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Epithelioid smooth muscle tumors of the uterus do not express CD1a: a potential immunohistochemical adjunct in their distinction from uterine perivascular epithelioid cell tumors☆

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Abstract Uterine epithelioid smooth muscle tumors and uterine perivascular epithelioid cell tumors (PEComas) are known to display such a substantial overlap in morphologic and immunophenotypic characteristics that the existence of the latter as a distinct clinicopathologic entity at this location has been called into question. Recent research suggests that the constituent entities of the PEComa family at all anatomical locations, including lymphangioleiomyomatosis of the uterus, uniformly display immunoreactivity for CD1a. The purpose of this study is to determine the proportion of uterine epithelioid smooth muscle tumors that may similarly be CD1a-positive. Representative sections from 18 archived epithelioid smooth muscle tumors of the uterine corpus (6 epithelioid leiomyosarcomas and 12 epithelioid leiomyomas), diagnosed and classified as such based on World Health Organization criteria, were subjected to immunohistochemical stains for CD1a and HMB-45. The epithelioid component of the tissue sections evaluated ranged from 10% to 100% (mean, 70%). Two cases were composed predominantly of cells with overtly clear cytoplasm. All cases were entirely negative for CD1a. Of 18 cases, 1 (5.5%) (an epithelioid leiomyosarcoma) displayed immunoreactivity for HMB-45 in scattered lesional cells that constituted approximately 5% of the overall tumoral volume for the case. All others were HMB-45–negative. Given their rarity, future studies are required to confirm that all PEComas of the uterus are indeed uniformly positive for CD1a. However, if the latter staining pattern is confirmed, our findings herein suggest that CD1a may be a useful immunohistochemical adjunct in distinguishing uterine epithelioid smooth muscle tumors from uterine PEComas.
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Keywords: CD1a; HMB-45; Epithelioid leiomyoma; Epithelioid leiomyosarcoma; Perivascular epithelioid cell tumors; PEComa

1. Introduction

The family of neoplasms that have been designated "perivascular epithelioid cell tumors" (PEComas) include angiomyolipoma, clear cell "sugar" tumors, lymphangioleiomyomatosis, clear cell myomelanocytic tumor of the falciform ligament/ligamentum teres, and other "unusual clear cell tumors" from a multitude of anatomical locations [1-14]. These neoplasms are characterized and unified by their at least partial constituency of the putative "perivascular epithelioid cells" [13-15]. This cell type has been recognized in renal angiomyolipomas since 1943 [15] and has no known normal anatomical homologue. Tumors that are thought to be composed of perivascular epithelioid cells are characterized at least partially by admixtures of spindle and epithelioid cells that display clear to eosinophilic/granular cytoplasm, perivascular arrangements, immunoreactivity for melanocytic markers (eg, HMB-45, micropthalmia transcription factor

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(miTF), melan A, melanoma antigens recognized by T cells, human melanosome-associated antigen 1), and with less frequency, "muscular" markers (eg, actin and desmin) [1-15]. The nebulous category that has previously been designated "perivascular epithelioid cell tumors not otherwise specified" (PEComa-NOS) essentially includes the aforementioned "unusual clear cell tumors" [4-8]. Henceforth in this report, we use the term PEComa to refer to these "unusual clear cell tumors" [9], that is, mass-forming uterine PEComas that cannot be classified as lymphangioleiomyomatosis or conventional angiomyolipomas. This includes cases reported as epithelioid angiomyolipomas and conceptually encompasses those reported as or morphologically identical to clear cell myomelanocytic tumor of the falciform ligament/ligament teres [16]. The PEComas are generally considered to be anatomically ubiquitous [4,6,13,14]. However, the uterus, an anatomical site where PEComas are recognized in the World Health Organization (WHO) classification [17], undoubtedly represents one of their most frequently reported anatomical sites of origin, with more than 50 reported cases in the medical literature [4,18-42]. As we have detailed elsewhere [7,8], cases reported as PEComas of the uterus [4,18-42] and those reported as uterine epithelioid smooth muscle tumors [43-48] display a substantial overlap in morphologic and immunophenotypic characteristics and may therefore be a source of diagnostic difficulty. Recent research suggests that the constituent entities of the PEComa family at all anatomical locations, including lymphangioleiomyomatosis of the uterus, uniformly display immunoreactivity for CD1a [49]. The purpose of this study is to determine the proportion of conventional epithelioid smooth muscle tumors that may similarly be CD1a-positive.

2. Materials and methods

Eighteen cases diagnostically coded as epithelioid smooth muscle tumors were retrieved after a search of the computerized databases of the Pathology Departments at Wilford Hall Medical Center (Lackland AFB, TX) and Stony Brook University Hospital (Stony Brook, NY). Selected slides were reviewed to confirm the reference interpretations. The 18 cases could be classified into epithelioid leiomyomas (n = 12) and epithelioid leiomyosarcomas (n = 6) according to WHO criteria [17]. Smooth muscle tumors with any epithelioid component were included. One section from each case was selected for immunohistochemistry. Sections (5-μm-thick) were cut from each corresponding paraffin block and mounted on positively charged glass slides. After heating, deparaffinization in xylene, rehydration in graded alcohols, blockage of endogenous peroxidase, pretreatment with Reveal (1:10 dilution with deionized water; Biocare Medical Corp., Concord, CA) solution and heat-induced epitope retrieval of these tissue-mounted slides, immunohistochemical assays were carried out in an Axiom 36 autostainer (LabVision Corporation, Fremont, CA) using mouse monoclonal antibodies to HMB-45 (Thermo Fisher Scientific, Fremont, CA; prediluted, 25-minute incubation time for primary antibody, 10-minute secondary antibody incubation times for both the probe and horseradish peroxidase polymer, 3′3′diaminobenzidine [5 minutes] as chromogen)

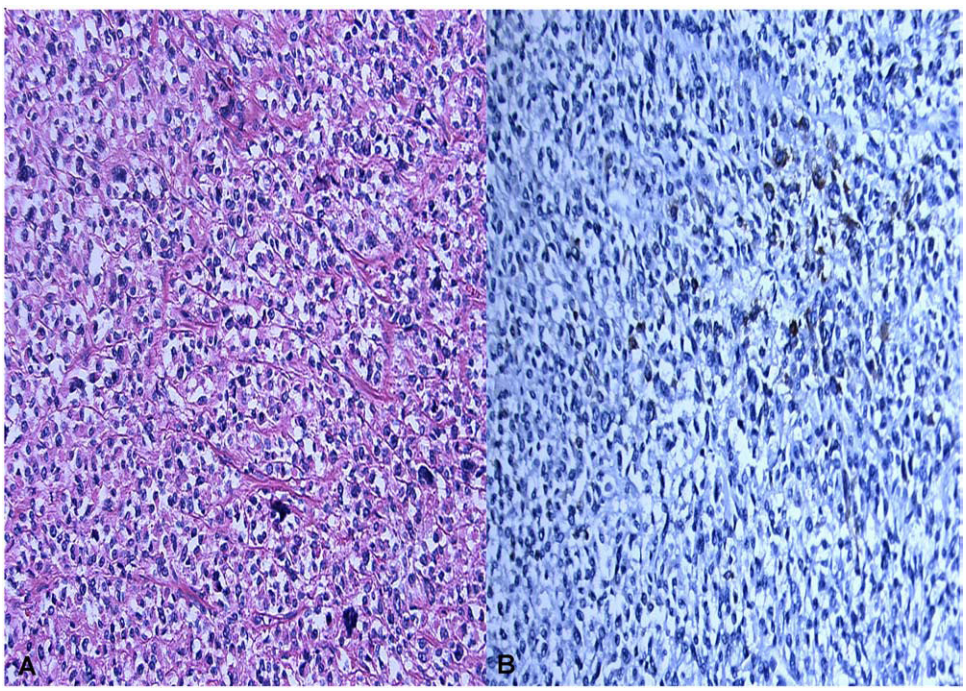

Fig. 1. (A), An epithelioid leiomyosarcoma (hematoxylin and eosin, ×100 magnification). (B), Same case as (A) showing scattered HMB-45–positive cells (immunoperoxidase, ×100 magnification).