin-peroxidase complex (ABC) method using Vectastain ABC kit (Vector Lab, Burlingame, CA). The primary antibodies used were cat sera against FIV, feline syncytial virus (FeSV), or feline herpesvirus (FHV), and anti-FeLV and anti-feline parvovirus (FPV) monoclonal antibodies (mAb). All antibodies were provided from the Department of Veterinary Microbiology, Graduate School of Agricultural and Life Sciences, the University of Tokyo. Biotin-labeled anti-cat IgG or biotin-labeled anti-mouse IgG was used as the secondary antibody. In addition, ultrastructural examination was performed on liver samples of Case 1. Small pieces of the liver were fixed in 2.5% glutaraldehyde in 0.1 M phosphate buffer (PB) (pH 7.4), postfixed in 1% osmium tetroxide in the same buffer, and embedded in Epok 812 (Ohken, Tokyo). Ultrathin sections were double-stained with uranyl acetate and lead citrate and observed under a JEM-1200EX electron microscope (Nihon-Denshi, Tokyo).

In Case 1, the mediastinal tumor was composed of a lot of anaplastic lymphoblastic cells and diagnosed as malignant lymphoma. The liver showed congestion, destruction of lobular structure, massive necrosis around the central veins and portal tracts, and bile duct proliferation in the portal interstitium. Hepatocytes were generally swollen and multinucleated giant hepatocytes were simultaneously found (Fig. 2). Bile plugs were found in the bile canaliculi. In the centrilobular and periportal areas, lymphoblastic tumor cells similar to those in the mediastinal tumor and inflammatory cells such as lymphocytes, neutrophils and macrophages were sparsely observed. The hepatic nodules also showed almost similar features except that infiltrating cells were mainly composed of eosinophils and macrophages (Fig. 3) and fibrosis was observed in some portions. The viral antigens were not detected in the liver. Electron microscopic examination revealed swelling of mitochondria and endoplasmic reticula being common to swollen hepatocytes and...
Remnants of cell membranes were never found in any hepatocytes.

In Case 2, the histopathology of the mediastinal mass and the liver was almost the same with that of Case 1. The mediastinal mass was diagnosed as malignant lymphoma. The liver was congestive accompanying with centrilobular necrosis. Hepatocytes were generally swollen, and multinucleated giant hepatocytes were also observed (Fig. 4). In this case, there were no lesions in the bile duct system. Lymphoblastic tumor cells similar to those in the mediastinal tumor were found among inflammatory cells.

In the present study, we reported two cases of hepatitis characterized by formation of multinucleated giant hepatocytes in young cats. Histopathological findings of the lesion were similar to those of human PIGCH [5]. Therefore, the present feline hepatic lesions may be diagnosed as giant cell hepatitis (GCH). It is speculated that the cause of feline GCH is similar to that of human PIGCH. Immunohistochemical and electron-microscopic examinations did not reveal any viral antigens and particles in any hepatocytes. Moreover, cell membrane remnants which are often detected in syncytial cells were not observed in multinucleated giant hepatocytes by electron-microscopic examination, suggesting that giant hepatocytes might be formed by

**Fig. 1.** Gross appearance of the whole (a) and dissection (b) of the liver in Case 1. Light brown masses (allowheads) are found in the right medial lobe (a, b) and quadrate lobe (a).

**Fig. 2.** Liver in Case 1. Multinucleated giant hepatocytes are seen with infiltration of lymphoblastic tumor cells as well as inflammatory cells. HE, ×100.

**Fig. 3.** Nodule in the liver in Case 1. Multinucleated giant hepatocytes are seen with infiltration of eosinophils and macrophages. HE, ×150.

**Fig. 4.** Liver in Case 2. Multinucleated giant hepatocytes are seen with infiltration of lymphoblastic tumor cells as well as inflammatory cells. HE, ×100.
failure of cytoplasmic division but not by cell fusion which is known as one of the viral cytopathic effects. Therefore, virus infection may be excluded as the cause of feline GCH. Next, we checked the relation of drugs with feline GCH. The drug commonly used in the two cases was prednisolone which is usually used for the treatment of human PIGCH [1, 8]. Therefore, it is also difficult to consider that the drug is the cause of feline GCH. Moreover, the possibility of the involvement of autoimmunity may also be very low, because the results of Coomb’s test was negative in Case 1. These two cats had similar clinical backgrounds such as age (1.5 years and 2 years old, respectively), positive reaction to FeLV and bearing thymic malignant lymphoma. Therefore, it is considered that feline GCH is a novel disease caused by complication of several factors. More cases should be collected to clarify the nature and the cause of the disease.

REFERENCES