April 2016 Case of the Month

A 42-year-old woman with a liver mass

Contributed by:


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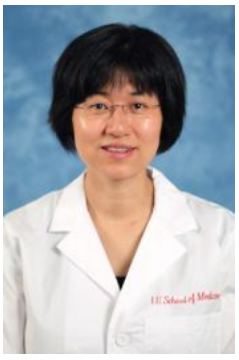
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Clinical history: A 42-year-old woman with a history of stage IV invasive ductal carcinoma of the breast status post mastectomy and chemo- and radiation therapy presents with a 3.1-cm liver mass detected on surveillance chest CT. Radiologically the lesion demonstrated prompt arterial enhancement and gradual washout excluding a possibility of focal nodular hyperplasia. Her laboratory studies including liver function tests were unremarkable. Findings of the fine needle aspiration and needle core biopsy procedures prompted surgical management with the right partial hepatectomy. A 12-months clinical follow-up showed no tumor recurrence, and liver function tests remained normal.

Gross examination: Examination of the right partial hepatectomy specimen revealed a well-demarcated gray-yellow indurated mass with dimensions of 3.2 x 2.9 x 2.5 cm in the background of a red-brown parenchyma (Figure 1).

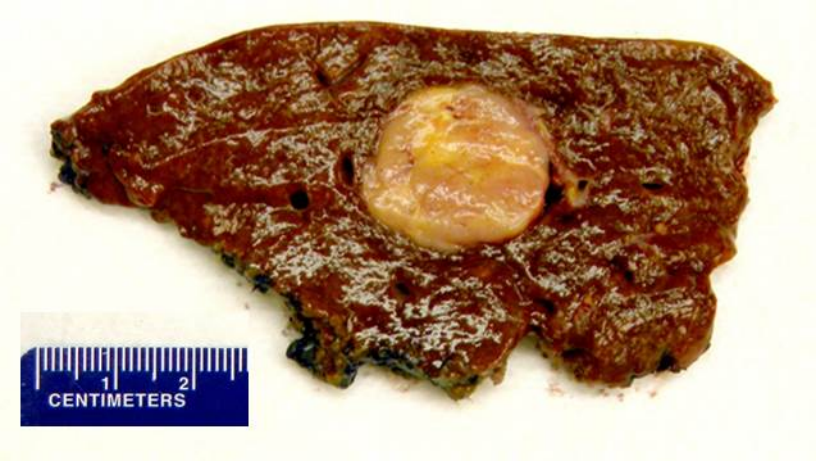
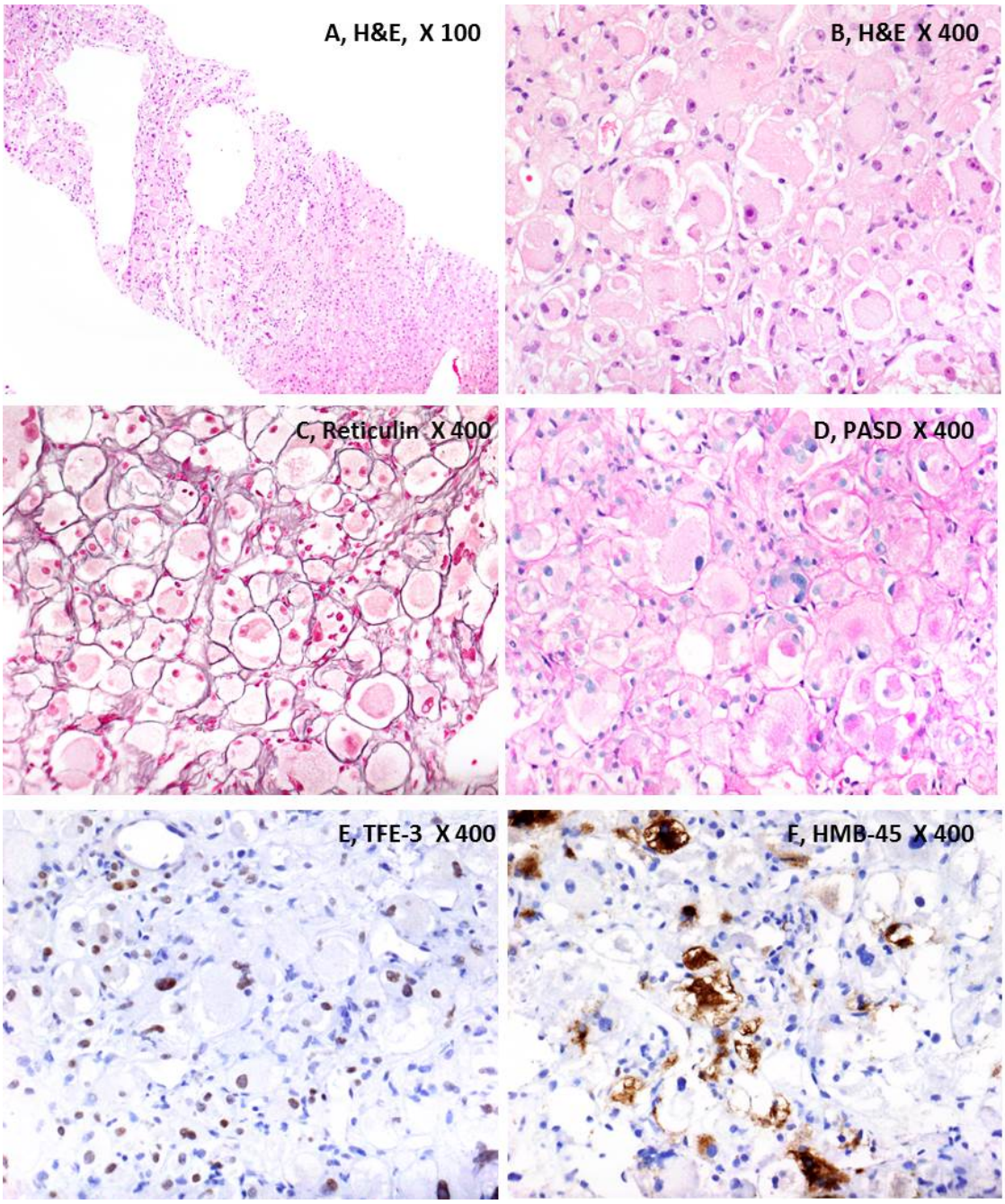


Figure 1. Gross photograph of the right hepatectomy specimen reveals a well-circumscribed gray-yellow indurated mass.

Microscopic examination and immunohistochemistry: Microscopy demonstrated an infiltrative neoplastic process with solid to vaguely organoid pattern of growth composed of large plump tumor cells remarkable for epithelioid and plasmacytoid appearance (Figure 2 A). These tumor cells had abundant eosinophilic cytoplasm with low nuclear to cytoplasmic ratios and frequent multinucleated giant cells (Figure 2B). Mitotic figures were rare, and necrosis was not detected. The background liver exhibited no features of chronic hepatitis or cirrhosis. Reticulin stain demonstrated positive fiber mesh surrounding individual tumor cells and PASD revealed occasional irregular intracytoplasmic granules (Figure 2 C and D, respectively). The immunohistochemical studies showed that the tumor cells were reactive with antibodies to HMB-45 (strong patchy, cytoplasmic), TFE-3 (moderate, diffuse, nuclear), cathepsin K (moderate, patchy, cytoplasmic), and MITF (moderate, focal, nuclear). The tumor cells were negative for AE1/3, Cam 5.2, ER, PR, S100, melan A, arginase 1, INI-1, CD31, E-cadherin, SMA, desmin, and inhibin. The electron microscopy study failed to reveal any intracytoplasmic crystals. The FISH assay for rearrangement of TFE-3 locus gene at Xp11.2 was negative.

Figure 2. Microscopic and ancillary studies: A core biopsy reveals perivascular lesion with solid growth pattern (A); Cytologic features are remarkable for large and giant plasmacytoid and epithelioid cells with abundant cytoplasm (B); Reticulin highlights a delicate meshwork surrounding individual cells (C); PASD reveals occasional cells with intracytoplasmic eosinophilic irregular granules (D); Immunohistochemical stains show moderate in intensity nuclear TFE-3 positivity (E) and strong patchy cytoplasmic HMB-45 reaction.



Final diagnosis: Perivascular epithelioid cell neoplasm (PEComa) of liver

Discussion: Perivascular epithelioid cell neoplasm (PEComa) is a family of tumors composed of histologically and immunohistochemically distinctive perivascular epithelioid cells [1]. This group includes renal and extra-renal angiomyolipoma, lymphangiomatosis, clear cell "sugar" tumor of the lung, myelomelanocytic tumor and abdominopelvic sarcoma of perivascular epithelioid cells. PEComas have been predominantly described in women with the average age of 46, though the range spans 15 to 97 years [2]. Since PEComa is associated with tuberous sclerosis (6-10% of cases), overactive mTOR pathway is possibly contributing to tumorigenesis [3]. PEComa of liver is an exceedingly rare tumor.

Historically, renal angiomyolipoma has been recognized for a long time whereas lymphangiomatosis and sugar tumor of the lung were formally described in the 1960-1970ies [4-5]. Pea at el. identified HMB-45 immunoreactivity in premelanosomes in renal angiomyolipoma in 1990ies [6]. Since then premelanosomes were confirmed in PEComas of other organs.

Grossly, the lesion occurs as a yellow to gray mass, reaching in size up to 20 cm. On microscopy, PEComa is composed of clear to lightly eosinophilic cells that grow in distinctive nested or sometimes sheet-like patterns. The cells organize in a radial fashion around blood vessels. The blood vessel types range from thin spider web-like capillary networks to dilated, hyalinized, thick-walled arterioles. Both epithelioid and myoid elements are prominent, with the epithelioid cells comprising the more immediate perivascular space and the spindle-shaped myoid cells farther away. Multinucleated giant cells are characteristic. Many cells may demonstrate cytoplasmic distention with glycogen or lipid. PEComas are considered benign neoplasms if they lack malignant morphologic features. Tumors that are "symplastic" or large in size are considered uncertain in terms of malignant potential. Dimorphic cellular composition of this tumor makes fine needle aspiration and core biopsy diagnosis difficult as it was witnessed in our case. Higher grade and cellularity corresponds to higher malignant potential. If more than two "worrisome" histologic features are identified, the tumor is considered malignant.

The immunohistochemical feature to distinguish PEComa from other neoplasms is the unique coexpression of both melanocytic and smooth muscle markers. The most important diagnostic criterion according to WHO classification of tumors of the liver and intrahepatic bile ducts is the presence of HMB-45-positive myoid cells. PEComas with a predominant component of clear cells also show extensive TFE-3 and cathepsin K positivity and they are not typically associated with TSC mutations [7], as in our case.

The chief histologic differential diagnosis in our case included metastatic mammary carcinoma, hepatocellular carcinoma, alveolar soft part sarcoma and malignant melanoma. The review of previous mastectomy slides and negative immunohistochemistry ruled out metastatic mammary carcinoma. Organoid pattern with loosely cohesive epithelioid to plasmacytoid cells with granular intracytoplasmic PASD positive inclusions made us consider alveolar soft part sarcoma. This entity was excluded by electron microscopy and TFE-3 gene Xp11 rearrangement negative studies. Lack of malignant features such as frequent mitotic figures and necrosis together with negative S100 and Melan A study excluded malignant melanoma.

Currently, the only curative option for liver PEComa is surgical excision with wide margins [2]. Adjuvant therapy has no define role in treatment of metastatic disease. Rapamycin, an inhibitor of mTOR pathway, may be beneficial for patients with metastatic disease [8].

List of References

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