B-Cell Immunoblastic Lymphoma with Multinucleated Giant Cells in a Cat

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ABSTRACT. A 10-year-old male mixed breed cat died after six months history of intermittent vomiting and weight loss. At necropsy, large white-colored foci were found in both kidneys, and whitish thickening of the gastric wall was present at the pyloric part of the stomach. Histopathological examination revealed that both lesions consisted of proliferation of large-sized neoplastic lymphocytes intermingled with multinucleated giant cells. Immunohistochemically, the neoplastic cells were positive for both B-cell antigen receptor complex (CD 79α cy) and MHC class II, although multinucleated giant cells were negative. The present case was diagnosed as B-cell immunoblastic lymphoma with multinucleated giant cells.

KEY WORDS: B-cell immunoblastic lymphoma, feline, multinucleated giant cell.

PATHOLOGY

Lymphoma is a very popular tumor in domestic animals. The tumor is classified as low, intermediate, or high grade in malignancy according to the National Cancer Institute Working Formulation [3, 7]. Among them, high grade lymphoma contains immunoblastic, lymphoblastic, small non-cleaved, and Burkitt types [3, 7]. Large cell lymphomas, which are the most commonly occurring tumors in the cow, cat, horse and pig, are classified into T-cell-rich B-cell lymphoma, large cell immunoblastic lymphoma, diffuse large B-cell lymphoma, thymic B-cell lymphoma and intravascular large B-cell lymphoma in WHO classification [8].

In humans, immunoblastic type is known to contain bizarre cells such as binucleated or multinucleated cells, and Reed-Sternberg-like cells [5]. However, immunoblastic lymphoma with multinucleated cells is rare in animals. Only a few reports of immunoblastic polymorphous type, which is a mixture of small, medium and large sized neoplastic lymphocytes including bizarre cells such as binucleated or multinucleated cells and Reed-Sternberg-like cells, have been reported in non-human primates [2] and ferrets [1]. In cat, to our knowledge, three cases of histiocytic lymphosarcoma with multinucleated giant cells have been reported, while the origin of tumor cells (T-cell or B-cell) is not demonstrated [4]. This report describes a case of feline B-cell immunoblastic lymphoma with multinucleated giant cells.

A 10-year-old male mixed breed cat died after six months history of intermittent vomiting and weight loss. Hematological and biochemical examinations performed 4 days before death, revealed severe neutrophilia (42,400/µl), and increased levels of blood urea nitrogen (BUN) (>140 mg/dl), and creatine kinase (CK) (>2000 U/L).

A complete necropsy was performed. Grossly, white-colored foci were observed in both kidneys (Fig. 1). Similar foci were also seen in the walls of gastric pyloric part, and gastric and pancreaticoduodenal lymph nodes. Other gross findings included muscular discoloration in the majority of skeletal muscles.

Tissue samples were fixed in 10% neutral buffered formalin, embedded in paraffin, sectioned at 3 µm, and stained with hematoxylin and eosin (HE). Immunohistochemistry was performed by a labeled streptavidin-biotin (LSAB) method using monoclonal antibodies against B-cell antigen receptor complex (Human CD 79α cy) (Dako, Denmark) and MHC class II (Dako), and polyclonal antibodies against lysozyme (Dako) and pan T-lymphocytes marker (CD 3) (Dako). Antigen recovery was accomplished by exposure to microwaves. An in-situ apoptosis detection kit (Apop Tag plus; Oncor Inc, Gaithersburg, Maryland, U.S.A.) was used in accordance with manufacturer’s recommendation to assess DNA fragmentation in the neoplastic lesions.

Histologically, the lesions of the kidneys and stomach consisted of proliferation of large-sized neoplastic lymphocytes. The neoplastic cells were arranged in a solid pattern with diffuse architecture (not showing follicular architecture) and invaded the parenchyma with necrosis in both organs (Fig. 2). The nucleus of tumor cells was large (>15 µm in diameter) with round to oval or cleaved and with a prominent single central nucleolus. Their cytoplasm was rich in size (Fig. 3). Mitotic figures were frequently observed. Among neoplastic lymphocytes, many multinucleated giant cells and some plasma cells were also seen. Multinucleated giant cells often had 10 or more nuclei and tiny to large vacuoles in the cytoplasm, and occasionally showed apoptotic nuclei (Fig. 4a). TUNEL method resulted in positive reaction in several apoptotic multinucleated giant cells as well as several lymphocytes (Fig. 4b). No gross and histological evidences of tumor metastasis to other organs were found expect for the gastric and pancreaticoduodenal lymph nodes. Immunohistochemically, many neoplastic lymphocytes were weakly positive for CD 79α cy and some
Fig. 1. Left kidney. White-colored foci are observed (arrows).

Fig. 2. Tumor tissue of the left kidney. Neoplastic lymphocytes are arranged in a solid pattern. Many multinucleated cells are also observed. HE. Bar = 65 µm.

Fig. 3. Left kidney. The nucleus of tumor cells is large with round to oval in shape or often cleaved and possesses a prominent single central nucleolus. Their cytoplasm is rich in size. Bar = 22 µm.

Fig. 4a. Left kidney. Multinucleated giant cells often have cytoplasmic vacuoles (arrowhead) and show apoptotic nuclei (arrows). HE. Bar = 22 µm.

Fig. 4b. Left kidney. TUNEL method reveals positive result in some apoptotic multinucleated giant cells (arrows). A non-apoptotic cell is TUNEL-negative. Bar = 32 µm.

Fig. 5. Left kidney. Many neoplastic cells are weakly positive and some cells are strongly positive for Human CD 79 α cy (B cell marker). LSAB method. Bar = 32 µm.
cells were strongly positive (Fig. 5). Almost all the neoplastic cells were positive for MHC class II, but negative for lysozyme and CD3. A few lymphocytes were positive for CD3. Multinucleated giant cells were negative for all the markers used.

In the present case, immunohistochemistry demonstrated that the tumor cells were originated from B lymphocytes. Furthermore, based on histological findings; ie. diffuse architecture of neoplastic lymphocytes and round to oval or cleaved nucleus with a prominent central nucleolus, the present case was diagnosed as large cell (B-cell) immunoblastic lymphoma according to the WHO classification [8]. Feline immunoblastic lymphoma has been reported to account for 34.4% of all the feline lymphoma cases [7], but the presence of multinucleated giant cells is very rare [3, 7].

In animals other than cats, only a few cases of immunoblastic lymphoma have been reported in non-human primates [1] and ferrets [2]. The neoplastic lymphocytes in the present case were more uniform in cell size than those in the previous cases. Histological findings in the present case were rather similar to those in human immunoblastic lymphoma with multinucleated cells in which most neoplastic lymphocytes showed abundant cytoplasm and prominent nucleus with plasma cell differentiation [5]. This may be the first report of a feline case of diffuse large cell immunoblastic lymphoma with multinucleated giant cells.

The first differential diagnosis for the present case is diffuse large B-cell lymphoma. The nucleus of the tumor cells in diffuse large B-cell lymphoma have been established to have two to three nucleoli [8], which is different from the present case. The second differential diagnosis is T-cell-rich B-cell lymphoma. Immunohistological study using CD3 antibody disclosed a minimal number of T lymphocytes in the neoplastic lesion of the present case. This finding enabled us to exclude a diagnosis of T-cell-rich B-cell lymphoma. Hodgkin’s-like lymphoma should be the third differential diagnosis because it is characterized by the presence of multinucleated giant cells with a large prominent nucleolus (Reed-Sternberg cells) [3, 6, 7, 9]. However, the present case did not have lymphadenopathy nor did the case show a heterogeneous population of lymphoid and inflammatory cells which characterize Hodgkin’s-like lymphoma. Furthermore, typical Reed-Sternberg cells (binucleated, mirror-image) were not found [5]. Therefore, the present case seemed to be different from Hodgkin’s-like lymphoma.

Another point of discussion is the origin of the multinucleated giant cells. The origin of the cells is considered neoplastic B-lymphocytes in human immunoblastic lymphoma [5]. In the present case, however, multinucleated giant cells were negative for both pan B-and T-cell markers and for lysozyme as well as previously reported in feline Hodgkin’s-like lymphoma [9]. Therefore, the origin of the multinucleated giant cells still remains obscure although apoptotic figures of the multinucleated giant cells may suggest that the cells would be a neoplastic cell population.

REFERENCES