Multiple hepatocellular adenomas presenting in a male 8 years post-pancreaticoduodenectomy for islet cell tumor of the pancreas

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Abstract

We report the case of a 29-year-old male who presented with vague right upper quadrant pain, 8 years following a pancreaticoduodenectomy for a symptomatic pancreatic islet cell tumor. Subsequent imaging revealed multiple lesions in the right lobe of the liver. A diagnosis of metastatic disease could not be out ruled and hence a formal resection was performed. A formal retrospective review of case notes, preoperative imaging, operative notes, subsequent histology as well as a review of the current literature using the Medline, CINAHL, and EMBASE databases was performed. Histologic analysis showed these lesions to be hepatocellular adenomas. We highlight in this case the importance of preoperative imaging and workup, discuss hepatocellular adenomas in males and hypothesize as to the underlying pathophysiology in this particular case based on the available evidence.

Key words: Hepatocellular adenoma, pancreatic islet cell tumor, pathophysiology

BACKGROUND

Multiple hepatocellular adenomas are extremely rare in males, so much so that their etiology should always be questioned. Common associated factors include the use of exogenous estrogens, anabolic steroids, and glycogen storage disorders (GSDs); however there are no reports in the literature relating their development to islet cell pancreatic tumors or previous pancreatico-duodenal resections.

CASE REPORT

We present the case of a 29-year-old male patient presented to our surgical clinic with a 5 month history of vague right upper quadrant pain. His background was significant for having undergone a radical pancreatico-duodenectomy (Whipple's procedure) 8 years earlier in another country for a pancreatic head islet cell tumor, which initially presented with recurrent episodes of hypoglycemia. At this time, histologic examination

showed the tumor to be completely excised and his symptoms resolved completely. Follow-up scans postoperatively revealed 1 sub-centimeter lesion in the segment 6 of the liver, which was stable for 5 consecutive years and he attended no further follow-up thereafter.

Clinical examination and routine bloods were noncontributory; however a computed tomography abdomen revealed multiple low attenuation lesions in the right lobe of the liver, with no other obvious abnormalities. The main differential at this stage was metastatic disease. A double contrast magnetic resonance imaging (MRI) scan was subsequently performed, which revealed four distinct lesions [Figure 1]. The fat content and superparamagnetic iron oxide uptake were not specifically indicative of malignant tumors; however, considering the interval change in the size of the lesion in segment 6, the unusual nature of the suspected primary (insulinoma) and the vascular enhancement pattern of these lesions, the overall impression favored a diagnosis of four insulinoma metastases in the right lobe of the liver. An octreotide scan was performed, which failed to show any uptake but this was not surprising as not all tumors with somatostatin receptors will bind with octreotide. An ultrasound guided biopsy of one of these lesions was performed, which revealed a core of liver with mild fatty change only; no metastatic tumor was appreciated.

Given this patient's history, the nature of the lesions seen on MRI and the fact that one of the lesions had grown substantially since previous imaging, it was elected to proceed to formal resection. The liver parenchyma was transected to the right of the principle plain because of his previous Roux loop and satisfactory margins were achieved. An uneventful recovery ensued.

Histologically [Figures 2, 3a and b], these lesions were found to be hepatocellular adenomas. Each lesion was similar; unencapsulated, containing no portal tracts. The nonlesional parenchyma was normal without evidence of a co-existing glycogen storage disease.

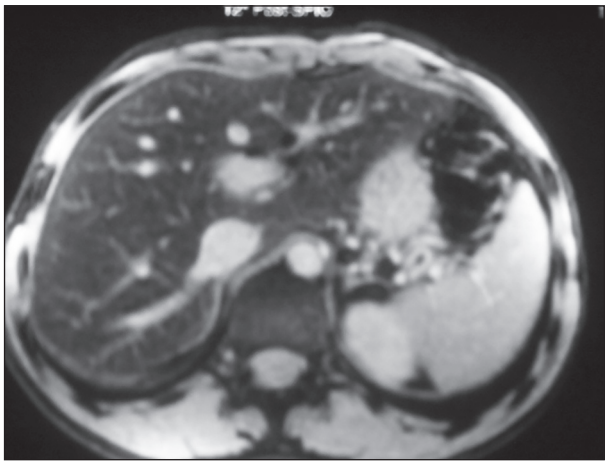

Figure 1: T2-weighted magnetic resonance image showing multiple lesions in the right lobe of the liver

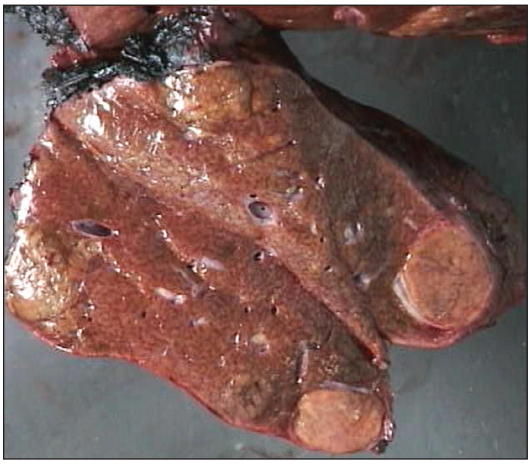

Figure 2: Macroscopic view of resected specimen (opened), containing multiple soft pale-brown well-circumscribed lesions

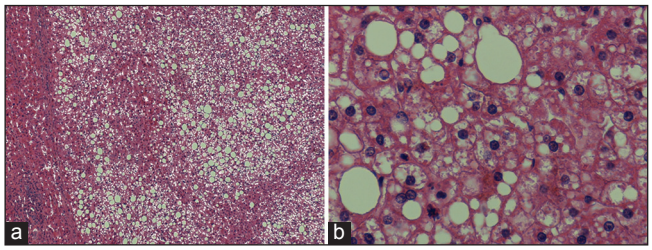

Figure 3: Microscopic view of one of the liver lesions stained with hematoxylin and eosin (a, ×10; b, ×40) showing uniform small hepatocytes arranged in sheets and a moderate degree of macrovesicular steatosis. No cytological atypia is present and the lesions are unencapsulated and contain no portal tracts

DISCUSSION

Hepatocellular adenomas are rare benign tumors occurring predominantly in women of child-bearing age. In males they are very rare, representing approximately 10% of cases,[1] and in the absence of risk factors, such as glycogen storage disorders (GSDs or exposure to anabolic steroids, are almost never multiple.

The pathophysiology underlying the development of multiple hepatic adenomas in a young male several years after complete resection of an insulinoma is at the very least, thought-provoking. Adenomas have been associated with diabetes mellitus,[2] leading to speculation as to whether imbalances between insulin and glucagon play a role in their development. This is

further evidenced by reports that GSD-related adenomas can seemingly disappear with dietary manipulation.[3] The Bordeaux group[4,5] have recently reported that hepatic adenomas are monoclonal tumors and probably develop from an interaction between gene defects and environmental changes such as oral contraceptives and steatosis. Genetic changes have been well described within hepatocellular adenomas. For example, a germline mutation of the hepatocyte nuclear factor (HNF-1 alpha) was described in two families that had both diabetes mellitus and liver adenomatosis.[6] Tumor cell analysis showed bi-allelic inactivation of HNF-1 alpha. This case can be considered to add another possible alternative to the environmental side of the equation, in the form of a glucagon-insulin imbalance attributable to a pre-existing insulinoma.

CONCLUSION

This case represents a conundrum both in relation to the initial work-up and the decision for surgery. The presence of multiple liver lesions in the setting of a previous pancreatico-duodenectomy for a neoplastic process really only raises one strong oncological possibility in the mind of a surgeon regardless of all other investigations, and this warranted exclusion ultimately in the form of resection. The subsequent histology raised many further questions, albeit at an academic level, regarding the ongoing evolution in theories of the pathophysiology behind hepatocellular adenomas.

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