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Case Report

Hepatocellular adenoma with activation of the β-catenin mutation pathway mimicking intrahepatic cholangiocarcinoma: Case report ☆

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ABSTRACT

Hepatocellular adenomas are relatively rare benign tumors of the liver that primarily develop in young women, particularly those who use oral contraceptive pills. There are 4 distinct subtypes of these tumors. Among them, β-catenin-mutated adenomas constitute approximately 10% to 15% and are notable for their potential to undergo malignant transformation. In this report, we present the case of a young patient who had a 4 cm hepatic lesion. The initial imaging studies, particularly an MRI, suggested that the lesion might be an intrahepatic cholangiocarcinoma. However, upon further histological examination, the lesion was identified as a benign hepatic adenoma, with activation of the β-catenin mutation pathway. Due to the associated risk of malignant transformation, the treatment plan included surgical resection of the adenoma. This approach is critical in managing such lesions to prevent any potential progression to hepatocellular carcinoma.

Introduction

Hepatocellular adenomas (HCAs) are rare benign liver tumors that primarily occur in young women taking oral contraceptives. The molecular classification identifies 4 subtypes of adenomas with significantly different evolutionary profiles. β-catenin-mutated adenomas account for 10%-15% of HCAs and are associated with malignant transformations to hepatocellular carcinoma [1]. Magnetic resonance imaging (MRI) is superior to other imaging modalities for diagnosis and surveillance of HCA allowing for subtype differentiation in up to 80%

Abbreviations: ALP, Alkaline phosphatase; GGT, Gamma Glutamyl transferase; HCA, Hepatocellular adenoma; MRI, Magnetic resonance imaging.

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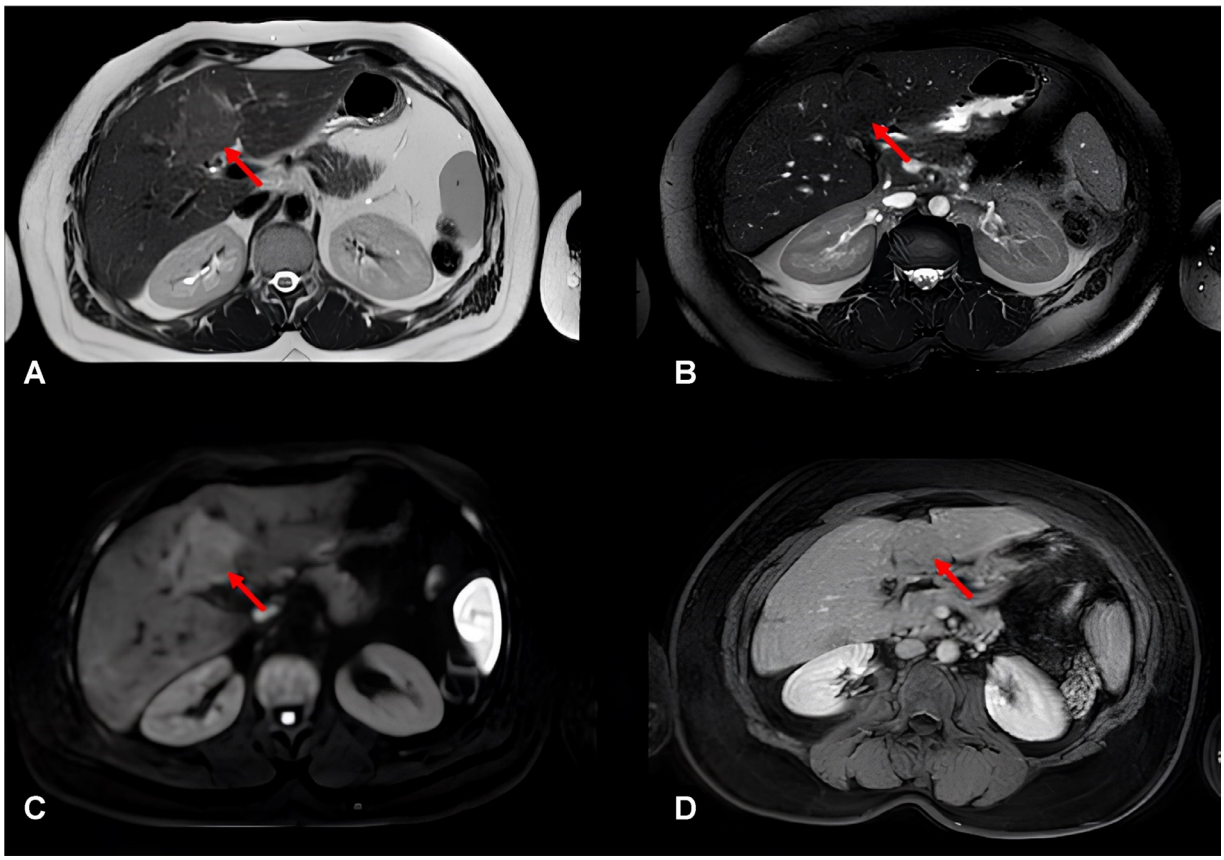

Fig. 1 – Axial T2 sequence images without (A) and with FAT SAT (B) showing a lesion in segment IV that is slightly hyperintense (red arrows), with slight diffusion restriction (C) and moderate enhancement after gadolinium injection (D).

of cases. However, histology should be performed when the MRI is inconclusive [2].

Case report

We report the case of a 50-year-old female patient with controlled hypertension on Valsartan and amlodipine, with no history of long-term oral contraceptive use. She presented to the consultation with right upper quadrant pain lasting for 2 months, accompanied by a weight loss of 5 kg in the absence of any other digestive or extra-digestive symptoms. Clinical examination revealed a patient in good general condition, non-icteric.

Hepatobiliary ultrasound showed a gallbladder with multiple stones and a slightly hyperechoic and heterogeneous image in segment IV, measuring approximately 40 mm with slight Doppler signal uptake.

Biological assessment indicated cholestasis (ALP: 2N, GGT: 3N) with normal bilirubin levels.

Liver MRI revealed a liver of normal size with regular contours, showing a lesion in segment IV measuring 41 mm, hypointense on T1 and T2, with slight diffusion restriction and moderate late enhancement after gadolinium injection, primarily suggesting intrahepatic cholangiocarcinoma (Fig. 1). The intrahepatic bile ducts and the main bile duct appeared thin, with no obstructive images.

A CT-guided biopsy was performed, and histology suggested benign cellular proliferation composed of hepatocytes with normal morphology, arranged in disorganized and branched trabeculae, with a normal reticulin framework on special reticulin staining. The immunohistochemical study on the DAKO platform showed diffuse membranous positivity for anti-β-catenin antibodies and diffuse cytoplasmic positivity for anti-glutamine synthetase antibodies, suggesting a hepatocellular adenoma with activation of the β-catenin pathway (Fig. 2).

Management consisted of curative surgical treatment with cholecystectomy and tumor resection.

The postoperative course was uneventful, with no complications.

Discussion

Hepatocellular adenomas (HCAs) are generally benign liver tumors resulting from abnormal hepatocyte proliferation. These tumors are frequently linked to hormonal or metabolic disruptions, often associated with the use of oral contraceptives or androgenic steroids [3]. The molecular classification identifying 4 subtypes of adenomas where the B-catenin mutated subtype accounts for 10%-15% [1]. B-catenin mutations have also been identified in hepatocellular carcinomas related to hep-

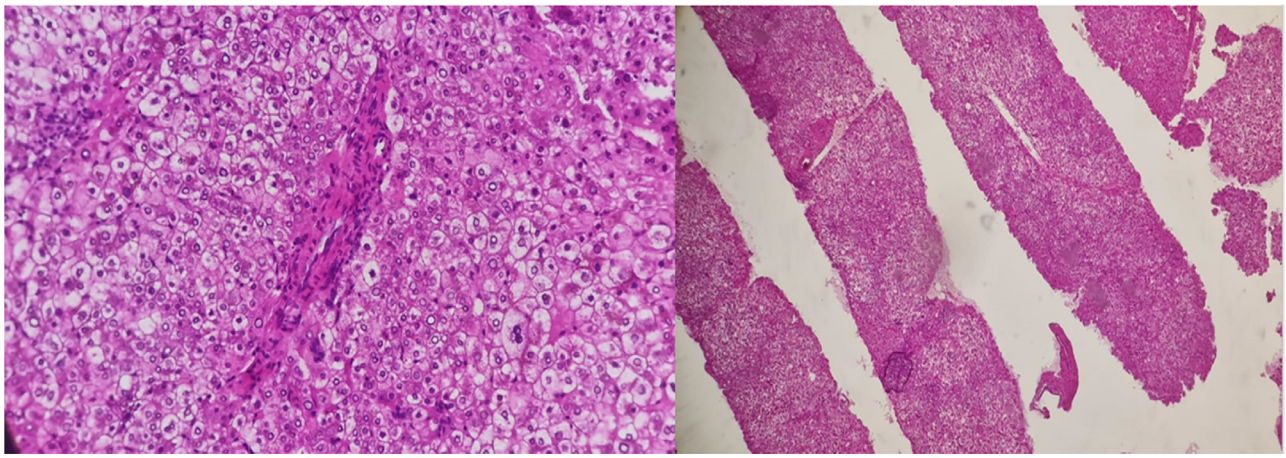

Fig. 2 – Histological image on special reticulin staining showing a hepatocellular adenoma, with immunohistochemistry supporting a β-catenin-activated adenoma.

atitis C virus infections. These mutations are associated to an increased risk of bleeding and malignant transformation [3,4].

HCA is commonly diagnosed in women between the ages of 35 and 40, with a female-to-male ratio of 10:1. Numerous studies have highlighted the possible influence of sex hormones in HCA development. Long-term use of oral contraceptives is associated with a 30 to 40-fold increase in the incidence of HCA [5].

β-catenin-activated hepatocellular adenomas are characterized by mutations in the β-catenin gene (CTNNB1), initially identified in exon 3 and more recently in exons 7 and 8. These mutations are associated with an elevated risk of malignant progression to hepatocellular carcinoma. β-HCAs display morphological features such as cellular atypia, pseudoglandular formations, and cholestasis. Tumor hepatocytes show a distinct immunophenotypic profile, with diffuse and typically strong positivity for glutamine synthetase (a β-catenin target), as well as nuclear β-catenin expression [6].

HCA is no longer considered a single entity, as imaging now reflects its various subtypes. Magnetic resonance imaging is superior to other modalities, such as contrast-enhanced ultrasound and CT scans, due to its ability to detect fat and vascular spaces, allowing for subtype differentiation in up to 80% of cases. However, β-catenin HCAs present less distinctive imaging features and can be difficult to differentiate from hepatocellular carcinoma (HCC). These lesions typically appear heterogeneous and hyperintense on T2-weighted images and hypointense on T1-weighted images, with a central scar but no signal loss on chemical shift sequences. On contrast-enhanced imaging, they generally show arterial enhancement and may retain or reduce signal intensity in the portal venous phase [2]. In Ba-Ssalamah et al.'s study, 5 out of 6 β-catenin HCAs retained gadoxetic acid in the hepatobiliary phase, a feature observed in both inflammatory and β-catenin HCAs, and linked to the expression of the biliary transporter OATP1B1/B3 [7].

Typically, intrahepatic cholangiocarcinoma presents as a well-defined intrahepatic mass with irregular margins, biliary stricture, and upstream bile duct dilation. It often shows peripheral rim enhancement during the arterial phase and progressive centripetal enhancement. However, in certain forms of cholangiocarcinoma, particularly the small duct type, there may be variable signal intensities on T1 and T2 sequences, without associated bile duct dilation around the lesion, making the imaging diagnosis even more challenging. It is in such atypical cases that distinguishing between adenoma and cholangiocarcinoma on imaging becomes particularly difficult [8].

Biopsy may be considered within a benign liver tumor experienced multidisciplinary team to exclude malignancy [9]. All guidelines recommend that a biopsy should be performed when imaging results are inconclusive, as it is essential for making informed treatment decisions [10].

When tissue samples are available for diagnostic purposes, curative intervention is recommended for β-catenin-activated mutated HCAs, regardless of tumor size. The European Association for the Study of the Liver (EASL) advises resection of HCAs in men, and in any case where a β-catenin mutation is confirmed, irrespective of the lesion's size [2].

Conclusion

β-catenin-HCAs are benign tumors accounting for 10%-15% of HCAs with a higher risk of hemorrhage and malignant transformation. Our case report presents a case of β-catenin-mutated HCA in a woman with no risk factors, mimicking a cholangiocarcinoma on MRI, and was effectively treated with curative surgery.

Patient consent

Written informed consent for the publication of this case report was obtained from the patient.

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