

Pedunculated Hepatocellular Adenoma: A Presentation of a Rare Disease

A report of Two Cases with Review of Literature

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ABSTRACT

Background: Liver cell adenomas are rare tumors of the liver that shows increased incidence in some circumstances, as the peculiar increase in incidence with the use of contraceptive drugs in females of child-bearing age, or idiopathic. These tumors carry the risk to transform to hepatocellular carcinoma. Grossly, these tumors usually present as a single or more tumor masses and rarely present as a pedunculated mass. Recent histological, immunohistochemical and molecular studies conclude distinct patterns with clear prognostic implications.

Case presentation: We present two cases of liver cell adenoma, both in young adult females with history of contraceptive pill use for some years, both cases presented as single large pedunculated liver tumors. Both tumors were resected completely and successfully. Both cases showed typical histological picture of liver cell adenoma with prominent fatty infiltration 'Steatotic subtype'.

Conclusion: Liver cell adenomas can be rare tumors that can be precancerous in some of the cases.

Keywords: Liver cell adenoma, Liver tumors, Contraceptive pills.

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Liver cell adenomas (LCA), also called hepatocellular adenoma or hepatic adenoma, are rare benign epithelial liver tumors that occur in 1-1.3/million case per year. LCA cases are seen mostly in young females, making up 90% of cases, especially older than 30 years of age with long use of contraceptive drugs⁽¹⁾, and increasing yearly incidence to 3-4/100,000. Although few cases are reported with a short history of contraceptive drugs and in few cases, tumors developed even after stoppage of these drugs. Other possible predisposing causes are anabolic steroids, tyrosinemia and glycogen storage diseases⁽²⁾.

The clinical presentation is variable between cases, so patients can present as right upper abdominal pain, abdominal mass or acute abdomen with abdominal hemorrhage that may sometimes prove fatal. Physical examination is also not specific, so can be symptomless, or may detect signs of abdominal hemorrhage or abdominal mass⁽³⁻⁵⁾.

The definitive treatment is surgical resection. Asymptomatic small tumors less than 5 cm in diameter can be managed conservatively with close monitoring, or sometimes with laparoscopic resection⁽⁶⁻⁸⁾.

Grossly, these tumors can present as smooth tan colored, encapsulated, vascular, sometimes with obvious necrotic areas, usually as a single tumor, or more than one liver mass, with a variable size that may reach 20 cm in diameter. These tumors can present as multiple tumors, and called hepatic adenomatosis if 10 or more masses found, and these may occur equally rare in both males and females with no known drug

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or other risk factor⁽⁹⁾. Less than 10% of cases can grossly present as a pedunculated mass⁽²²⁾.

Histologically, LCA is an epithelial liver tumor, cells usually resemble well differentiated hepatocytes, with no portal triads nor central veins, and the tumor is not connected to the portal system⁽¹⁰⁾.

Tumor pathogenesis is thought to be from drug effect on liver vasculature causing vascular ectasia, probably with some interaction of defected gene(s). The estimated risk to develop malignancy is up to 13% in some studies, with an overall risk of 4.2%⁽¹¹⁻¹⁴⁾. The recent Bourdeux classification of hepatocellular adenoma is currently being evaluated^(15,16). Subtyping is established using immunohistochemical markers and molecular pathology to detect specific mutations, combined with histological criteria⁽¹⁷⁻²¹⁾, and accordingly these subtypes are recognized, with a fourth unclassified subtype: 1. Inflammatory type (40-55%) with serum amyloid-A overexpression. A higher risk of bleeding and lower risk of malignancy is noted in this subtype. 2. Steatotic type with hepatocyte nuclear factor (HNF) 1 α gene mutation, and liver fatty acid binding protein (LFABP). Almost no increased risk for malignancy is noted. 3. β -catenin mutated and overexpression of glutamine synthetase enzyme, and higher risk to develop hepatocellular carcinoma. This subtyping is useful for the assessment of malignancy risk, which is higher in β -catenin mutated group. Useful immunostains include liver fatty acid binding protein (LFABP), serum amyloid-A (SAA) protein, β -catenin, C-reactive protein and glutamine synthetase⁽²²⁾. This panel however can't distinguish it from hepatocellular carcinoma.

Case Report

The first case, WHA, is a 43-year old female who presented with epigastric pain, discomfort and vomiting for one month duration. Upon physical examination, the patient was in good general status, with a palpable epigastric mass noted. Ultrasound

study and endoscopy were not remarkable. Investigations for liver tests, renal function tests, blood counts were all unremarkable. CT scan suggested an epigastric mass probably related to the stomach. Laparotomy was eventually done and the mass was explored, and found to be related to the right lobe of the liver as a pedunculated mass with a thin pedicle, grossly measuring 11x8 cm. The mass and the pedicle were completely excised, hemostasis was controlled. No other abdominal lesion was found and the rest of the liver is normal.

The second case was SMN, a 34-year old female, presented as abdominal pain, on physical examination, the general condition was also good, with a palpable epigastric mass. Abdominal CT scan revealed a mass related to the liver. The mass was completely excised with proper hemostasis, and the tumor was sent for histopathological study, the mass measures 9x7 with a short pedicle.

Both cases did well post-operatively with no complications and discharge with a short regular follow-up.

Histopathologic study for both cases showed similar picture, with moderate fatty changes, mixed macrovesicular and microvesicular, prominent vascular pattern and disorganized portal tracts and central veins. Few areas of hemorrhage and necrosis are noted. No mitotic figures nor pleomorphic changes seen and the histological picture is consistent with pedunculated LCA, steatotic type. No immunohistochemical tests were done because all the immune markers useful for these cases were not available.

On further questionnaire, the two patients were using contraceptive pills, the first case (WHA) for the last five years and the second (SMN) for more than two years.

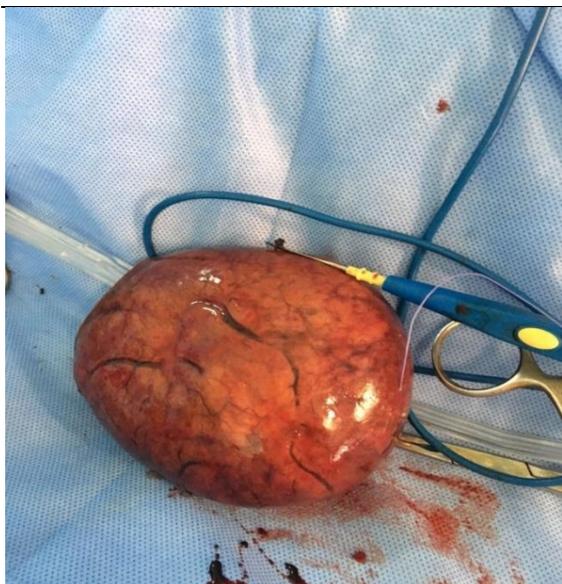


Figure 1: Liver cell adenoma gross view.



Figure 2: Liver cell adenoma, pedunculated, with part of the pedicle (Rt. margin).

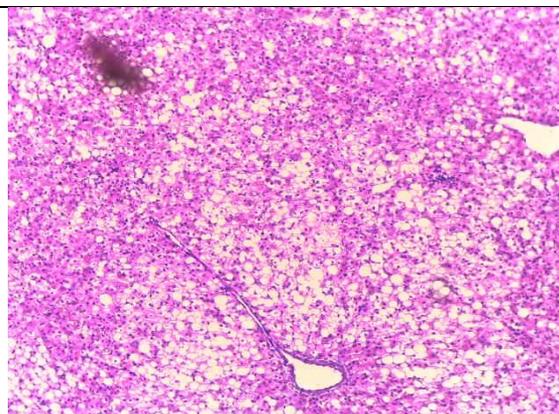


Figure 3: LCA microscopy showing large veins, lack of portal triads and prominent steatotic changes

Discussion

LCAs are rare but clinically important because of the relatively young age group of patients, the risk of complications and an increased risk of developing hepatocellular carcinoma. Diagnosis of these cases is not always easy, and sometimes the diagnosis is established only after laparotomy. Pedunculated cases are uncommon, comprising about 10% of these tumors⁽²²⁾. Pedunculated tumors may present as an epigastric mass that may show false relation to organs in the vicinity as the stomach.

Diagnosis can be reached after proper history clinical examination, imaging studies and ultimately surgical excision. Microscopy of the two cases showed steatotic pattern with no evidence of pleomorphic changes, mitosis or necrosis. The most important differential diagnosis that needs to be kept in mind for these tumors may include hepatocellular carcinoma. Mitosis, necrosis, pleomorphic changes and excluding vascular invasion are especially important to look for, and multiple sections need to be routinely taken in these tumors^(10,21). Focal nodular hyperplasia can be differentiated by the fibrous scar and the absence of fibrous capsule. Care should be taken for potential complications, especially hemorrhage, which on occasions are fatal⁽²³⁾.

In conclusion; Association of these tumors can be suspected with the long use of contraceptive pills.

Recommendations: A center for liver pathology equipped with the proper immunohistochemical panels and molecular testing can be very helpful in diagnosis and proper subtyping of these tumors according to the Bourdeaux classification, which is of significant prognostic value.

Conflict of interest: None to declare.

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