Contraceptive-related hepatic adenoma

The patient had been taking oral contraceptives for two years. On ultrasound, performed for vague abdominal pain, a nodule with 5.5 cm in diameter was detected in S2 of the liver.

Imaging Findings:

1.5 T1w MRI: The hepatic nodule is isointense to the liver on T1w GRE in-phase MRI; the nodule signal markedly drops on T1w GRE out-of-phase MRI (Fig. 1a, b); the nodule is slightly high in signal on T2x MRI (not shown). Intralesional blooming artefact, consistent with previous haemorrhage, is detectable on T2* MRI (Fig. 1c). The nodule is hypervascularized on arterial phase of dynamic sequences with liver-specific contrast medium, and shows a washout phenomenon during the venous phase; no take-up of the contrast medium in the hepatobiliary phase (Fig. 2).

3T MRI after 3-month contraceptive withdrawal: The nodule is isointense to the liver on T1w GRE out-of-phase MRI (Fig. 3a); post-contrast MRI shows decrease in size of the nodule, measuring 39 mm in diameter (Fig. 3b).

Discussion:

Pathologic and genetic studies recently widened our comprehension of hepatic adenomas (HAs), which encompass lesions having distinct imaging features, natural history and clinical behaviour influencing therapeutic management. HAs are currently distinguished in four types: inflammatory HAs, hepatocyte nuclear factor (HNF) 1?–mutated HAs, ?-catenin–mutated HAs, and unclassified subtype, the latter without peculiar genetic abnormality [1, 2]; main characteristics of HA subtype are summarized in Fig. 4.

Approximately one third of all HAs are of HNF-1?–mutated type, the development of which relies on biallelic inactivating mutations of the HNF-1? gene, a tumour suppressor gene encoding the HNF-1? protein, a transcription factor involved in hepatocyte differentiation [1-3]. In 90% of patients with a HNF-1?–mutated HA the biallelic mutation is somatic; in the remaining 10% of patients one mutation is somatic and one germline; association with maturity-onset diabetes of the young, type 3, and familial hepatic adenomatosis can be found in subjects with germline mutation [2, 4]. HNF-1?–mutated HA with somatic mutation is found in women only, 90% of which are oral contraceptive users [2]. Increased incidence of HA in women after widespread diffusion of oral contraceptive and regression, exceptionally complete, of a HA after contraceptive withdrawal strongly show the tight relationship between oestrogens and HAs [3]. Oestrogens are considered endogenous genotoxic mediators causing somatic mutation of HNF-1? gene, the outcome being increased lipogenesis, hepatocellular proliferation and intracellular fat
HNF-1α–mutated HAs are usually hyperintense or isointense on T1w in-phase MRI, hypointense on T1w out-of-phase MRI because of intracellular fat deposits, isointense or slightly hyperintense to the liver on T2w imaging. Surrounding parenchyma may be also hypointense in T1w out-of-phase imaging because of fatty infiltration in cases of maturity-onset diabetes of the young, type 3, or associated steatosis [2, 6]. HNF-1α–mutated HAs show mild enhancement on arterial phase of dynamic post-contrast imaging, with a wash-out phenomenon on portal and delayed phases [7]; when a liver-specific contrast medium is administered, they do not take up the contrast medium in the hepatobiliary phase. MRI characterization of HNF-1α–mutated HAs is clinical important because they have no tendency to malignant transformation and bleeding [2].

**Differential Diagnosis List:** Hepatocyte nuclear factor (HNF) 1α–mutated hepatic adenoma, Focal nodular hyperplasia, Hepatocellular carcinoma, Haemangioma

**Final Diagnosis:** Hepatocyte nuclear factor (HNF) 1α–mutated hepatic adenoma

**References:**


Figure 1

a

**Description:** T1w out-of-phase imaging shows a hepatic 0.5-cm hypointense nodule in S2. **Origin:** UO Radiologia, Ospedale San Bortolo, Vicenza, Italy

b

**Description:** The nodule is isointense to the liver on T1w in-phase imaging. **Origin:** UO Radiologia, Ospedale San Bortolo, Vicenza, Italy
Description: T2* imaging depicts intratumoral blooming artifact. Origin: UO Radiologia, Ospedale San Bortolo, Vicenza, Italy
Figure 2

a

**Description:** Mildly enhancement of the hepatic nodule in the arterial phase. **Origin:** UO Radiologia, Ospedale San Bortolo, Vicenza, Italy

b

**Description:** The nodules is hypointense relative to the liver parenchyma in the venous phase. **Origin:** UO Radiologia, Ospedale San Bortolo, Vicenza, Italy
Description: The lesion does not take up the liver-specific contrast medium in the hepatobiliary phase.
Origin: UO Radiologia, Ospedale San Bortolo, Vicenza, Italy
Figure 3

a

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Gender</th>
<th>Frequency</th>
<th>Clinical Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory HA (IL6ST mutations)</td>
<td>Female most frequently</td>
<td>40-55%</td>
<td>Obesity, alcohol, hepatic steatosis; risk of bleeding; 10% express beta-catenin (risk of HCC)</td>
</tr>
<tr>
<td>HNF-1α-mutated HA</td>
<td>90% women using oral contraceptive</td>
<td>30-50%</td>
<td>Tend to adenomatosis; maturity-onset diabetes of the young type 3</td>
</tr>
<tr>
<td>β-Catenin-mutated HA</td>
<td>male/female</td>
<td>10-18%</td>
<td>Associated with male hormone administration and glycogen storage disease; increased risk of progression to HCC</td>
</tr>
<tr>
<td>Undetermined</td>
<td></td>
<td>10%</td>
<td></td>
</tr>
</tbody>
</table>

**Description:** Synthetic clinical features hepatic adenomas. **Origin:** from ref. 1, 2

b

<table>
<thead>
<tr>
<th>Subtype</th>
<th>T1w GRE MRI in-phase</th>
<th>T1w GRE MRI out-of-phase</th>
<th>T2w MRI</th>
<th>Dynamic MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory HA</td>
<td>Iso-mildly hyper</td>
<td>No signal ←</td>
<td>Hyperintense</td>
<td>Intense enhancement persisting in delayed phases</td>
</tr>
<tr>
<td>HNF-1α-mutated HA</td>
<td>Hyper-iso</td>
<td>Signal ←</td>
<td>Iso- slightly hyper</td>
<td>Wash-in wash-out</td>
</tr>
<tr>
<td>β-Catenin-mutated HA</td>
<td>Unspecific pattern</td>
<td>Unspecific pattern</td>
<td>Unspecific pattern</td>
<td>possible wash-in wash-out mimicking HCC</td>
</tr>
</tbody>
</table>

**Description:** Synthetic radiologic feature of hepatic adenomas. **Origin:** from ref. 1, 2
Figure 4

a

Description: The nodule is isointense to the liver parenchyma on T1w out-of-phase imaging. 

Origin: UO Radiologia, Ospedale San Bortolo, Vicenza, Italy

b

Description: Contrast-enhanced MRI (venous delayed phase) shows low signal of the hepatic nodule, currently measuring 3.9 cm in the largest diameter. 

Origin: UO Radiologia, Ospedale San Bortolo, Vicenza, Italy