Lymphoplasmacytoid Lymphoma in a Cow

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ABSTRACT. Lymphoplasmacytoid lymphoma was found in an 8-year-old Holstein cow uninfected with bovine leukemia virus (BLV). The neoplastic tissue was composed of lymphoid and plasmacytoid cells, and intracytoplasmic IgM (\(\lambda\)) was detected in the latter. The diagnosis was based on the presence of small lymphoid cells and the expression of CD5, which were suggestive of a close relationship with chronic lymphocytic leukemia. Areas of immunoblastoid cells were reminiscent of histologic progression into immunoblastic lymphoma. The neoplastic cells at different stages of differentiation were distinct from those of BLV-associated pleomorphic lymphoma.

KEY WORDS: cattle, immunoglobulin, lymphoma.

NOTE Pathology

In the Kiel classification of human non-Hodgkin’s lymphoma, lymphomas composed of small B lymphocytes and plasmacytoid or plasma cells are divided into two subtypes, lymphoplasmacytoid and lymphoplasmacytic [6]. The lymphoplasmacytoid subtype is usually CD5 positive, whereas the lymphoplasmacytic subtype is always CD5 negative [6]. Other mature B cell neoplasms such as mantle cell lymphoma, marginal zone lymphoma and follicular lymphoma may show plasmacytic differentiation [10]. Swine [4, 9] and equine [2] lymphoplasmacytic lymphomas have been reported, but it is not known in which category the lymphomas belong due to lack of CD marker studies. Small lymphocytic lymphoma with plasmacytoid differentiation has been recorded in a cow [12], but no clinical, macroscopic, histologic or immunohistochemical findings were available. In this paper, we report a case of lymphoplasmacytoid lymphoma in a cow that was characterized by positive immunoreactivity for cytoplasmic immunoglobulin-M (cIgM) and CD5.

Just before calving, an 8-year-old Holstein cow with a 1-month history of slight emaciation was examined hemato logically because of enlargement of the parotid and mammary lymph nodes. Hematological values were as follows: hematocrit, 23%; hemoglobin, 7.8 g/dl; red blood cell count, 3.84 \(\times 10^{12}/\mu\)l; white blood cell count, 19,400/\(\mu\)l, with 96% lymphocytes, 2% segmented neutrophils, and 2% monocytes. Antibodies to bovine leukemia virus (BLV) were not detected by the agar gel immunodiffusion test. Based on these findings, a presumptive diagnosis of sporadic lymphoma was made. One month after normal calving, the animal was euthanatized because of anorexia, severe emaciation and markedly decreased milk production.

At necropsy, the majority of the superficial, thoracic and abdominal lymph nodes were highly enlarged, and they were homogeneous and firm on cut section. There were disseminated white foci on the diaphragmatic surface of the liver. The gallbladder wall became thickened up to 10 cm due to neoplastic tissue, which extended to the hepatic capsule but was not invasive into the hepatic parenchyma. A few white masses 3 to 4 cm in diameter were on the surfaces of the right apical, right middle and left apical lobes of the lung. The kidneys were diffusely enlarged, and white infiltrates and remaining parenchyma created a mosaic appearance. The wall of the abomasum was thickened with multiple elevations 5 mm in diameter on the mucosal surface. The spleen was slightly enlarged.

Tissues were fixed in 10% buffered formalin, embedded in paraffin, sectioned at 4 \(\mu\)m, and stained with hematoxylin and eosin (HE) and Giemsa. Immunohistochemical staining was carried out by the streptoavidin-biotin complex/horseradish peroxidase (SAB-PO) method on histologic sections using Histofine SAB-PO kits (Nichirei, Tokyo, Japan). The primary antibodies utilized were rabbit polyclonal antibodies to human CD3 (Dako, Glostrup, Denmark), human CD5 (Lab Vision, Fremont, CA, U.S.A.), bovine IgM (\(\mu\)-chain specific) (Bethyl Laboratories, Montgomery, TX, U.S.A.), bovine IgA (\(\alpha\)-chain specific) (Bethyl), human \(\lambda\)-light chain (BioGenex Laboratories, San Ramon, CA, U.S.A.) and \(\kappa\)-light chain (BioGenex), sheep polyclonal antibody to bovine IgG (heavy-chain specific) (Bethyl), and mouse monoclonal antibody to human CD79a (Dako). Small blocks of formalin-fixed tissues were post-fixed in 1% osmium tetroxide, and embedded in epoxy resin. Ultrathin sections were stained with uranyl acetate and lead citrate, and examined by electron microscopy (EM).

Histologically, in the lymph nodes examined, the normal architecture was completely effaced by neoplastic tissue, with severe neoplastic infiltrates in the capsule. There were widespread necrotic areas in some lymph nodes. The spleen was entirely packed with neoplastic cells. Accumulations of neoplastic cells were present in the majority of portal triads in the liver, and diffuse neoplastic growths were in the gallbladder wall. Neoplastic cells were present not only in the macroscopically visible lesions but also in the lumina of...
alveolar capillaries in the lung. In the kidneys, tumor cells proliferating in interstitium formed foci of various sizes. There was diffuse neoplastic infiltration throughout the wall of the abomasum. The lamina propria and submucosa of the duodenum were heavily infiltrated with neoplastic cells, and those of the ileum were less heavily infiltrated. The endometrium of the uterus was affected moderately. The stroma of the mammary glands were extensively infiltrated...
with tumor cells. A few neoplastic cell accumulations were found in the reticulum, rectum, and urinary bladder.

The tumor cells showed marked variation in cytology and were divided into small lymphoid cell, plasmacytoid cell, and immunoblastoid cell types. The small lymphoid cells were 3.5–5 μm in diameter, having heterochromatic nuclei, inconspicuous nucleoli and scant cytoplasm (Fig. 1A). The plasmacytoid cells were 5–7 μm in diameter, and the majority showed medium-sized nucleoli, moderately condensed chromatin and less abundant cytoplasm than that of typical plasma cells (Fig. 1B). The immunoblastoid cells 7–13 μm in diameter possessed large vesicular nuclei with prominent nucleoli, and the cytoplasm was relatively abundant (Fig. 1C). These cytologically variegated cells were intermingled in varying proportions (Fig. 1D), though areas composed exclusively of a single cell type were detected in places (Fig. 1A–C). The mitotic count ranged from 3 to 5 mitotic figures per high-power field (HPF) in most regions, with areas of immunoblastoid cells reaching 8 mitoses/HPF, but mitoses were few (1–2/HPF) in areas of small lymphoid cells.

Immunohistochemically, the tumor cells were positive for CD79a, and CD5-positive neoplastic cells were frequently observed (Fig. 2A). Cells expressing κ and λ chains (IgM) were plasmacytoid or immunoblastoid (Fig. 2B).

Ultrastructurally, most neoplastic cells contained slightly irregular nuclei. Moderate to slight development of rough endoplasmic reticulum (RER) was observed in the majority of neoplastic cells (Fig. 3A, B), though some smaller cells were characterized by few organelles and heterochromatic nuclei. Neoplastic cells whose RER was well developed as in normal plasma cells were rare, and no cartwheel pattern of heterochromatin aggregates was observed.

In the Kiel classification of human lymphoid neoplasms, immunocytoma is divisible into two subtypes, lymphoplasmacytoid and lymphoplasmacytic [6]. The lymphoplasmacytoid subtype is usually CD5 positive, and more often leukemic. In contrast, the lymphoplasmacytic subtype is always CD5 negative [6]. In the present study, white blood cell count was 19,400 with 96% lymphocytes 1 month before euthanatization. In addition, histologic examination disclosed the presence of many neoplastic cells within alveolar capillaries in the lung. These suggest that a great number of neoplastic cells were present in the peripheral blood just before euthanasia [7, 11]. On the basis of the peripheral blood involvement, CD5 expression and plasmacytic differentiation, a diagnosis of lymphoplasmacytoid lymphoma was made [6]. In humans, the lymphoplasmacytoid subtype is more like chronic lymphocytic leukemia of B cell type (B-CLL) than the lymphoplasmacytic subtype [6]. In the current case, areas consisting principally of small lymphoid cells, which were reminiscent of B-CLL/small lymphocytic lymphoma, were thought to be evidence to support the diagnosis [8]. Moreover, the plasmacytoid cells did not show the characteristic cartwheel distribution of heterochromatin aggregates, which is found in normal plasma cells and has been observed in a CD5-negative lymphoplasmacytic lymphoma in a cow [unpublished data]. Unlike in a bovine plasmacytoma whose neoplastic cells are ultrastructurally characterized by abundant RER [5], most of the plasmacytoid cells had smaller amounts of RER.

Nearly all of the previous reports about mature B cell lymphoma in cattle have been characterized by the presence of a prominent immunoblastoid component [8]. As in the human counterpart neoplasm [8], areas consisting chiefly of immunoblastoid cells were detected in the present case, and were interpretable as evidence of histologic progression into immunoblastic lymphoma. A similar phenomenon has been observed in a swine lymphoma [3]. However, the lymphoma was diagnosed as composite lymphoma because the immunoblastic element constituted a considerable proportion of the neoplastic lesion. Since the frequency of mitotic figures in areas of immunoblastic differentiation was higher than in the other areas, the present lymphoma would have progressed to composite lymphoma or would have been replaced by immunoblastic lymphoma if the cow had not been euthanatized.
neoplasms in cattle are those of BLV-associated B cell lymphomas. Yin et al. [14] divided these lymphomas into B-1a, B-1b and B-2 cell types in a study of surface markers. Vernau et al. [13] applied immunohistochemistry to paraffin sections from 35 cases of adult-form lymphoma; surface IgG was detected in all cases, but no reference was made to cytoplasmic immunoglobulin (cIg). This indicates the absence of cIg in the cases. This type of lymphoma is considered unable to differentiate into Ig-producing tumors despite of the frequent cytologic pleomorphism [1]. Although little is known of Ig-producing neoplasms in cattle, a case of plasma cell myeloma has been described and was accompanied by hypergammaglobulinemia [5]. Because many IgM-bearing neoplastic cells were observed in the present study, it is probable that the animal had macroglobulinemia.

REFERENCES


