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Long-term follow-up of hepatic adenoma and adenomatosis: analysis of size change on imaging with histopathological correlation

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AIM: To analyse the change in size on follow-up of hepatic adenomas (HAs) and adenomatosis, and to investigate the relationship of imaging features with size change.

MATERIALS AND METHODS: The study included 44 patients (142 lesions) who underwent magnetic resonance imaging (MRI) or computed tomography (CT) for diagnosis and follow-up of HA. The imaging features and percentage change in maximum tumour dimension were observed over a follow-up duration of up to 139 months.

RESULTS: With an average follow-up of 43 months, 37% lesions decreased in size, 58% were stable, 4% increased; one lesion regressed completely. Adenomas were stratified into size groups (<3, 3–5, and ≥5 cm). Size change among the three groups was similar ($p>0.05$). Percent size change was different for lesions followed for ≤12 months (−7.2%) compared with lesions followed for 13–60 months (−20.5%), and those followed for ≥60 months (−23.5%; $p<0.05$); there was no difference between lesions followed for 13–60 months and ≥60 months ($p=0.523$). Baseline size and percent size change was similar between the hepatocyte nuclear factor 1α-inactivated HA (HA-H) and inflammatory HA (HA-I) subtype ($p>0.05$).

CONCLUSION: Most adenomas were either stable or regressed on follow-up. Size change was independent of baseline size. After an initial size decrease within 5 years, no further size reduction was noted on extended follow-up. The percent size change in the HA-H and HA-I subtype was similar.

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Introduction

Hepatic adenoma (HA) is the third most common benign solid liver tumour after haemangioma and focal nodular hyperplasia. HA is usually found in young women aged between 20–40 years and increased prevalence is seen in women with a history of prolonged oral contraceptive (OCP) intake.[1] The estimated incidence of HA is 3 per million per year and increases to 30–40 per million among long-term OCP users.[2] Hepatic adenomatosis[3] is defined by the presence of 10 or more HA involving both hepatic lobes. It is not associated with a specific HA subtype[4] and its imaging features are similar to those of solitary HA.[5]

HA are often asymptomatic but can be associated with a risk of rupture, haemorrhage, and malignant transformation into hepatocellular carcinoma (HCC). The reported incidence of macroscopic haemorrhage and malignant transformation in adenomas <5 cm is 5% and 2%, respectively; the risk increases to 25% and 9%, respectively, for adenomas ≥5 cm.[6] Hepatic adenomatosis can be seen in either sex with or without oral contraceptive use[5]; other risk factors for adenoma include glycogen storage disease and hepatic steatosis.[7] In addition, adenoma formation may be associated with germ-line HNF1A (hepatocyte nuclear factor 1α) gene mutations.[5,8,9] Risk of complication in both HA and adenomatosis is related to the size of the largest lesion and underlying histopathological subtype.[10] As HA are associated with OCP use, they have been reported to regress or disappear after OCP withdrawal,[2,11–15] although this may not be true for hepatic adenomatosis.[16]

With recent recognition of HA as a complex entity, there has been an increasing interest in categorising subtypes of adenomas. Based on the molecular characteristics, HA can be divided into four subtypes[1]: HNF1A-inactivated HA (HA-H),[2] β-catenin-activated HA (HA-B),[3] inflammatory HA (HA-I), and[4] unclassified HA (HA-U).[17] Studies have emphasised the importance of this histopathological classification of HA on the patient management.[18–20] Based on studies[21,22] suggesting that HA-B subtype may demonstrate a high risk of malignant transformation, authors have proposed that this subgroup be surgically resected regardless of its size at presentation.[19] On the other hand, HA-H subtype demonstrates a much lower risk of malignant transformation in comparison to other subtypes. Therefore, surgical resection or even biopsy can be avoided in favour of imaging follow-up if this subtype can be recognised, particularly for small HAs (<5 cm) in women.[19] For HA-I subtype, biopsy to rule out coexisting β-catenin mutation (that is associated with increased malignant potential) is suggested.[19] Authors have also shown the successful role of MRI in this subtype characterisation of HA.[23,24] About 30–35% of HA are of the HA-H subtype, and are characterised by steatosis within the lesion.[17,19]

Size is an important factor in the management of adenoma as it relates to risk of complications and malignant transformation; however, the natural history of adenoma size is not well described. As such, the objective of the current study was to analyse the change in size on follow-up of hepatic adenomas and adenomatosis and the relationship of imaging features with the size change.

Materials and methods

Patient population

This was a retrospective, institutional review-board approved, Health Insurance Portability and Accountability Act-compliant study with waived patient consent. Review of the medical records identified 44 patients (age range, 20–58 years; mean age, 41 years) between October 2004 and May 2016, including 27 patients with HA (nine patients with solitary HA; 18 patients with multiple HA) and 17 patients with hepatic adenomatosis. Among patients with more than five HA, up to five lesions with at least ≥1 month follow-up were included to reduce selection bias; thus a total of 142 lesions were evaluated. Pathological diagnosis along with histological subtype was established for 67 lesions in 21 patients. For remaining lesions, diagnosis was made by characteristic imaging findings. All patients underwent imaging with computed tomography (CT) and/or magnetic resonance imaging (MRI) for diagnoses and follow-up. Nineteen patients (n=61) underwent both MRI and CT, 22 patients (n=73) had MRI only, whereas three patients (n=8) had CT only. The protocol used for MRI and CT studies performed is shown in Table 1.

Imaging analysis

MRI and CT images were analysed by one experienced abdominal radiologist with 7 years of experience in abdominal MRI. Each lesion was evaluated for signal intensity (SI) or density (relative to surrounding liver parenchyma), homogeneity, presence of capsule, and presence of fat or haemorrhage within the lesion and enhancement characteristics. All region of interest (ROI) measurements were performed using circular ROIs measuring at least 1 cm^2 with the aim of covering maximum area of the lesion while avoiding peripheral 1 mm of the lesion to avoid volume averaging. Homogeneity was defined as uniform SI or density. Heterogeneity was defined as any difference in SI or density within the lesion on T1- or T2-weighted imaging (WI) or CT images. Capsule was defined as a thin low-SI or low density rim surrounding all or a part of the lesion. The dropout of signal on chemical-shift images or fat-suppression sequence was interpreted as intralesional fatty infiltration. Haemorrhage was defined as areas of high-SI on T1- and T2WI with or without low-SI on T2WI suggesting haemosiderin deposition, or hyper-density on unenhanced CT.

The longest dimension of the lesion was measured at baseline and follow-up images. All the lesion measurements were performed on contrast-enhanced images in the hepatic arterial or portal venous phase using CT/MRI T1W three-dimensional (3D) fat-suppressed spoiled gradient-echo images. As HAs demonstrate variable enhancement profiles, it was decided not to use the same enhancement

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