Clinical history

A 61 year-old man was referred with mild hepatomegaly and slight abdominal pain in the right hypochondrium.
Computed tomography scans showed a large cystic mass (20 cm ∅) in the right hepatic lobe with.a mural nodule of 6,5 cm in diameter and thick irregular walls.
2 months later (October 2007) the cystic lesion was resected (bisegmentectomy: segment V and VI). No others tumor was found outside the liver.

Macroscopic features:
The excised mass consisted of an unilocular cystic lesion, 20 cm Ø, with haemorrhagic, thick irregular walls. A mural nodule, 6,5 cm Ø, with spongy-like appearance was present.

Microscopic features:

The well demarcated mural nodule showed an honeycomb appearance. A vague stellate scar was present in the center of the neoplasm. The cysts were smaller than 1.0 cm and were separated by thin fibrovascular septa. The tumor dysplayed mainly pushing margins without infiltrating the surrounding hepatic parenchyma. The adjacent hepatic parenchyma showed a mild reactive lymphocytic infiltration of portal tracts The cyst were filled with clear, watery, straw-colored fluid. They were separated by thin fibrovascular septa and lined by a single layer of uniform, clear cuboidal cells. The clear cells contained abundant intracytoplasmic glycogen sensitive to diastase digestion. The sorrrounding large cystic lesion was characterized by absence of lining epithelium, fibrosis, haemorrhage and degenerative changes of the cystic wall. Some cysts are were rarely lined by flattened epithelial layer, with cells resembling simple squamous epithelium and lacking clear cytoplasm. More compact cellular areas without cystic changes were also rarely detected. Nuclear atypia and mitoses were absent. Immunohistochemical analysis showed diffuse postivity for NSE, CK 7, CK19 and MUC1. Some rare cells stained positive for CK8. Chromogranin, synaptophysin, S-100, □-inhibin, PAX8, vimentin, RCC, MUC2, MUC3 MUC5AC and MUC6 stainings resulted negative.

Diagnosis:

Microcystic serous cystadenoma of the liver

Discussion

Serous cystadenoma of pancreatic type is characterized by multiple small locules lined by a single layer of glycogen-rich cuboidal cells with clear cytoplasmand lacking the ovarian-type mesenchymal stroma. The sponge-like gross appearance that brings this tumor the name microcystic is diagnostic of the entity. This benign tumour is exceedingly rare in the liver where only very few cases have been reported (1-4). In the pancreas four variants of serous cystic adenoma have been described: a) macrocystic serous cystoadenoma (serous oligocystic and ill-demarcated adenoma ,SOIA), b) serous microcystic adenoma (SMA), c) von Hippel-Lindau-associated cystic neoplasm (VHL-CN), d) combined well-differentiated endocrine neoplasm/serous cystoadenoma, e) solid serous adenoma (5-8). Serous cystoadenoma and its variants display similar cytological and immunohistochemical features. They are decorated by keratins 7, 8, 18 and 19. Alpha-inhibin, MUC6 and MUC1 are expressed in 82%, 705 and 34% of serous cystoadenoma respectively. Positivity for MUC6 and MUC1 lends support to a centroacinar differentiation of these tumors.

Serous cystoadenoma may be sporadic or occur in the context of von Hippel-Lindau (VHL) syndrome . Up to 90% of patients with VHL develop serous cystic neoplasms. The VHL syndrome is an autosomal dominant familial cancer syndrome arising from germ-line inactivation of the VHL gene on the short arm of chromosome 3. Affected patients are at increased risk for developing multiple synchronous or metachronous benign or malignant, cystic, and vascular neoplasms of various organs. The characteristic neoplasms associated with von Hippel-Lindau are hemangioblastoma of the central nervous system and retina, clear cell renal cell carcinoma, and pheochromocytoma, but other lesions as serous cystic pancreatic tumors are common. Loss of heterozygosity at the VHL gene locus, has been observed in two of two serous cystadenoma associated with VHL disease and in 40-70% of sporadic cases. The overwhelming majority of serous cystic neoplasms of the pancreas are benign serous cystadenomas; however, a handful of malignant serous cystic neoplasms, serous cystadenocarcinomas, have been reported. Malignancy is defined by the presence of metastases to extrapancreatic organs or tissues. However many of these are morphologically

identical to adenomas, raising the question of whether they may have been multifocal tumors rather than true metastasis.

Due to the absence of pancreatic primary site the presented case can be interpreted as a primary hepatic lesion. Primary hepatic serous cystadenoma is an extremaly rare lesion and so far only 5 cases have been reported. Other primary or metastatic clear cell tumors of the liver can mimic serous cystoadenoma (Table 1). Among these entities a cystic form of metastatic renal clear cell carcinoma has to be mainly considered in the differential diagnosis. However the immunohistochemical profile (negativity for RCC, PAX8 and vimentin) together with the absence of renal lesions on ultrasound examination ruled out such diagnosis. Intrahepatic cholangiocarcinoma clear cell variant is also an extremely rare hepatic tumor, and only few case are on record (9,10) . This neoplasia however usually displays a papillary or solid pattern, without cystic changes.

Table 1. Clear cell tumors of the liver

- Clear cell Hepatocellular Carcinoma
- Intrahepatic cholangiocarcinoma, clear cell variant
- Angiomyolipoma
- Mestatatic clear cell carcinomas : > renal, adrenal, ...
- Metastatic sarcoma: > GIST, liposarcoma, ...
- Metastatic melanoma

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