

T Cell Lymphoma in An Akkaraman Sheep

Songül ÇERİBAŞI *  Mustafa ÖZKARACA ** Ali Osman ÇERİBAŞI * Harun ÖZER *

* Department of Pathology, Faculty of Veterinary Medicine, Firat University, TR-23119 Elazığ - TURKEY

** Veterinary Control Institute, TR-23119 Elazığ - TURKEY

Makale Kodu (Article Code): KVFD-2012-8161

Summary

Lymphocytic T cell lymphoma was detected in liver and kidneys of a 3 year old Akkaraman sheep which was submitted to the pathology department for diagnosis. Macroscopically, nodular formations with white colour and about 1 cm size were observed in the cortex of both kidneys. The irregular nodules were observed in the liver, similar to the lesions in the kidneys. Microscopically, the nodular lesions in the liver and kidneys were consisted of uniform lymphocytic accumulations. These lymphocytes were similar to the mature lymphocytes although they were bigger and had less chromatin. Immunohistochemically, tumor cells had positivity with CD3, but negativity with CD20 and CD79a. Thus, the tumor was described as type of lymphocytic T cell lymphoma.

Keywords: Akkaraman sheep, Immunohistochemistry, Lymphoma

Bir Akkaraman Koyunda T Hücreli Lenfoma

Özet

Teşhis amacıyla Patoloji Anabilim dalına karaciğer ve böbrekleri getirilen 3 yaşında Akkaraman ırkı bir koyunda lenfositik tipte T hücreli lenfoma olgusu tanımlandı. Makroskopik olarak, her iki böbreğin korteksinde, beyaz renkli, yaklaşık 1 cm çapında, nodüler formasyonlar saptandı. Karaciğerde de böbreklerdeki lezyonlara benzeyen düzensiz nodüller mevcuttu. Mikroskopik olarak; karaciğer ve böbrekteki nodüler lezyonların, üniform yapıda lenfosit birikimlerinden oluştuğu gözlemlendi. Olgun lenfositlere benzeyen ancak boyut olarak daha büyük ve daha az kromatin içeren bu hücreler lenfositik tipte lenfoma hücreleri olarak değerlendirildi. İmmunohistokimyasal olarak tümör hücreleri, CD3 ile pozitif, CD20 ve CD79a ile negatifti. Bundan dolayı, tümör T hücreli lenfositik tipte lenfoma olarak tanımlandı.

Anahtar sözcükler: Akkaraman koyun, İmmunohistokimya, Lenfoma

INTRODUCTION

Lymphoma is a rare neoplastic condition in sheep ¹⁻³. Although many cases have been reported in older sheeps, lymphoma was also identified in lambs ⁴. No predisposition has been found in sheep in terms of breed and gender. However, the number of affected female cases has been reported to be higher among adult animals ¹. Both enzootic and sporadic forms of lymphoma occur in sheep ⁵. Retrovirus infection has been suggested to be a cause of enzootic lymphoma in sheep, and bovine leukemia virus (BLV) can be experimentally transmitted to sheep and ovine lymphoma has been reported to develop within 3 years following the inoculation of BLV ⁶. Retroviral etiology has also been documented epidemiologically and virologically in spontaneous lymphoma cases in sheep ⁷.

The distribution of lesions in sheep is usually similar to cattle. Ovine lymphoma has several anatomic forms including primarily the multicentric type, the alimentary form and, rarely thymic and skin forms ⁸. Multicentric form results in skin form in rare cases ⁵. Although the most constant feature of ovine lymphoma is the enlargement of affected lymph nodes and progressive spread of neoplastic tissue to other lymphoid and non-lymphoid organs, enlargement of peripheral lymph nodes may not be observed in some cases. Organs next to the lymph nodes such as spleen, liver, kidney, digestive tract, skeletal muscles and heart are commonly affected in sheep ¹. While the liver and the spleen are the most commonly affected organs in spontaneous lymphoma cases in sheep ⁹, common involvement of the



İletişim (Correspondence)



+90 424 2370000/4033



songulozer@firat.edu.tr

uterus, heart and abomasum has been reported in experimental infections ¹⁰. Sometimes the only macroscopical lesions are detected in kidney associated with ovine lymphoma ⁷.

Focal or generalized diffuse accumulation of neoplastic lymphocytic cells are generally observed microscopic changes in affected organs ^{1,6,7}. The most common observed lesion of lymphoma is the existence of undifferentiated neoplastic cells in other animal species, but well differentiated lymphoid cells are reported to be dominant in sheep ¹.

This is the first report about the diagnosis of T cell lymphoma with the aid of immunophenotypic methods in an Akkaraman sheep in Turkey.

CASE HISTORY

The study material was composed of the liver and the kidneys of a 3 year old Akkaraman sheep which was submitted to the pathology department for diagnosis. Following examination of the organs, tissue samples obtained from the liver and the kidneys were fixed in 10% neutral buffered formalin, embedded in paraffin, and cross sections were stained with hematoxylin and eosin (HE). Liver and kidney sections were immunohistochemically stained with the

avidin-biotin-peroxidase complex (ABC-P) for CD3, CD20 and CD79a monoclonal antibodies. Rabbit anti-human CD3 (Early T cell marker) (Thermo Scientific, Cat No: RM-9107-S0), mouse anti-human CD20 (Dako Corp, Carpinteria, CA, Cat No: M7254, IR604) and mouse anti-human CD79a/mb1 B cell marker (Thermo Scientific, Cat No: MS-1171-P0) kits were used. A mediastinal lymph node from a sheep with ovine pulmonary adenomatosis served as a positive control for all antibodies, and nonimmune serum was used as a negative control. The primary antibodies were diluted to 1:50. The immune complexes were stained with diaminobenzidine tetrahydrochloride (DAB) and counterstained with Mayer's hematoxylin (M-H).

Macroscopically, multiple nodular formations with yellow-white colour and about 1 cm size were observed in the cortex of both kidneys (Fig. 1A). Evaluation of the cross section surface in the kidneys revealed thinning of the medulla and the enlargement of the pelvis (Fig. 1B). The liver was observed to be enlarged, pale and fatty; capsular fibrosis and nodules with irregular size were detected on both surfaces (Fig. 2A). In addition, prominent enlargement was observed in the hilar lymph node of the liver (Fig. 2B).

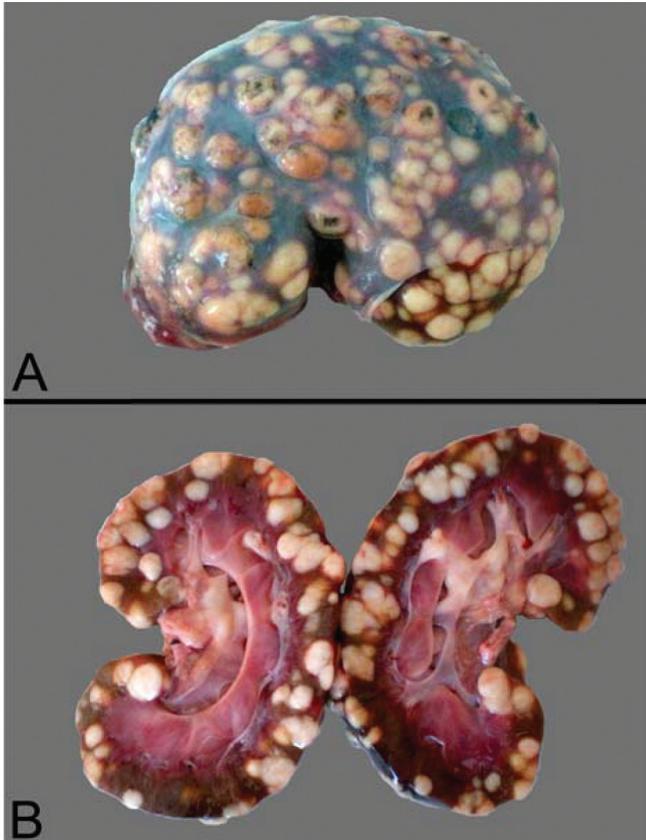


Fig 1. A- Nodular formations in kidney cortex, B- Macroscopical appearance sagittal section of kidney

Şekil 1. A- Böbrek korteksinde nodül formasyonları, B- Böbreğin kesit yüzünün görünümü

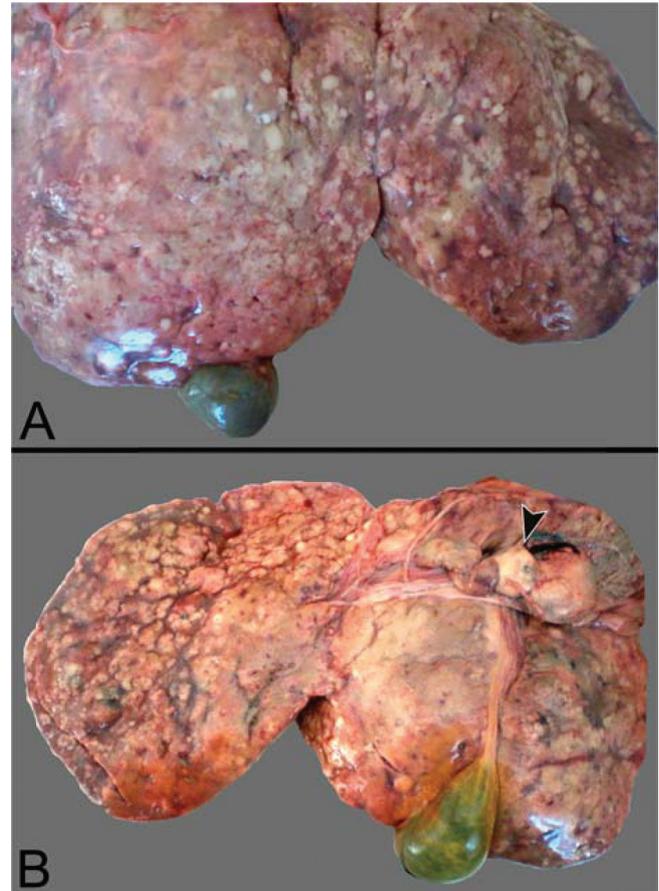


Fig 2. A- Nodular formations and capsular fibrosis on diaphragmatic surface of liver, B- Pale and fatty appearance on visseral surface of liver with enlargement hilar lymph node (arrow head)

Şekil 2. A- Karaciğerin diafragmatik yüzünde kapsüler fibrozis ve nodül formasyonları, B- Karaciğerin visseral yüzünün solgun ve yağlı görünümü ile birlikte hilar lenf düğümünde büyüme (ok başı)

Microscopically, the nodules in the liver and the kidneys were observed to be composed of neoplastic lymphocyte accumulations, similar to uniform and mature lymphocytes though they were bigger and had less chromatin. Lymphocyte accumulations were seen in the overall liver parenchyma, while the infiltration was especially more

severe in the portal area (Fig. 3A). Due to the neoplastic cell infiltrations, the normal liver structure was completely destroyed in the midzonal and periacinar regions and small islands of hepatocytes were seen between the affected areas. Although intrasinusoidal accumulation was observed in the liver, no intravascular neoplastic cells were

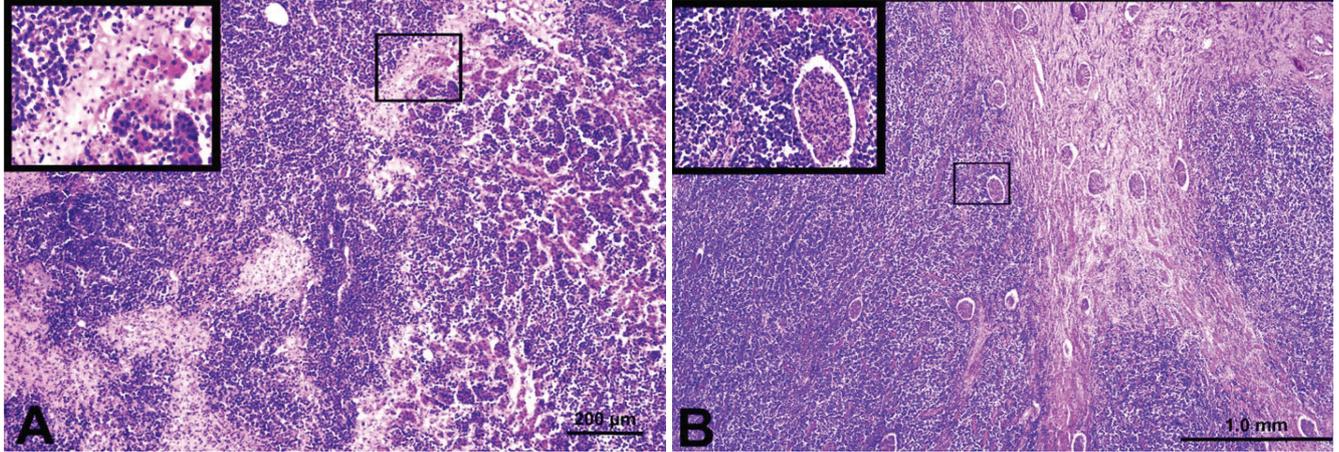


Fig 3. A- Diffuse lymphocytic infiltration in liver parenchyma, H-E, 10x B- Diffuse infiltration in intersitium of kidney and remains of destroyed tubules, H-E, 4x

Şekil 3. A- Karaciğer parankiminde diffüz lenfositik infiltrasyon, H-E, 10x, B- Böbrek intersitiumunda diffüz infiltrasyon ve yıkılmış tubulus kalıntıları, H-E, 4x

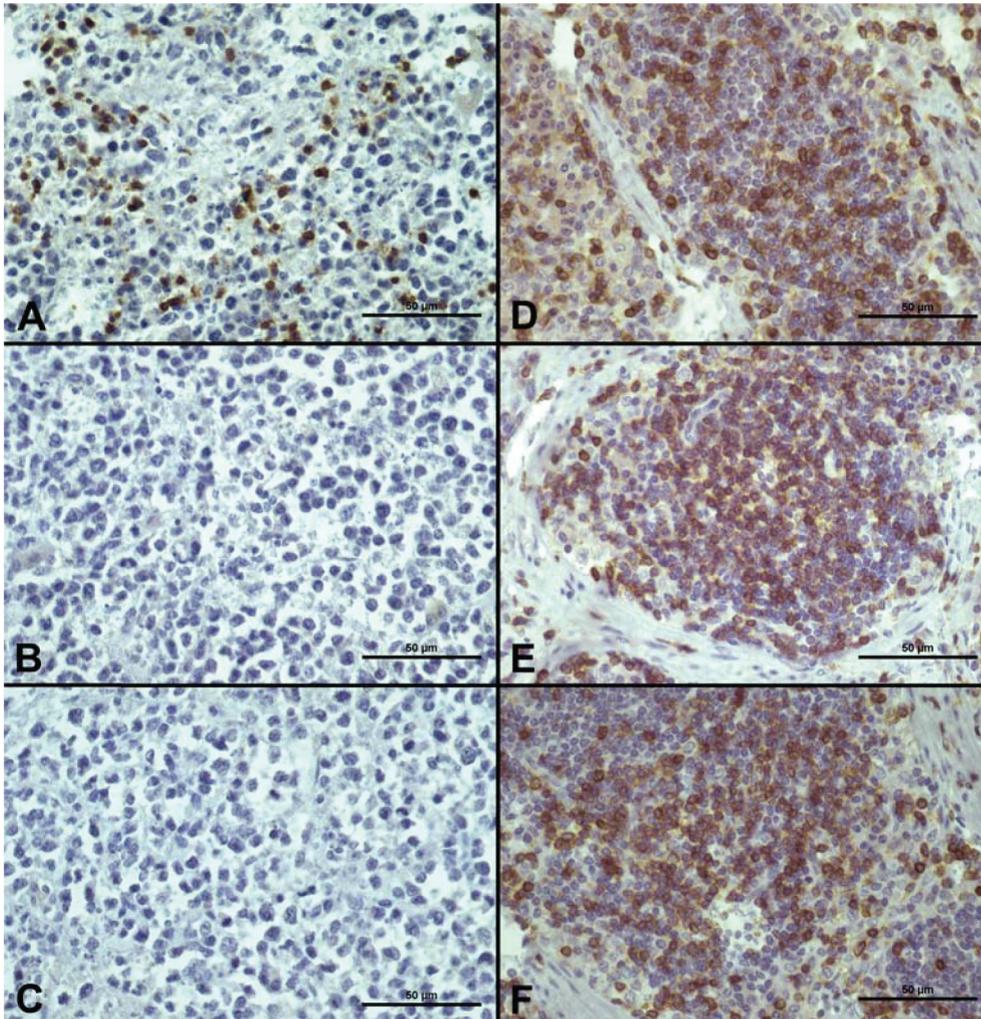


Fig 4. A- CD3 positivity in neoplastic lymphocytes, M-H, liver, ABC-Px40, B- CD20 negative reaction in lymphoma cells, M-H, liver, ABC-Px40, C- CD79a negative reaction in neoplastic cells, M-H, liver, ABC-Px40, D- CD3 positivity in T cell lymphocytes, M-H, lymph node, ABC-Px40, E- CD20 positivity in B cell lymphocytes and follicular dendritic cells, M-H, lymph node, ABC-Px40, F- CD79a positivity in B cell lymphocytes, M-H, lymph node, ABC-Px40

Şekil 4. A- Neoplastik lenfositlerde CD3 pozitifliği, M-H, karaciğer, ABC Px40, B- Neoplastik lenfositlerde CD20 negatifliği, M-H, karaciğer, ABC Px40, C- Neoplastik hücrelerde CD79a negatifliği, M-H, karaciğer, ABC-Px40, D- T lenfositlerde CD3 pozitifliği, M-H, lenf düğümü, ABC-Px40, E- B lenfositleri ve foliküler dentritik hücrelerde CD20 pozitifliği, M-H, lenf düğümü, ABC-Px40, F- B lenfositlerinde CD79a pozitifliği, M-H, lenf düğümü, ABC-Px40

detected. In the kidney, progressive lymphocytic infiltration of cortical interstitial tissues led to the eventual destruction of the affected region (Fig. 3B).

Immunohistochemical staining showed that the tumor cells had positive results with CD3, a specific marker for T lymphocytes (Fig. 4A), and had negative results with CD20 (Fig. 4B) and CD79a (Fig. 4C), a specific marker for B lymphocytes. The antibodies employed accurately identified B, T, follicular dendritic cells in the control sheep lymph node (Fig. 4 D,E,F).

DISCUSSION

Although the anatomical classification differs in sporadic or enzootic cases in sheep, macroscopic changes are mainly observed in the liver and kidneys^{1,6,7}. In the multicentric form, varying numbers of enlarged profound and superficial lymph nodes are observed, accompanied by alterations in the spleen, liver, kidneys, lungs, heart, digestive tract and bone marrow⁶. In the alimentary form, together with the intestines, Peyer's patches, mesenteric lymph nodes and the liver are mainly affected^{1,6}. Only the thymus is affected in some cases of thymic form, but in most cases, enlarged mediastinal lymph nodes, spreading to the internal organs are observed⁶. Because the material comprised only two organs in the presented case no comments could be made about the form of lymphoma.

Intravascular neoplastic cells, characteristic finding of leukemia⁵, were determined in the liver and spleen in sheep with lymphoma in sporadic cases¹¹. It has been reported that although leukemia and bone marrow were not involved in ovine lymphoma in a study⁸, but chronic lymphocytic leukemia and bone marrow involvement were described in sheep in another study¹⁰. Development of persistent lymphocytosis was reported in sheep infected by BLV⁴. Furthermore, leukemia was reported to develop following the late stages of solid lymphoma⁵. In the present case, macroscopic and microscopic findings in the liver and the kidneys show similarity to previous studies; however, intravascular neoplastic cell groups associated with leukemia were not found.

Lymphomas are histologically classified as lymphoblastoid, prolymphocytic, lymphocytic, histiocytic or reticular types^{5,6}. The most common type in sheep has been reported as the lymphoblastoid type⁷. Based on atypical mononuclear cells found in the liver and the kidneys in our case exhibiting similar characteristics to mature lymphocytes, the case was regarded as lymphocytic lymphoma.

Lymphoma originates from T and B lymphocytes and histiocytes, which comprise the immune system. Differentiation of these cells is made by revealing the phenotypic and molecular characteristics of the tumor

cells⁸. Immunophenotypic and haematological studies indicate that enzootic bovine lymphoma are mostly B cell origin^{12,13}. Immunophenotypic studies in sheep show that lymphoma is the B and T cell origin; however, B cell lineage was identified in most cases⁵. In addition, alimentary form lymphomas are usually originated from B cell¹⁴. A lymphoma case in a sheep was examined by immunohistochemical staining with CD79a, CD20, CD3, CD68 kits and, the only positivity was determined with CD79a, a diagnostic marker of B cell leukemia¹¹. In the present case, the case was regarded as T cell lymphoma due to the neoplastic cells showed positivity with CD3, but negativity with CD20 and CD 79a.

In conclusion, lymphocytic T cell lymphoma was described by histological and immunophenotypical examination for the first time in the Akkaraman sheep in Turkey. It is therefore believed that this finding may provide significant contribution to the literature in this area.

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