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CASE REPORT

Trabecular Angiomyolipoma Mimicking Hepatic Cell Carcinoma

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Hepatic angiomyolipomas are rare tumors, especially in comparison with those occurring in the kidney. Nevertheless, it is important to be aware of their existence, especially when occurring in the liver, where they might have different subtypes. Not infrequently they are composed of rather irregular cells with epithelioid appearance. In these cases hepatocellular carcinoma or the possibility of other malignant tumors has to be ruled out, with the aid of numerous immunohistochemical reactions. The authors present a case of a female patient, whose liver lesion was first diagnosed on cytological examination as a hepatocellular carcinoma. Based on the preoperative cytological diagnosis, a large liver lobe resection was performed. Histological examination found an angiomyolipoma of the above-mentioned type, and the final diagnosis was ascertained with the aid of vimentin, smooth muscle actin (SMA), and HMB-45. (Pathology Oncology Research Vol 6, No 3, 224–226, 2000)

Keywords: hepatic tumor, angiomyolipoma, trabecular, epithelioid

Introduction

Angiomyolipoma (AML) is a benign mesenchymal tumor which occurs relatively frequently in the kidneys. AML's of the liver are much less frequent, about 80 cases have been reported in the English literature since 1976, following the first description by Ishak.[1,7] Sporadic cases have also been reported in other anatomical sites , as hard palate, skin, uterus, vagina, penis, spermatic cord and lung.[4] With the increased number of ultrasound-screening examinations of asymptomatic patients, probably more cases will be discovered. Angiomyolipomas are composed of a heterogeneous mixture of fat cells, smooth muscle cells and vessels, however, they may show variant histological patterns: trabecular, angiomatoid, pelioid, inflammatory.[1] Even in a single tumor there may be variation of the above mentioned forms.[1,3] Of the listed histological types, the trabecular form can present some differential diagnostic difficulties, since its histological picture may be similar to a hepatocellular carcinoma, or a liver angiosarcoma. Unequivocal diagnosis nowadays is usually based on HMB-45 positivity of the tumor cells, (besides others, see below), which is rather characteristic of this type of tumor.[1,2,3,9]

Our case was a hepatic angiomyolipoma of the trabecular type. Besides the preoperative cytological diagnosis (liver cell carcinoma) the histological picture was also "frightening", and first the only strong clue to question the malignant nature of the tumor was the fact, that no mitotic figure could be found after thorough examination. After the use of a huge panel of immunohistochemical reactions a hepatic angiomyolipoma was diagnosed.

Clinical history

Our patient was a 38 year old female, who underwent a routine ultrasound (US) examination in a county hospital, – organised as a screening program for teachers – which revealed a 7 cm mass in the right lobe of her liver. At the same department US guided fine needle aspiration biopsy (FNAB) was performed, and cytological examination suggested a hepatocellular carcinoma. After the cytological diagnosis the patient was admitted to the 1st Department of Surgery of the Semmelweis University and the liver mass was resected. (An intraoperative US examination was needed to find the tumor since it was not palpable.)

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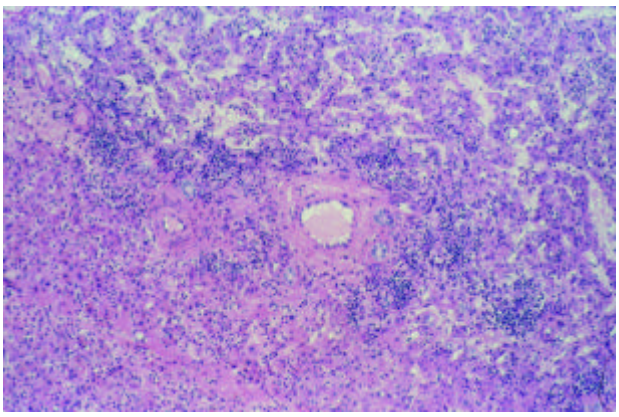

Figure 1. Low power view of the tumor, which is unencapsulated, but has a pushing margin.

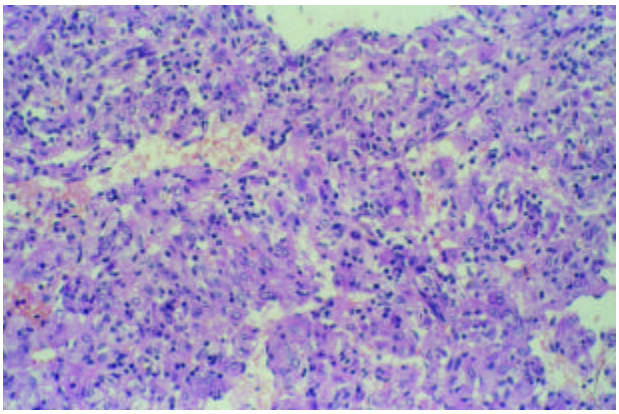

Figure 2. Higher magnification of the epithelioid cells forming trabecules. Vesicular nuclei with prominent nucleoli are readily visible. Note intrasinusoidal lipid droplets.

Pathological findings

Macroscopically the cut surface of the liver resection specimen showed a grayish brown, well circumscribed spongy tumor. The tumor also contained areas of haemorrhage. On microscopic examination the tumor had no capsule, but a pushing margin (*Figure 1*), and was composed of mainly epitheloid cells having rather "empty" looking nuclei, with irregular nuclear membranes, prominent nucleoli, and elongated cytoplasm, containing either granules or eosinophilic fibers. Tumor cells formed slender trabecuae, and each trabecule was covered by a thin endothelial cell layer. Only very few scattered fat cells were present, but fine lipid droplets were detectable in the cytoplasm of the trabecular cells, and also in the lumen of the sinusoid-like structures. (*Figure 2*). There was a rather remarkable infiltration of lymphocytes, forming numerous follicles. Thick walled blood vessels lacking an elastica interna were few in number, and extramedullary haemopoiesis was not visible. At first sight a sinusoidal type hepatocellular carcinoma, or an angiosarcoma of the liver were in question, but since no mitotic figures were seen the possibility of either suggestion was ruled out. Immunohistochemical reactions showed no positivity with the monoclonal antibodies usually positive in hepatocellular carcinoma, (CK, EMA, CEA, AFP, progesterone, oestrogen). CD31 and CD34 revealed positivity only in the sinusoidal cells, but not in the epithelioid cells forming the trabecules. (*Figure 5*). Further reactions with desmin, smooth muscle actin and HMB- 45 antibodies showed strong positivity in the cytoplasm of the epithelioid cells. (*Figures 3,4*). The scattered lymphocytes were T and B cells, and adipocytes showed positivity with S-100 antibody. Based on both the microscopical features and immunohistochemistry, an epithelioid angiomyolipoma of trabecular type was diagnosed.

Discussion

On the basis of the different morphologic appearances, and the relative proportion of different cell types, AML-s are divided to different patterns, composed of different

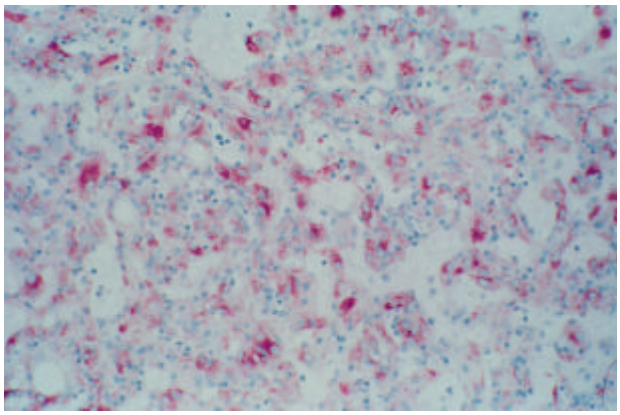

Figure 3. HMB-45 positivity of the epithelioid cells.

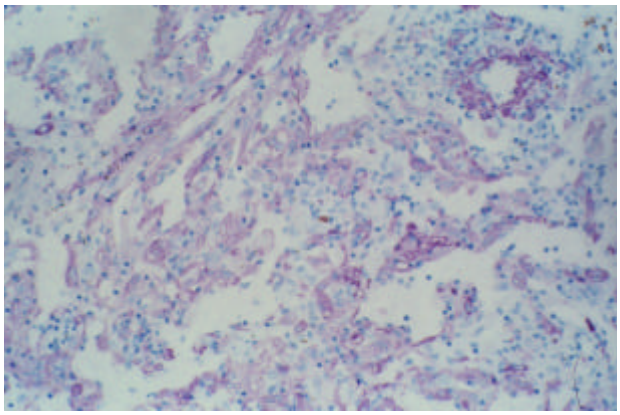

Figure 4. Smooth muscle actin positivity in the blood vessels and in the cytoplasm of epithelioid cells.

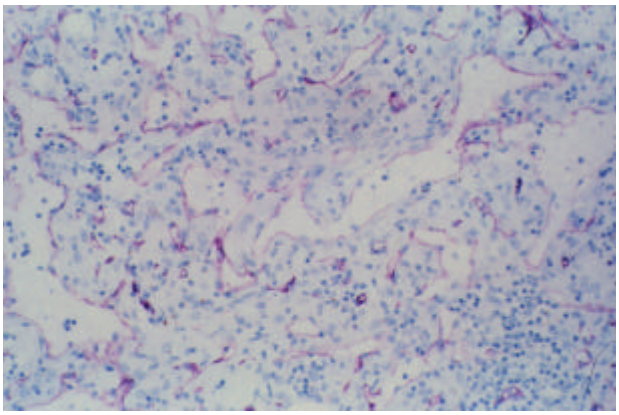

Figure 5. CD 31 positivity in the endothelial cells lining the sinusoidal spaces. Note that epithelioid cells are not stained.

dominating cell types (conventional mixed, myomatous, lipomatous and oncocytic).[1] Regarding the growth pattern, trabecular, (smooth muscle cells forming trabecules), pelioid, (spaces without endothelial lining containing serous fluid in the vicinity of areas of haemorrhage), and inflammatory (prominent lymphoid infiltrate with mixed population of B and T cells, macrophages, with entrapped spindle cells, reminiscent of inflammatory pseudotumor) subtypes may be discerned. The different growth patterns may occur in the same tumor. Vessels are usually large and thick walled, similar to vascular malformations. Smooth muscle cells may show various morphology, usually not showing the conventional morphology (slender cytoplasm and dense cigar shaped nuclei), but possessing a rather irregular granulated cytoplasm, and clear nucleus with irregular nuclear membrane and discernible nucleolus. In numerous cases, smooth muscle cells may have an epitheloid appearance.[3,10,11] In these cases, when adipocytes are rather few in number, and the dominant cell type is the rather "ugly looking" epitheloid cell, the tumor may be morphologically similar to a sinusoidal type hepatocellular carcinoma.[11] However, the lack of mitoses and the use of immunohistochemical examinations (CK,AFP,EMA, estrogen negativity and positivity with smooth muscle actin, desmin, and HMB-45 of the epithelioid cells) help in the differentiation of the two tumors, and a correct diagnosis can readily be made.[1,3,6]

Several authors consider that AML's are real neoplastic proliferations, which originate from perivascular mesenchymal cells.[5] These cells differentiate toward spindle cells possessing immunohistochemical characteristics of smooth muscle cells , (smooth muscle actin, desmin positivity) or epitheloid cells, with the characteristic HMB-45 positivity.[9] The latter epithelioid cells might show coexpression of both smooth muscle and premelanosome antigens.[9] Many authors regard AML, clear cell (sugar) tumor of the lung and pancreas, lymphangiomyomatosis, and rhabdomyoma of the heart, as closely related tumors based on their similar morphology and common immunohistochemical characteristics (HMB-45 positivity).[1,3,9] Others regard AML-s and lymphangiomyomatosis as hamartomatous lesions of smooth muscle cells.[2]

Hepatic angiomyolipomas may cause diagnostic difficulties for both the radiologists and the pathologists, especially in cases of angiomatoid types with a trabecular pattern, when neither adipocytes, nor dilated vascular spaces help in the prompt diagnosis. Pathologists should be aware of the existence of the several subtypes of AML , especially when these tumors occur in the liver. The use of several immunohistochemical panels , (9) can help the pathologist to avoid a regrettable misdiagnosis .

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References

1.²*Tsui WMS, Colombari R, Portmann BC:* Hepatic angiomyolipoma A clinicopathologic study of 30 cases and delineation of unusual morphologic variants Am J Surg Pathol 23:34-48, 1999.
2.²*Chan JKC, Tsang WYW, Pau MY, et al:* Lymphangiomyomatosis and angiomyolipoma:closely related entities characterized by hamartomatous proliferation of HMB-45 positive smooth muscle. Histopathology 22:445-455, 1993.
3.²*Eble JN, Amin MB, Young RH:* Epithelioid angiomyolipoma of the kidney: a report of five cases with a prominent and diagnostically confusing epithelioid smooth muscle component. Am J Surg Pathol 21:1123-1130, 1997.
4.²*Guinee DG, Thornberry DS, Azumi N, et al:* Unique pulmonary presentation of an angiomyolipoma. Am J Surg Pathol 19:476-480, 1995.
5.²*Martignoni G, Pea M, Bonetti, et al:* Carcinomalike monotypic epithelioid angiomyolipoma in patients without evidence of tuberous sclerosis: a clinicopathologic and genetic study. Am J Surg Pathol 22:663-672, 1998.
6.²*Nonomura A, Mizukami Y, Muraoka K:* Angiomyolipoma of the liver with pleomorphic histological features. Histopathology 24:279-281, 1994.
7.²*Kaiserling E, Kröber S. XiaoJ-C, et al:* Angiomyolipoma of the kidney. Immunoreactivity with HMB-45, light and electron-microscopic findings. Histopathology 25:41-48, 1994.
8.²*Wick MR, Humphrey PA, Ritter JH:* Pathology of pseudoneoplastic lesions. Lippincott-Raven, 1997, pp 163-165.
9.²*Sturtz CL, Dabbs DJ:* Angiomyolipomas: the nature and expression of the HMB45 antigen. Mod **(???)** Pathol 7:842-845, 1994.
10.²*Tsui WMS, Yuen AKT, Ma KF, et al:* Hepatic angiomyolipoma with deceptive trabecular pattern and HMB-45 reactivity. Histopathology 21:569-573, 1992.
11.²*Tsui WMS, Ng IOL, Colombary R, et al:* Hepatic angiomyolipomas (letter). Histopathology 22: 602-603, 1993.
12.²*Ma TKF, Tse MK, Tsui WMS, et al:* Fine needle aspiration diagnosis of angiomyolipoma of the liver using a cell block with immunohistochemical study. A case report. Acta Cytol 38:257-260, 1994.