

Hepatic adenomas in male patients

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Background

Hepatic adenomas are benign tumours of the liver most commonly seen in premenopausal women. However, it is now clear that adenomas may occur in males. This small series reviews the characteristics of hepatic adenomas in males.

Case outlines

Three cases of solitary hepatic adenoma occurring in otherwise well male patients (age 22–48 years) are presented. Two patients presented with abnormal liver function tests while one presented with abdominal pain. Imaging of the lesions demonstrated typical appearances of hepatocellular adenoma, resection was undertaken in all cases and all patients remain alive and well.

Discussion

Up to 20% of adenomas are documented as occurring in male patients. Most are solitary and occur in patients without recognised risk factors (steroid therapy and glycogen storage diseases types I and III). However, multiple adenomas are most commonly seen in male patients with risk factors. The imaging characteristics and presentation of adenomas in males are similar to female patients and, most importantly, intraperitoneal rupture and malignant transformation are documented in untreated adenomas in males.

Keywords

Liver adenoma, complications, demographics

Introduction

Hepatic adenomas are benign tumours of the liver, the growth of which may be positively influenced by oestrogenic hormones [1, 2]; they are most commonly seen in premenopausal women [1–3]. A number of reports have documented adenomas in men undergoing steroid therapy [4], or in types I and III glycogen storage diseases [5]. However, it is now clear that hepatic adenomas may also affect men without these risk factors [3, 6–9]. While the behaviour of hepatic adenomas in women has been closely evaluated, the specific characteristics of hepatic adenomas in men have not been described.

We report the presentation of hepatic adenoma in three men with no history of hormone use or glycogen storage disease and have reviewed the behaviour, diagnosis and management of these tumours.

Case reports

Case no. 1

A 48-year-old man presented with an incidental finding of abnormal liver function tests and an ultrasound scan showing a single mass in the right lobe of the liver measuring $7 \times 6 \times 6$ cm. CT scan confirmed a solitary central hepatic lesion extending through segments I, IV

and VIII. Alkaline phosphatase (ALP) was mildly raised at 158 U/L (normal range 40–130 U/L). Serum alpha-fetoprotein (α FP) was normal and there was no serological evidence of active hepatitis B or C. Percutaneous biopsy confirmed hepatocellular adenoma, with fatty change in the rest of the liver. Following an extended right hepatectomy [10] the patient remains alive and well at 36 months later with no evidence of recurrent disease.

Case no. 2

A 22-year-old man was noted to have mildly abnormal liver function tests while receiving isotretinoin for the treatment of acne. The medication was discontinued, and hepatic ultrasound scan and CT scan were performed. A 6-cm lesion was identified in segments VI and VII that enhanced briskly following the injection of intravenous contrast. The patient's liver function tests were normal apart from a gamma-glutamyl transferase (γ GT) level of 110 U/L (normal range 0–60 U/L). There was no evidence of active hepatitis B or C, and α FP was within the normal range. A biopsy of the lesion was consistent with hepatocellular adenoma, and the rest of the liver showed mild macrovesicular fatty change. The patient was treated with a right posterior sectionectomy

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Table 1. Summary of male patients with hepatic adenomas reported in the literature

Reference	Date	Total	Males	Solitary vs multiple	Steroid use	Glycogen storage disease	Diameter	Comment
Wilkens et al. [11]	2001	10	2	Solitary	NS	NS	6 cm 7.5 cm	
Terkivatan et al. [12]	2001	12	2	Solitary	Yes	No	NS	Presented with rupture
Mamada [9]	2001	1	1	Solitary	No	No	4.5 cm	Focal lesional haemorrhage
Ichikawa et al. [13]	2000	25	4	Solitary	No	No	NS	
Weiman et al. [7]	1997	44	9	NS	NS	NS	NS	
Nagorney [3]	1995	24	2	NS	NS	NS	NS	
Arrive et al. [16]	1994	29	2	Solitary	NS	NS	NS	
Foster and Berman [18]	1994	5	1	Multiple	Yes	NS	NS	Developed HCC
Paulson et al. [6]	1994	14	3	Solitary	No	Yes	NS	
Leese et al. [8]	1988	18	3	Solitary	No	No	14 cm 13 cm 2 cm	
		6	5	Multiple	No	Yes	NS	Also ref. 18
Sale and Lerner [4]	1977	1	1	Multiple	Yes	No	NS	
Foster and Berman [19]	1977	37	2	Solitary	No	No	15 cm 23 cm	Presented with rupture
			1	Multiple	No	No	4 cm	
Howell et al. [5]	1976	8	6	Multiple	No	Yes	NS	

NS, not stated.

[10] (Couinaud segments VI and VII) and remains well without evidence of recurrent disease 18 months later.

Case no. 3

A 38-year-old male presented with intermittent right upper quadrant pain, and a liver mass was identified on ultrasound scan. There was no history of steroid use, his liver function tests were normal, hepatitis B and C serology was negative, and α FP was normal. Triphasic CT demonstrated a 12-cm exophytic mass in segment VI that was hypervascular in the arterial phase with no evidence of a central scar. He proceeded to segment VI resection and histology confirmed hepatic adenoma. He remains well with no evidence of recurrence at 31 months.

Discussion

Hepatic adenoma is widely regarded as a tumour that only affects women, or males who are on steroids or suffering from types I or III glycogen storage diseases. However, several series have documented that 16–20% of adenomas affect men (Table 1) [3, 6–9, 7, 11, 12]. Most of these reports have been of single adenomas occurring in histologically normal livers without evidence of cirrhosis or fibrosis and in men without recognised risk factors [8, 9, 13, 14]. Although multiple adenomas are also recognised in men, most of these patients do have recognised risk factors [4, 5, 8]. Of the six patients with

multiple adenomas reported by Leese and colleagues [8], five were men and, of them, four of them suffered from glycogen storage disease. Male patients have also been reported with multiple adenomatosis (which is defined as the presence of >10 liver adenomas in an otherwise normal hepatic parenchyma, in patients without a history of glycogen storage disease or androgenic steroid therapy [4, 5, 8], and Flejou and associates [15] have emphasised that liver adenomatosis affects men and women equally.

The typical symptomatology of hepatic adenomas is largely based on data from women whose lesions have been associated with oral contraceptive use. At least 50% of adenomas present as an incidental finding [16], as in two of the three cases reported here; acute or chronic abdominal pain or discomfort precipitate diagnosis in the remainder [3, 8, 16]. Intra-tumoral or intra-peritoneal haemorrhage may be associated with acute abdominal pain in 39–50% of patients [3, 12]. Liver function tests in hepatic adenoma are seldom abnormal but mild elevations in γ GT have been observed in 7% of patients and [7] ALP may be raised in up to 23% [15].

As in women hepatic adenomas are often first detected by ultrasound scan where they appear as well demarcated hyperechoic, hypoechoic or isoechoic lesions [2]. The CT appearance is of hypervascular tumours with typical features of adenomata including sharply defined margins and smooth non-lobulate masses. Adenomas are encapsulated in 25% of cases and rarely show evidence of calcification [12]. Magnetic resonance imaging (MRI)

appearances are of well-defined contrast-enhancing lesions that are mostly hyperintense on T₁- and T₂-weighted images [6, 13]. The primary diagnostic consideration is to differentiate adenoma from hepatocellular carcinoma (HCC). Small HCCs are more commonly seen in men, and most are associated with a raised serum α FP [17]. The presence of a radiologically suspicious lesion in a male patient with a normal α FP is an indication for biopsy.

The risk of tumour rupture and malignant transformation are the most important complications of hepatic adenoma, both for men and women. Up to 50–60% of adenomas have evidence of intra-tumoral haemorrhage [9, 12], and can present with haemoperitoneum, hypotension and shock [3, 8] due to intraperitoneal rupture. While intraperitoneal rupture of a hepatic adenoma is classically seen in premenopausal women, it has been described in men [9, 12]. Although the size of the ruptured lesions was not specified, it is likely that the risk of rupture in males is related to lesional diameter as it is in females [8].

Malignant transformation of hepatic adenoma is a rare phenomenon. Foster and Berman [18] reviewed 76 adenomas treated non-operatively and reported malignant transformation in 5 out of 76 cases of adenoma occurring over a 30-year period. The specific risk of malignant transformation of hepatic adenoma in men is not known, but 1 of the 5 cases (20%) reported by Foster and Berman was male [8, 18, 19], suggesting a similar risk to that in women.

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