Human Pathology (2009) **40**, 374–380

ELSEVIER

Human PATHOLOGY

www.elsevier.com/locate/humpath

Original contribution

Lymphatic differentiation in renal angiomyolipomas

Stephen M. Bonsib MD*, **Mana Moghadamfalahi MD**, **Ami Bhalodia MD**

Louisiana State University Health Sciences Center, Shreveport, LA 71130, USA

Received 25 April 2008; revised 6 August 2008; accepted 8 August 2008

Keywords:
Angiomyolipoma;
Lymphatic;
Podoplanin;
D2-40

Summary Renal angiomyolipomas are mesenchymal neoplasms with varying proportions of smooth muscle, adipose tissue, and abnormal blood vessels. Although the presence of lymphangiomatous-like foci is frequently noted in large series of angiomyolipoma, lymphatic differentiation has not been previously studied. Twelve angiomyolipomas from 10 patients were identified. All tumors expressed a melanocytic marker, HMB-45 or Melan-A. Twenty-eight paraffin blocks (1-4 per tumor) were stained for lymphatic endothelial cell markers, podoplanin, and D2-40, and the presence and distribution of lymphatic differentiation were recorded. The angiomyolipomas ranged from typical triphasic tumors to leiomyoma-like and lipoma-like tumors. All 12 tumors showed positive staining with podoplanin, and all 6 tumors stained for D2-40 were also positive, indicative of lymphatic differentiation. Lymphatic differentiation was variably observed throughout the tumors. It was most prevalent in myoid areas of the triphasic angiomyolipomas and in the leiomyoma-like variant, but infrequent and widely scattered within the adipose regions of triphasic angiomyolipoma and in the lipoma-like variant. The lymphatics were usually small, often irregularly shaped, and isolated vessels in fat, whereas in myoid regions lymphatics were clustered and in some areas formed a sinusoidal or labyrinth-like pattern. Lymphatics were commonly adjacent to abnormal arteries. However, unlike the lymphatics in the normal renal cortex, a consistent adventitial association was not observed and the clustering around arteries is regarded as reflecting the myoid regions that typically exist in these areas. In conclusion, lymphatic differentiation is common in angiomyolipomas, preferentially located in myoid regions. These data expand the mesenchymal pluripotential profile of renal angiomyolipomas.

1. Introduction

Angiomyolipoma (AML) is a member of a complex family of neoplasms believed to be derived from the perivascular epithelioid cell (PEC) [1-3]. Neoplasms within this family exhibit remarkable morphologic diversity that ranges from epithelial-appearing tumors such as the clear cell tumor of the lung and pancreas, epithelioid AML, oncocytoma-like AML, and clear cell PEComs of visceral organs and soft tissue, to mesenchymal-appearing neoplasms such as AML, pulmonary lymphangioleiomyomatosis, cardiac rhabdomyoma, and a very rare neoplasm, clear cell myomelanocytic tumor of the falciform ligament, and ligamentum teres [4-9]. A unifying attribute of the PEComa family is their distinctive immunohistochemical signature, expression of melanocytic antigens such as HMB-45, Melan A/Mart-1, and microophthalmia transcription factor [1-3].

The mesenchymal cell profile that may be encountered in members of this family is broad and includes

* Corresponding author.
E-mail address: sbonsi@lsuhsc.edu (S. M. Bonsib).

0046-8177/$ – see front matter © 2009 Elsevier Inc. All rights reserved.
doi:10.1016/j.humpath.2008.08.010

adipocytes; smooth muscle cells; cardiac muscle cells; a variety of endothelial cell–lined vascular structures such as abnormal arteries, arterioles, and capillary-sized vessels; and lymphatics in lymphangioleiomyomatosis. Slit-like and curvilinear lymphatic-like channels and lymphangioleiomyomatosis-like foci are well known in the classic triphasic AML and in the monomorphic smooth muscle dominant variants [10-15].

In a recent report of cystic AML, Davis et al. [15] described lymphatic-like spaces similar to findings in lymphangioleiomyomatosis that exhibited lymphatic endothelial cell (LEC) differentiation based upon staining with D2-40 [16]. D2-40 is a reliable LEC marker that reacts with podoplanin, an antigen that resides within the lymphatic endothelium but is absent in hematogenous epithelium [17-19]. Lymphatic differentiation in an AML may be no surprise in light of the cell phenotypic diversity within PEC-derived neoplasms mentioned above, and because one member of this group, lymphangioleiomyomatosis, is believed to be derived from and often connected to the lymphatic system [20-22]. As lymphatic differentiation has not been studied in AMLs in detail, we extend the observations of Davis et al and describe the incidence and morphologic appearance of LEC differentiation in a group of 12 AMLs that range from the classic triphasic form to monomorphic leiomyoma-like and lipoma-like varieties.

2. Material and methods

In this study, 12 AMLs of diverse types from 10 patients were collected (Table 1). Five patients had tuberous sclerosis and 2 of these had end-stage renal disease. All 12 tumors expressed melanocytic markers, HMB-45 and/or Melan A. The cases included 5 triphasic AMLs, 3 of which presented as tumor nodules. One bilateral triphasic case entirely replaced both kidneys without formation of a mass lesion, herein referred to as angiomyolipomatosis. Five tumors were leiomyoma-like and 2 tumors were lipoma-like variants.

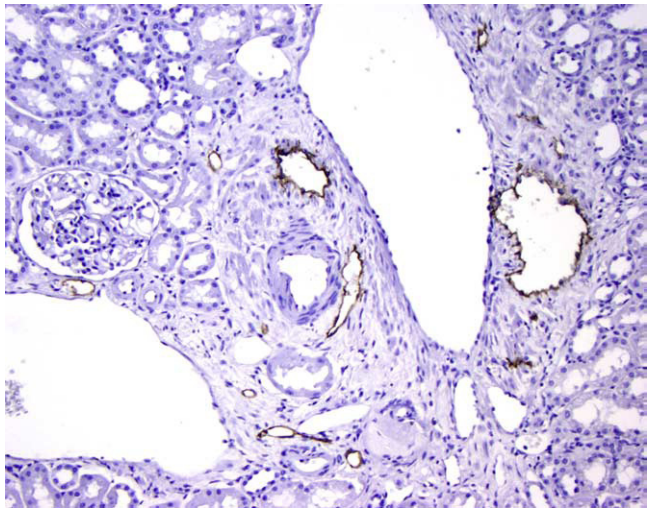

Fig. 1 Normal cortex. Notice that lymphatics are restricted to the adventitial region of the interlobular arteries. Immunoperoxidase stain for podoplanin.

Twenty-eight formalin-fixed paraffin-embedded blocks, 1 to 4 per case, were selected for immunohistochemical study. Immunoperoxidase stains were performed with the LEC marker podoplanin (AngioBio Co, Del Mar, CA; 1:100 dilution) in all cases. A second endothelial marker, D2-40 (Signet, Dedham, MA; 1:400 dilution), was also used in 6 cases to validate the results of podoplanin staining. Skin and tonsil tissue were used as positive controls.

Lymphatic differentiation was defined as a podoplanin-positive and D2-40–positive endothelial-lined structure. Endothelial-lined structures with a negative staining pattern for podoplanin and D2-40 were regarded as lined by hematogenous endothelial cells (HEC). Internal controls consisted of adjacent nonneoplastic renal cortex where LEC staining was limited to the adventitial regions of interlobular arteries, as previously reported (Fig. 1) [18].

Table 1 Clinical and morphologic information

Patient no.	Age/sex	Size (cm)	Clinical	Type of AML	No. of blocks
1	56F	2.2		Triphasic	3
2	68F	2.9		Triphasic	1
3	47F	20.0		Triphasic	3
4-Lt	38F	N/A	TS/ESKD	Triphasic, angiomyolipomatosis	2
4-Rt	38F	N/A	TS/ESKD	Triphasic, angiomyolipomatosis	2
5	61F	1.9		Lipoma-like	4
6-Rt	58F	0.5	TS/ESKD	Lipoma-like	1
6-Lt	58F	2.5	TS/ESKD	Leiomyoma-like	2
7	76M	3.4	TS	Leiomyoma-like	2
8	76M	2.5	TS	Leiomyoma-like	2
9	38F	1.8		Leiomyoma-like	2
10	21F	4.0	TS	Leiomyoma-like	4

Abbreviations: M, male; F, female; Lt, left; Rt, right; TS, tuberous sclerosis; ESKD, end-stage kidney disease; N/A, not applicable.