Human Pathology (2011) **42**, 1013–1018

ELSEVIER

Human PATHOLOGY

www.elsevier.com/locate/humpath

Original contribution

Adrenal lymphangioma: clinicopathologic and immunohistochemical characteristics of a rare lesion☆

Carla L. Ellis MD, MS[a], Priya Banerjee MD[a], Erin Carney MD[a], Rajni Sharma PhD[a], George J. Netto MD[a,b,c,*]

[a]*Department of Pathology, The Johns Hopkins Hospital, Baltimore, MD 21287, USA*
[b]*Department of Urology, The Johns Hopkins Hospital, Baltimore, MD 21287, USA*
[c]*Department of Oncology, The Johns Hopkins Hospital, Baltimore, MD 21287, USA*

Received 31 August 2010; revised 18 October 2010; accepted 20 October 2010

Keywords:
Adrenal;
Lymphangioma;
D2-40

Summary Adrenal lymphangiomas, also known as cystic adrenal lymphangiomas, are rare, benign vascular lesions that usually remain asymptomatic throughout life. Although previously adrenal lymphangioma lesions were primarily found at autopsy, they are currently detected during imaging work-up for unrelated causes and are likely to imitate other adrenocortical or adrenal medullary neoplasms. We aimed to retrospectively review all adrenal lymphangioma cases at our hospital and further document their lymphatic origin by immunohistochemical staining. A search of surgical pathology records (1984-2008) was conducted. All hematoxylin and eosin sections were retrieved from archives and reviewed by 2 pathologists in the study. Clinical information was gathered from electronic medical records. Representative paraffin-embedded sections from each case were selected for immunohistochemical analysis using monoclonal antibodies D2-40 and AE1/AE3. A total of 9 adrenal lymphangioma cases were identified (6 women and 3 men). All 9 patients were adults at time of diagnosis with a mean age of 42 years (range, 28-56 years). There were 7 white patients, 1 African American patient, and 1 Asian patient. The average size of an adrenal lymphangioma lesion was 4.9 cm (range, 2.0-13.5 cm). Adrenal lymphangioma was twice more frequently located on the right side (6 right-sided and 3 left-sided). Clinically, 4 (44%) of the 9 lesions presented with abdominal, flank, or back pain. One lymphangioma was found during work-up for labile hypertension. The remaining 4 lesions (44%) were asymptomatic and incidentally found during imaging studies for unrelated causes. Surgical removal was achieved by total adrenalectomy in 8 of the 9 lesions and by partial adrenalectomy in the remaining case. No evidence of recurrence or development of a contralateral lesion was encountered in any of the patients. Histologically, our adrenal lymphangiomas showed a typical multicystic architecture with dilated spaces lined by flattened, bland, simple lining. The cystic channels/spaces occasionally contained proteinaceous material and lacked red blood cell content. On immunohistochemical stains, D2-40 cytoplasmic staining was positive in all 9 examined lesions, whereas AE1/AE3 was negative, thus, confirming their lymphatic nature. D2-40 staining was diffuse in 2 and focal in the 7 remaining lesions. Adrenal lymphangiomas are very rare, benign lymphatic neoplasms with a female, right-sided predominance in our current series. They may clinically present

☆ Presented in part at the 2009 United States and Canadian Academy of Pathology Annual Meeting in Boston, USA.

* Corresponding author. The Johns Hopkins Hospital, 401 North Broadway, Weinberg 2242, Baltimore, MD 21287, USA.
E-mail address: gnetto1@jhmi.edu (G. J. Netto).

doi:10.1016/j.humpath.2010.10.023

with abdominal pain or can be incidentally found during adulthood as a mass, necessitating surgical removal to rule out other types of adrenal neoplasms.

1. Introduction

Primary adrenal "cysts" are very rare lesions with an incidence of approximately 0.06% in the general population [1]. Most of these lesions are clinically asymptomatic, with incidental discovery during imaging or surgery for an unrelated complaint or at autopsy [2-4]. The differential diagnosis of adrenal cystic lesions includes a primary or metastatic cystic neoplasm (including endothelial and epithelial lined cysts), hemorrhage, pseudocysts, and infections including echinococcal cysts [3,5,6]. Adrenal cysts are divided into 4 main histologic subtypes: pseudocysts, parasitic cysts, epithelial lined cysts, and endothelial lined cysts. The latter are further subdivided into angiomatous and lymphangiomatous cysts [3,4]. Adrenal lymphangioma (AL), also known as cystic AL, is a benign vascular lesion first reported in 1965, with currently less than 50 cases reported in the literature. Advancements in radiographic techniques have improved the ability to clinically characterize adrenal cystic lesions. Despite current improved capabilities, benign and malignant adrenal tumors including adrenocortical neoplasms and pheochromocytomas remain in their clinical differential diagnosis, thus, necessitating surgical removal [2]. The current study is a retrospective review of clinical and pathologic features of all AL treated in our hospital during the last 24 years.

2. Materials and methods

2.1. Patient cohort

A retrospective search of all electronic surgical pathology records (Pathology Data Systems) from 1984 to 2008 in The Johns Hopkins Hospital Department of Pathology was conducted. A total of 9 AL cases were identified. No autopsy cases were found. All hematoxylin and eosin sections and previously performed immunohistochemical slides were retrieved from archives and reviewed by 2 pathologists in the study. Clinical information was retrospectively retrieved from electronic medical records. A representative formalin-fixed, paraffin-embedded block from each case was selected for additional immunohistochemical analysis.

2.2. Immunohistochemistry

Immunohistochemical staining for D240 and AE1/AE3 was performed on 5-μm-thick, formalin-fixed, paraffin-embedded sections using automated staining systems. Slides were deparaffinized and hydrated, and heat-induced antigen retrieval was performed. Incubation with primary antibody using optimal conditions was followed by development of immunostaining and counterstaining as per manufacturer's instructions. The antibody specifications are summarized in Table 1. Immunoexpression of each marker was evaluated for extent and intensity. Extent of positive staining was characterized as focal (<25%) or diffuse. Intensity of positive staining was categorized as weak (1+), moderate (2+), and strong (3+).

3. Results

3.1. Clinicopathologic characteristics

Clincopathologic findings are summarized in Table 2. There were 6 female and 3 male patients. All 9 patients were adults at time of diagnosis with a mean age of 42 years (range, 28-56 years). There were 7 white patients, 1 African American patient, and 1 Asian patient. The average lesion size was 4.9 cm (range, 2.0-13.5 cm). AL lesions were all unilateral and twice more frequently located on the right side (6 right-sided and 3 left-sided). Clinically, 3 patients presented with back or flank pain (33%), 1 patient presented with abdominal pain (11%), 1 patient presented with labile hypertension, and 4 patients (44%) presented with unrelated

Table 1 Immunohistochemical markers: clones, sources, dilutions, and methods of staining

Name/clone/source	Dilution	Antigen retrieval	Primary antibody incubation time	Autostainer
Antipancytokeratin, clone-AE1/AE3/PCK26 (Ventana Medical Systems, Inc, Tucson, AZ)	Predilute	Enzyme (protease 1 for 4 min)	16 min	Ventana benchmark (Ventana Medical Systems, Inc)
Antihuman, D240 clone-D2-40 (Dako North America, Carpentaria, CA)	1:200	ER2 (basic pH for 20 min)	15 min	Bond-Leica (Leica Microsystems, Bannockburn, IL)