Iranian Journal of Pathology (2009)4 (2), 88 - 91

Case Report

Littoral Cell Angioma: A Morphologic and Immunohistochemical Study

Mohsen Emami Aleagha[1], Etrat Javadi Rad[1], Siamak Shariat Torbaghan[2]

1-Dept. of Pathology, Kermanshah University of Medical Sciences, Kermanshah, Iran.
2-Dept. of Pathology, Tehran University of Medical Sciences, Tehran, Iran.

ABSTRACT

Littoral cell angioma is a splenic vascular tumor of splenic sinus lining cells that is considered benign in general. This report describes a case of littoral cell angioma with no malignant histological features. The lesion is composed of anastomosing vascular channels resembling splenic sinus; they are lined by endothelial cells which show mitotic activity very rare. Immunohistochemically, the tumor cells were positive for both endothelial (Factor VIII-AG, CD_{34}) and histiocytic markers (KP_1 or CD_{68}). The morphologic and immunohistochemical findings in this tumor confirm the presence of dual (endothelial / histiocytic) characteristics of the reticuloendothelial cells lining the splenic sinus, justifying the term littoral cell angioma.

Keywords: Angioma, Spleen, Iran

Introduction

Vascular tumors are the most common primary neoplasms of the spleen. Most of these lesions are derived from vascular endothelium (1,2). Less common is originated from the cells in the red pulp sinuses (littoral cells) (1,3). Littoral cell angioma is a unique splenic tumor that may be present with abdominal pain or may be an incidental finding. The tumor is characterized by a mixture of papillary and cystic areas lined by plump cells with nuclear enlargement, but lacks mitotic activity. Littoral cells have a mixed vascular and histiocytic origin. Normal littoral cells, express CD_8 but the lining cells of littoral cell angioma do not express CD_8 or CD_{34}, although express CD_{31}, CD_{68},CD_{163} (1,4-7).

Here we present a patient with a splenic tumor with morphologic and immunophenotypic features of littoral cell angioma. All antibodies were from DAKO company and used according to the standard methods at the Pathology Department, Kermanshah University of Medical Sciences.

Case Report

A 31-year-old man from west part of Iran presented with recent vague abdominal pain and discomfort with a history of brucellosis 3 years ago. Physical

Received: 20 April 2008
Accepted: 20 January 2009
Address communications to: Dr Mohsen Emami Aleagha, Department of Pathology, Kermanshah University of Medical Sciences, Kermanshah, Iran.
Email: draleagha@yahoo.com

examination disclosed only a mildly enlarged, non-tender spleen. Laboratory examination showed anemia of 11.1 g/dL hemoglobin. Leukocyte count, platelet count, liver function tests, and coagulation tests were normal. Abdominal ultrasound, and computed tomography (CT) scans confirmed mild splenomegaly with non-homogeneous texture and one round, hyperdense lesion, and a normal liver. Splenectomy was performed. The patient promptly recovered. No further therapy was administered.

The spleen was immediately placed in 10% buffered formalin solution, fixed for 24h, and routinely processed for paraffin embedding. Sections were stained with hematoxylin and eosin. Immunostaining was performed manually using routine steamer antigen retrieval and the envision system, HRP (DAB) kit (DAKO, Carpinteria, CA), following manufacturer's instructions. Negative and positive controls were run for each antibody (CD_{31}, CD_{34}, CD_{68}, Factor VIII. AG).

The enlarged spleen was 16x 8.5x 5.5cm. The capsule was intact. Cut sections, show a red, hemorrhagic tissue with a relatively well-circumscribed mass measuring 6.5x 5.5cm. It had spongy configuration with few delicate gray septa. Histological sections showed diffuse replacement of splenic parenchyma by vascular channels, a few with cystic dilation harboring intraluminal papillary projections and other areas with solid architecture. The cells lining the channels and papillary fronds and comprising the solid areas had abundant clear-to-eosinophilic cytoplasm and oval-to-spindle large vesicular nuclei, including indented and grooved nuclei (Fig. 1). Some cells had foamy cytoplasm, and a few showed erythrophagocytosis. Nuclear atypia was mild, and mitoses were not seen (Fig. 2). Remainder of splenic parenchyma was unremarkable.

On immunohistochemistry, the lining cells exhibit strong positivity for factor VIII and CD_{34} (Fig. 3, 4). In addition, they react with monoclonal antibodies against the macrophage-associated CD_{68} antigen. The cytoplasmic reactivity was granular and of variable intensity in the cell lining the vascular channels; however, reactivity was faint or absent in littoral cells with scant cytoplasm and small nuclei.

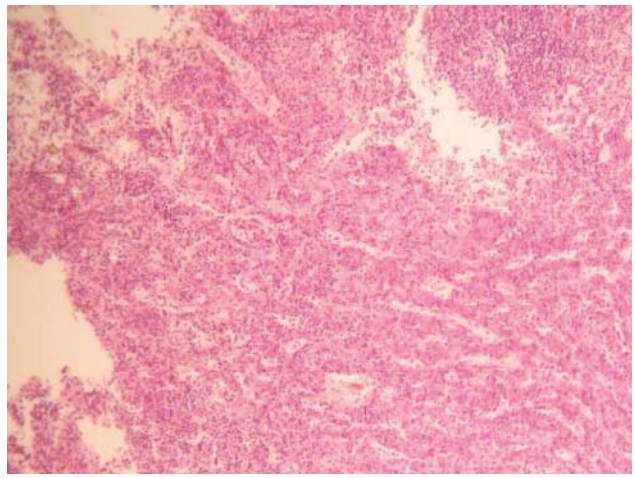

Fig. 1: Anastomosing vascular channels, a few with cystic dilation (.H&E Staining x100)

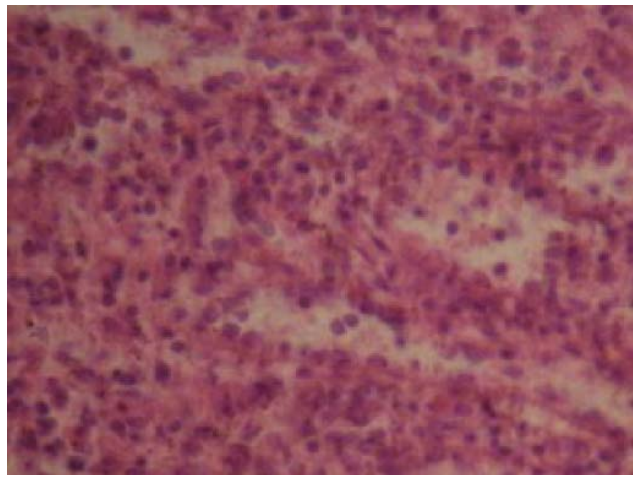

Fig. 2: The cells lining the channels showed clear to eosinophilic cytoplasm and oval large vesicular nuclei (H&E Staining x400).

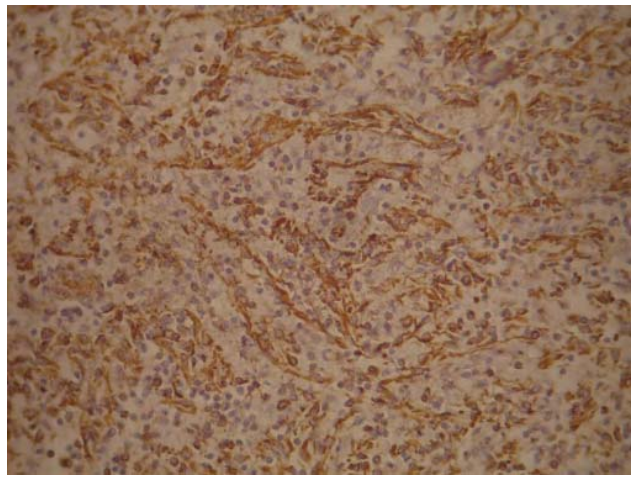

Fig. 3: The lining cells were positive for factor VIIIag

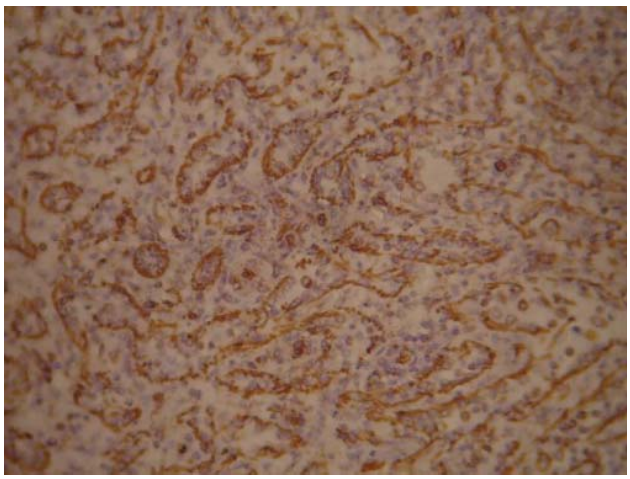

Fig. 4: The lining cells expressed CD34 (*100 magnification.IHC Staining).

Discussion

Littoral cell angioma (LCA) is a vascular proliferation unique to the spleen (5). The lesion may occur either as solitary nodules or as multiple lesions, but they are always situated within the splenic red pulp (1). Although its cellular origin is assumed to be the normal splenic sinus lining cells, the tumor cells show slight immunophenotypic differences from this normal cellular component of the spleen (4,8).

The basic morphologic feature is the presence of vascular channels that are reminiscent of splenic sinuses and that may anastomose with normal sinuses at the periphery of the tumor the appearance of these vascular channels is quite variable, because cyst like spaces, papillary fronds as well as solid intraluminal proliferations, may be present within the same lesion. The lining cells observed in the lesions point to sinus endothelium, as they may be morphologically indistinguishable from normal littoral cells, at least in some areas of the lesions (1,9). Characteristically, however, most areas of LCA show lining cells that possess vesicular nuclei and more abundant cytoplasm and may phagocytose as well as slough off into the vascular lumina (1,10). Immunohistochemically, the proliferating cells expressed both endothelial and histiocyte-associated antigen. Our case had morphologic and immunophenotypic findings similar to those previously described, with reactivity for the vascular marker CD_{31}, as well as expression of the CD_{68} antigen (3,11,12). Expression of the CD_{68} antigen was not unique to this type of tumor in the spleen and although CD_{68} antigen expression is common in histiocytic cells, its expression is also not lineage specific (1,5,13). Some of the hemangiomas as well as half of the angiosarcomas of the other studies also had lining cells expressing CD_{68}. However, CD_{21} expression was unique to the LCA cases. LCAs are proposed to be tumors of the splenic sinus lining cells or littoral cells (1,3,14).

LCA appears to be a benign neoplasm. Follow-up obtained for many cases reveals that patients with typical LCA did not develop either recurrence or metastatic disease, but in rare case metastasis has been reported (15). In our case, following up 14 years after splenectomy reveals no recurrence or specific pathologic finding. In summary, LCA constitutes a distinct clinicopathologic entity that broadens the spectrum of vascular tumors of the spleen and that must be considered in differential diagnosis of these lesions (splenic hemangioma, angiosarcoma, vascular hamartoma and peliosis) (1). Its peculiar morphologic and immunophenotypic properties reflect the dual, i.e., endothelial / histiocytic, differentiation potential of splenic sinus-lining cells and thus underline the importance of the "reticuloendothelial system" concept.

Acknowledgement

We are grateful to Professor Juan Rosai M.D from the Weil Medical College of Cornell University (NewYork , USA) and chairman of Nnational Cancer Institute (Milan , Italy) for his thoughtful review of the slides and confirming the diagnosis.

References

1. Falk S, Stutte HJ, Frizzera G. Littoral cell angioma. A novel splenic vascular lesion demonstrating histiocytic differentiation. Am J Surg Pathol 1991;15(11):1023-33.

2. Burke JS. Surgical pathology of the spleen: an approach to the differential diagnosis of splenic lymphomas and leukemias. Part II. Diseases of the red pulp. Am J Surg Pathol 1981;5(7):681-94.

3. Rosso R, Paulli M, Gianelli U, Boveri E, Stella G, Magrini U. Littoral cell angiosarcoma of the spleen. Case report with immunohistochemical and ultrastructural analysis. Am J Surg Pathol 1995;19(10):1203-8.

4. Fernandez S, Cook GW, Arber DA. Metastasizing splenic littoral cell hemangioendothelioma. Am J Surg

Pathol 2006;30(8):1036-40.

5. Arber DA, Strickler JG, Chen YY, Weiss LM. Splenic vascular tumors: a histologic, immunophenotypic, and virologic study. Am J Surg Pathol 1997;21(7):827-35.

6. Ben-Izhak O, Bejar J, Ben-Eliezer S, Vlodavsky E. Splenic littoral cell haemangioendothelioma: a new low-grade variant of malignant littoral cell tumour. Histopathology 2001;39(5):469-75.

7. Rosso R, Gianelli U, Chan JK. Further evidence supporting the sinus lining cell nature of splenic littoral cell angiosarcoma. Am J Surg Pathol 1996;20(12):1531.

8. Nguyen TT, Schwartz EJ, West RB, Warnke RA, Arber DA, Natkunam Y. Expression of CD163 (hemoglobin scavenger receptor) in normal tissues, lymphomas, carcinomas, and sarcomas is largely restricted to the monocyte/macrophage lineage. Am J Surg Pathol 2005;29(5):617-24.

9. Gregorc V, Ludovini V, Pistola L, Darwish S, Floriani I, Bellezza G, *et al.* Relevance of p53, bcl-2 and Rb expression on resistance to cisplatin-based chemotherapy in advanced non-small cell lung cancer. Lung Cancer 2003;39(1):41-8.

10. Hirasawa Y, Tokuhiro H. Electron microscopic studies on the normal human spleen: especially on the red pulp and the reticulo-endothelial cells. Blood 1970;35(2):201-12.

11. Buckley PJ, Dickson SA, Walker WS. Human splenic sinusoidal lining cells express antigens associated with monocytes, macrophages, endothelial cells, and T lymphocytes. J Immunol 1985;134(4):2310-5.

12. Garvin DF, King FM. Cysts and non-lymphomatous tumors of the spleen. Pathol Ann 1981;16: 61-80.

13. Falk S, Stutte HJ. Hamartomas of the spleen: a study of 20 biopsy cases. Histopathology 1989 Jun;14(6):603-12.

14. Pardo-Mindan FJ, Vazquez JJ, Joly M, Rocha E. Splenic hamartoma, vascular type, with endothelial proliferation. Pathol Res Pract 1983;177(1):32-40.

15. Rosso R, Paulli M. Littoral cell angiosarcoma: a truly malignant tumor. Am J Surg Pathol 2004;28(9):1255.