Cytological Features of Hepatic Epitheliotropic Lymphoma in A Cat

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Abstract

The cytological and histological features of an hepiteliotropic hepatic lymphoma from a cat are described. The cat was referred because clinical signs indicative of hepatopathy. A fine needle capillary sampling (FNCS) without aspiration, via the use of a 25 Gauge spinal needle of the hepatic parenchyma was performed. A variable number of medium-sized, round lymphoid cells, with bluish cytoplasm and round-to-ovoid, sometimes clivated nuclei, with clumped chromatin, were dispersed around the hepatocytes. These cells were frequently internalised into the cytoplasm of the hepatocytes, displacing the nuclei were observed in the cytoplasm of hepatocytes, sometimes displacing the nucleus. Similar features were observed in the histological sections. Immunohistochemistry showed diffuse CD3 expression of the lymphoid cells. The incorporation of neoplastic cells into the hepatocytes is believed to be the expression of a mechanism of emperipolesis. At the best of the author’s knowledge, this is the first description of the cytomorphological features of epitheliotropism expressed by lymphoid neoplastic cells in the liver.

Keywords: cytology, cell block, freeze, cryo, snap, pathology

Received August 19 2014; Accepted March 25 2015; Published April 2 2015

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Case Report

A 9-year-old, Shorthair, male cat was referred because of loss of weight and vomit; although the cat was alert, the clinical examination revealed cachexia and icteric mucous membranes. Evaluation of CBC data showed the presence of mild (4.84 x109 RBC, reference interval 6.35-9.50 x109), normocytic (MCV 39.5 fL, reference interval 38.0-49.5 fL) and normochromic (MCHC 34.5 g/dl, reference interval 31.0-35.0 g/dl) anaemia with leukopenia (WBC 1.4 x103, reference interval 5.0-11.0 x103) and thrombocytopenia (PLT 114 x103, reference interval 130-430 x103). Significant changes in serum biochemistry included an increase in hepatic enzyme activity (ALT 583 U/L, reference interval 32-87 U/L; AST 356 U/L, reference interval 15-35 U/L; ALP 112 U/L, reference interval 19-70 U/L; GGT 31 U/L, reference interval 0.1-0.6 U/L) and of total bilirubin (Total Bilirubin 2.1 mg/dl, reference interval 0.14-0.26 mg/dl). A test for Feline Immunodeficiency Virus gave positive results. On the basis of these data, a hepatopathy was suspected. Ultrasonographic investigation showed the presence of mild peritoneal effusion, hepatomegaly with many hypoechoic areas with perivascular location and a normal gallbladder. A fine needle capillary sampling (FNCS) without aspiration, via the use of a 25 Gauge spinal needle of the hepatic parenchyma was performed. Three smears were air-dried and stained with the Wright Giemsa method. On a bloody background, a high number of hepatocytes arranged in bidimensional sheets showed a variable amount of lipofuscin pigment in the cytoplasm, and some degree of vacuolar changes and round nuclei, with granular chromatin; a variable number of medium-sized, round lymphoid cells, with bluish cytoplasm and round-to-ovoid, sometimes clivated nuclei, with clumped chromatin, were dispersed around the hepatocytes (Figure n°1A). These cells were frequently internalised into the cytoplasm of the hepatocytes, displacing the nuclei. In some samples, a very thin clear line surrounding the rim of the lymphoid cells in the cytoplasm of the aggregated hepatocytes was evident (Figure 1B, C and D). A diagnosis of hepatic lymphoma with epitheliotropic activity was reported.
Figure 1: a large number of neoplastic lymphoid cells surrounds a cluster of hepatocytes (A); the neoplastic cells are internalised in the cytoplasms of hepatocytes, displacing the nuclei (B, C, D) 106 (WG, 100X)

Figure 2: histologic sections of liver tissue. Note the internalization of lymphoid cells into the cytoplasms of hepatocytes (A); HE, x40 objective). Neoplastic cells are diffusely CD3 positive (B) and locate also among the cells of biliary ducts (ABC complex, DAB chromogen, x100 objective)

In order to confirm the cytological results, two wedge-shaped fragments of liver tissue were obtained by laparotomy, immediately fixed in 4% buffered formalin and then processed and stained routinely. In periportal and in midzonal areas, a high number of lymphoid cells were distributed among regular rows of hepatocytes; in many instances, these cells were located in the cytoplasm of the hepatocytes, with a consequent peripheral displacement of the nucleus (Figure 2A); biliary epithelium was also diffusely involved. A definitive diagnosis of hepatic epitheliotropic lymphoma was made. Immunohistochemical investigation showed diffuse CD3 expression of the lymphoid cells (Figure 2B). After euthanasia, requested by the owner, a complete post-mortem necropsy was denied.

Discussion

Among haematopoietic hepatic neoplasms, malignant lymphoma is the most frequent type observed (Charles and al, 2006); an epitheliotropic variant of a T-cell malignant lymphoma, with marked emperipolesis of the tumour cells by the hepatocytes, has been previously described (Ossent et al., 1989; Suzuki et al. 2011). Emperipolesis is defined as "the active penetration of one cell by another which remains intact" (Humble et al. 1956). It differs from phagocytosis because the engulfed cell exists within another cell, remains viable, and can exit with no physiological or morphological consequences for either cell (Humble et al. 1956). Emperipolesis is believed to have no diagnostic significance and must be differentiated from “aggressive” emperipolesis, where neoplastic cells enter and destroy other cells (Bechtelsheimer et al. 1976). In normal conditions, T-cells are able to penetrate other tissue cells because they may move from blood to lymphoid tissues through, rather than between, the endothelial cells of the high endothelial venules (Sorokin 2010). T-cells are also able to infiltrate the epidermis (Neta, 2008) or the epithelium of mucous membranes (Coyne and Steinberg, 2004). The most interesting feature of our case is the presence of neoplastic lymphoid cells within the cytoplasm of normal hepatocytes; the overlapping of neoplastic cells to the hepatocyte membrane is excluded by the presence of a very thin line surrounding the external membrane edges of some neoplastic cells in the cytoplasm of hepatocytes. This represents a true incorporation of neoplastic cells, according to the mechanism of emperipolesis. In a previous study, electron microscopy revealed that neoplastic cells were contained within hepatocytes: the cell membrane of these internalised cells was intact and was surrounded by the cell membrane of the hepatocytes (Suzuki et al. 2011). This finding suggests that the neoplastic cells had invaginated into the hepatocyte, rather than directly crossing the membrane into the cytoplasm. Although a very low degree of cytoplasmic changes are evident in cytological samples of this liver, it is not clear whether the process is directly related to cellular and subcellular damage; we hypothesise that the marked increase in hepatic enzyme activity would be a direct consequence of this damage.
Conflict of Interest

All authors disclose any financial and personal relationships with other people or organisations that could inappropriately influence their work.

References


