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Perivascular Epithelioid Cell Tumors (PEComas)

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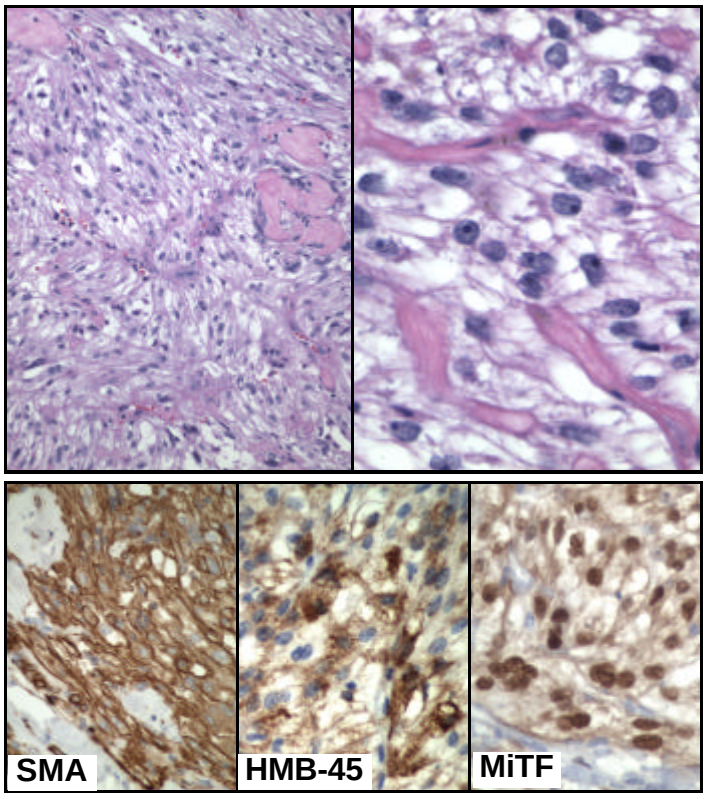
Bonetti first coined the term "perivascular epithelioid cell" in 1992. Since that time, a variety of neoplasms have been attributed to this unique cell that characteristically coexpresses smooth muscle and melanocytic markers. Angiomyolipoma, clear-cell "sugar tumor" (of the lung, pancreas, uterus, breast and eventually probably other organs), and lymphangioleiomyomatosis are all thought to arise from these cells, and it is interesting that a subset of patients with these tumors have tuberous sclerosis. In the past several years, additional neoplasms attributed to this cell have been described and reported by authors under the names "PEComa" and "clear cell myomelanocytic tumor". We recently had the opportunity to study a case presenting as a pelvic soft tissue mass, and thought it might be of interest to readers to briefly review some of the recent literature on these tumors.



H&E's and immunostains from a PEComa in the pelvis of a middle-aged female. Note clear-cell appearance with co-expression of smooth muscle and melanocytic markers.

In 2001, Bonetti and colleagues described four cases of "abdominopelvic sarcoma of perivascular epithelioid cells" arising in young females (ages 19 to 41), including 1 patient with tuberous sclerosis. The tumors ranged from 2.5 to 9 cm, and in 2 cases were attached to the serosa of the terminal ileum and serosa of the uterus, respectively. Another tumor presented as a 2.5 cm pelvic nodule thought to represent endometriosis, and the final tumor (in the patient with tuberous sclerosis) originated in the myometrium. Morphologically, all tumors resembled clear cell carcinoma of the kidney of low to intermediate grade. The tumor cells showed frequent clear cytoplasm with mild to moderate pleomorphism, variable nucleoli, and an associated prominent delicate capillary network in the background. Mitoses were rare, but focal necrosis and angiolymphatic invasion was observed. In 2 of the 4 cases, about 10% of tumor cells contained cytoplasmic pigment, presumably melanin. The tumors were negative for S100, cytokeratins (AE1, AE3, CAM5.2, KL-1), EMA, vimentin, chromogranin, myosin, desmin, and muscle-specific actin. HMB-45 was positive in all four cases, but only 2 of the 4 expressed MART-1. The Ki-67 proliferative fraction was 2-8%. One patient was lost to follow up, the 1 patient with tuberous scle-

rosis was well at 6 months follow-up, and the remaining 2 patients developed metastastes in the liver, lungs, or bone 10-28 months after surgery. Vang and Kempson subsequently reported a series of 8 uterine PEComas in patients ranging from 40 to 75, with variable percentages of tumor cells positive for HMB-45. All were S100 negative, SMA was positive in most but not all tumors, and MART-1 was present in some and absent in others.

The term "clear cell myomelanocytic tumor" was first employed by Folpe in a paper describing 7 tumors occurring in patients ranging from age 3 to 29, presenting in the region of the falciform ligament and ligamentum teres. The lesions ranged from 5 to 20 cm, and consisted of a proliferation of clear to light pink spindle cells growing in fascicles and nests, with at most modest cytologic atypia, and small but distinct nucleoli. There was an associated elaborate delicate vasculature. Mitotic activity was <1/20 HPF in all cases, and there was no necrosis or angiolymphatic invasion. All 7 tumors were HMB-45 positive and S100 negative, and 3 of the 7 tumors had paraffin blocks available for further study. All 3 of these tumors expressed (in addition to HMB-45) the melanocyte-related markers MART-1 and microphthalmia transcription factor (MiTF) (in greater than 50% of the cells). They were also positive for smooth muscle actin and myosin (in greater than 50% of cells), but negative for desmin. Electron microscopy was performed in one case, which documented the presence of premelanosomes. Follow-up was available in 6 of the 7 cases, with no evidence of recurrence in 5 patients, and 1 patient (the 29 year-old) having a presumed metastatic lesion in the lung on x-ray. Subsequently, case reports appeared in the literature of similar tumors occuring in the soft tissue of the thigh (3.5 cm tumor in a 43-year-old female) and in the muscle wall of the bladder (a 4 cm well-circumscribed tumor in a 33-year-old female). The thigh tumor was negative for S100 protein, desmin, cytokeratin, and MART-1, and positive for HMB-45, MiTF, and smooth muscle actin, and showed a low mitotic rate (<1 per 50 hpf). The bladder tumor did not show detectable mitotic activity and lacked necrosis. It was strongly positive for HMB-45 and SMA, but negative for MART-1 (clone A103), vimentin, desmin, S100, cytokeratin (KL-1), estrogen receptor, and progesterone receptor.

The recent case studied at ProPath (illustrated on the previous page) was positive for vimentin, smooth muscle actin, smooth muscle myosin, caldesmon, HMB-45, MiTF, and weakly positive for tyrosinase and muscle specific actin. It was negative for S100, desmin, MART-1, and cytokeratin.

In summary, perivascular epithelioid cells are thought to give rise to a number of different but related neoplasms, all sharing coexpression of smooth muscle markers and melanocytic markers, but characteristically lacking S100 protein. However, from the reported results in the literature, it is apparent that it may be necessary to perform multiple markers for smooth muscle and melanocytic antigens to recognize these tumors, since there is some variability in reported phenotypes. Because of their rarity, predicting clinical behavior is difficult, but is clear that at least some of these neoplasms are malignant.

References:

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