Angioma-like liver lesions in patients with chronic liver disease

A. Repiso, R. Gómez Rodríguez, C. González de Frutos, T. de Artaza, J. J. Sánchez Ruano, M. J. Pérez Grueso and J. L. Martínez Potenciano†

Service of Digestive Diseases. Virgen de la Salud Hospital. Toledo, Spain

RESUMEN

Objetivo: el objetivo de nuestro estudio fue valorar en nuestro medio las características clínicas, ecográficas y evolutivas de los pacientes con hepatopatía crónica y lesiones ecográficas sugestivas de angiomias hepáticos.

Material y métodos: estudio retrospectivo realizado entre los pacientes recogidos en la base de datos de la Unidad de Ecografía del Servicio de Aparato Digestivo entre enero de 2000 y junio de 2004. Incluimos en el estudio a pacientes que presentaban datos clínicos y/o analíticos compatibles con hepatopatía crónica de cualquier etiología y en los que la ecografía abdominal ponía de manifiesto la existencia de al menos una lesión hepática compatible con angioma. Se han recogido los datos epidemiológicos, clínicos, ecográficos y evolutivos de estos pacientes.

Resultados: durante el periodo de estudio se diagnosticaron 58 pacientes con hepatopatía crónica y lesiones hepáticas sugestivas de angiomias, de los cuales trece presentaban datos clínicos, analíticos, ecográficos y/o histológicos compatibles con cirrosis hepática. Ecográficamente se trataban de lesiones menores de 10 mm en el 50% de los pacientes y en la mayoría de los casos localizadas en lóbulo hepático derecho. Durante el periodo de medio de 35 meses (6 a 168 meses) se pudo comprobar cómo en dos pacientes (3%) las lesiones inicialmente interpretadas como angiomas se trataban en realidad de lesiones malignas (un hepatocarcinoma y unas metástasis de adenocarcinoma vesicular). En ambos casos los pacientes eran cirróticos. Por tanto, en el 15% de los pacientes cirróticos de nuestra serie se demostró la naturaleza maligna de las lesiones inicialmente interpretadas como angiomias.

Conclusiones: en pacientes con hepatopatía crónica, sobre todo en cirróticos, un porcentaje no despreciable de las lesiones ecográficas interpretadas inicialmente como angiomias se tratan realmente de lesiones malignas.


ABSTRACT

Objective: the aim of this study was to evaluate in our healthcare area the clinical, ultrasonographic, and evolutionary features of patients with chronic liver disease and angioma-like liver lesions on ultrasonography.

Materials and methods: we conducted a retrospective study amongst patients seen at the Ultrasonography Unit, Gastroenterology Department between January 2000 and June 2004. Included in the study were patients that presented with clinical and/or laboratory complaints consistent with chronic liver disease of any etiology, and those in which abdominal ultrasounds revealed the existence of at least one angioma-like liver lesion. All relevant epidemiological, clinical, ultrasonographic, and evolutionary data were carefully collected and recorded.

Results: in the course of our study, 58 patients were diagnosed with chronic liver disease and angioma-like liver lesions, of which 13 showed clinical, laboratory, ultrasonographic, and/or histological signs of liver cirrhosis. In 50% of patients these lesions were less than 10 mm in diameter, and in most cases were located in the right hepatic lobe. During an average follow-up period of 35 months (6-168 months) we verified that, in two patients, these lesions, initially interpreted as angiomas were in fact malignancies (one hepatocellular carcinoma and one metastatic adenocarcinoma of the gallbladder). In both cases, the patients were cirrhotic. Thus, our study revealed that 15% of lesions found in cirrhotic patients initially interpreted as angiomas were actually malignant.

Conclusions: our study revealed that, in patients with chronic liver disease, particularly in cirrhotic patients, a considerable percentage of ultrasonographic lesions originally interpreted as angiomas are in fact malignant tumors.

Key words: Angioma. Hepatocellular carcinoma. Liver neoplasms. Liver cirrhosis.


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Correspondence: Alejandro Repiso Ortega. Servicio de Aparato Digestivo. Hospital Virgen de la Salud. Avda. Barber, 30. 45004 Toledo, Spain. e-mail. arepisoo@sescam.jccm.es.
INTRODUCTION

Hemangioma represents the most frequent benign tumor of the liver, and is found in up to 5% of the adult population; ultrasonographically, its shape is very variable (1). However, we know that in the majority of cases they are round, hyperechogenic masses with well-defined borders and homogeneous sonographic patterns (2).

Patients with chronic liver disease, and particularly those with liver cirrhosis, are at high risk of developing malignant liver lesions (3,4), specifically hepatocellular carcinoma. This type of carcinoma is generally seen with ultrasounds as a well-defined, focal lesion of variable size with irregular borders and most frequently heteroechographical characteristics (2). On other occasions it appears as a hypoechoic, isoechogenic or hyperechogenic lesion (where a major fatty component exists) with hemorrhage or hypervascularization, in which case it may cause diagnostic problems, being indistinguishable from hepatic angioma (5).

Taking all this into account, the aim of our study was to evaluate in our immediate healthcare area the clinical, sonographic, and evolutionary characteristics of patients with chronic liver disease and sonographic angioma-like liver lesions.

MATERIAL AND METHODS

Study population

This study was performed at “Virgen de la Salud Hospital” in Toledo, Spain, in patients seen at the Ultrasounds Unit, Gastroenterology Department between January 2000 and June 2004.

The study includes those patients showing clinical and/or laboratory symptoms consistent with chronic liver disease of any etiology (persistent alteration of liver biochemistry tests for more than 6 months), and those in which abdominal ultrasounds had demonstrated the presence of at least one angioma-like liver lesion, defined as a solid, hypoechogenic, round focal lesion with well-defined borders (Fig. 1). Excluded were patients lost to follow-up (3 patients) and those with hypoechogenic, focal lesions that, because of their ultrasonic characteristics, led us to the diagnosis of “space-occupying, malignant lesion” as a first possibility in the initial exploration.

Ultrasound study

In the course of the study we used a Toshiba SSH-140 and a Hitachi EUB-6500 ultrasonograph with multi-frequency probes. The study was performed by 4 different endosonographers with at least 5 years’ experience in abdominal ultrasonography, all in the same unit and with the same working method.

Follow-up

Our patients received outpatient follow-up with visits every six months, and abdominal ultrasounds every six to twelve months depending on the etiology of liver disease, evolutionary status, and diagnostic confidence.

Variables

Assessed variables were as follows:
1. Clinical data included patient age at first ultrasonography; etiology of liver disease; and presence of cirrhosis, defined by clinical and/or histological, laboratory, and ultrasonographic data.

2. Ultrasonographic data: number, size and location of lesions (right and/or left hepatic lobe); diagnosis at first ultrasound exam or explorations performed during follow-up; existence of sonographic evidence of cirrhosis, defined as alterations in the echogenicity of the liver parenchyma, surface irregularities, hypertrophy of caudate lobe and/or direct data like ascites or signs of portal hypertension; diagnostic conformation obtained through follow-up with ultrasounds or following other tests such as CT and/or MRI. In general, we performed an abdominal CT and/or MRI in cirrhotic patients with focal liver lesions, and/or in those with liver lesions and no typical angioma-like characteristics, or when sonographic characteristics changed during follow-up.

3. Evolutionary data such as follow-up time; difference in lesion size between first and last ultrasound ex-
RESULTS

Among the 1950 patients in our database who were diagnosed with chronic liver disease, 58 (3%) showed angioma-like liver lesions in ultrasonographic explorations. Of these, 34 were males and 24 were females, with an average age of 52 ± 12 years, of which 13 (22%) presented with clinical, laboratory, ultrasonographic, and/or histological signs of liver cirrhosis.

In 39 patients, a sonographic diagnosis of angioma-like liver lesions was made after the first exploration. In 19 patients, the lesion was first ultrasonographically apparent during follow-up. Half of patients had lesions smaller than 10 mm. In most cases lesions were unique and located in the right hepatic lobe (Table I). In order to clarify the origin of the lesion, an abdominal CT was done in 27 patients, thus allowing us to visualize the previously defined lesion in 14 cases. Among 11 patients with lesions smaller than 10 mm, CT scans revealed the lesions previously described sonographically in only 2 cases. In 13 cirrhotic patients the use of abdominal CT and/or MRI was considered, and ruled out in 2 patients because of advanced age and poor health (Table II).

During an average follow-up of 35 months (6-168 months) the definitive diagnosis of 56 patients was a probable hepatic angioma. In this period we observed variations in the size of lesions (increase or decrease in size by more than 3 mm) in 13 patients (22%). In 9 patients (15%), we observed a decrease, and in 4 (7%), an increase. In all patients where a significant increase in lesion size was detected during follow-up (4 patients), we decided to obtain a CT and/or MRI (1 patient) scan. At some point during follow-up we were unable to identify ultrasonographically the lesions previously described in 20 patients (Fig. 2).

In 2 patients (3%), we could verify how lesions earlier described as angiomas were in fact malignant lesions. Specifically, in 1 patient, after 35 months of follow-up, we demonstrated histologically, upon distinguishing changes in ultrasonographic characteristics, that the lesion was a hepatocarcinoma (Figs. 3a and 3b); in another case, that it was a metastatic adenocarcinoma of the gallbladder. Both cases showed clinical, laboratory, and/or sonographic data consistent with cirrhosis of the liver (Table II). Therefore, in 15% of cirrhotic patients in our series we elucidated the malignant nature of lesions initially interpreted as angiomas.

Table I. Ultrasonographic findings of 58 patients with chronic liver disease and angioma-like lesions

<table>
<thead>
<tr>
<th></th>
<th>Number of patients</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasonographic findings of cirrhosis</td>
<td>13</td>
<td>22</td>
</tr>
<tr>
<td>Size of lesions: &lt; 10 mm</td>
<td>29</td>
<td>49</td>
</tr>
<tr>
<td>&gt; 20 mm</td>
<td>11</td>
<td>19</td>
</tr>
<tr>
<td>Number of lesions: Single</td>
<td>45</td>
<td>77</td>
</tr>
<tr>
<td>Multiple</td>
<td>13</td>
<td>22</td>
</tr>
<tr>
<td>Location: Right hepatic lobe</td>
<td>45</td>
<td>77</td>
</tr>
<tr>
<td>Left hepatic lobe</td>
<td>8</td>
<td>13</td>
</tr>
<tr>
<td>Both lobes</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Diagnostic: In the first exploration</td>
<td>39</td>
<td>67</td>
</tr>
<tr>
<td>In the follow-up</td>
<td>19</td>
<td>32</td>
</tr>
</tbody>
</table>

Table II. Characteristics of 13 cirrhotic patients with angioma-like liver lesions

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>Size at diagnosis (mm)</th>
<th>Ultrasonographic follow-up (months)</th>
<th>Abdominal CT</th>
<th>NMR</th>
<th>Citology/ histology</th>
<th>Evolution and treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>83</td>
<td>8</td>
<td>106</td>
<td>Not done</td>
<td>Not done</td>
<td>Not done</td>
<td>Follow-up</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>76</td>
<td>10</td>
<td>11</td>
<td>Not done</td>
<td>Not done</td>
<td>Not done</td>
<td>Death</td>
</tr>
<tr>
<td>3</td>
<td>V</td>
<td>81</td>
<td>5</td>
<td>20</td>
<td>None</td>
<td>Not done</td>
<td>Not done</td>
<td>Death</td>
</tr>
<tr>
<td>4</td>
<td>V</td>
<td>54</td>
<td>8</td>
<td>35</td>
<td>None</td>
<td>HCC</td>
<td>HCC</td>
<td>Resection; transplantation</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>45</td>
<td>6</td>
<td>3</td>
<td>None</td>
<td>Not done</td>
<td>ADC</td>
<td>Death</td>
</tr>
<tr>
<td>6</td>
<td>V</td>
<td>36</td>
<td>20</td>
<td>68</td>
<td>Undetermined</td>
<td>Angioma</td>
<td>Not done</td>
<td>Follow-up</td>
</tr>
<tr>
<td>7</td>
<td>V</td>
<td>54</td>
<td>10</td>
<td>20</td>
<td>Unspecific</td>
<td>Angioma</td>
<td>Non-malignant</td>
<td>Follow-up</td>
</tr>
<tr>
<td>8</td>
<td>V</td>
<td>62</td>
<td>10</td>
<td>12</td>
<td>Undetermined</td>
<td>Angioma</td>
<td>Non-malignant</td>
<td>Death</td>
</tr>
<tr>
<td>9</td>
<td>V</td>
<td>69</td>
<td>6</td>
<td>9</td>
<td>Unspecific</td>
<td>None</td>
<td>Not done</td>
<td>Follow-up</td>
</tr>
<tr>
<td>10</td>
<td>V</td>
<td>62</td>
<td>8</td>
<td>34</td>
<td>None</td>
<td>Angioma</td>
<td>Not done</td>
<td>Follow-up</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>58</td>
<td>15</td>
<td>88</td>
<td>Not done</td>
<td>Not done</td>
<td>Angioma</td>
<td>Transplantation</td>
</tr>
<tr>
<td>12</td>
<td>V</td>
<td>60</td>
<td>10</td>
<td>36</td>
<td>Angioma</td>
<td>Angioma</td>
<td>Not done</td>
<td>Follow-up</td>
</tr>
<tr>
<td>13</td>
<td>V</td>
<td>70</td>
<td>15</td>
<td>12</td>
<td>None</td>
<td>Angioma</td>
<td>Angioma</td>
<td>Transplantation</td>
</tr>
</tbody>
</table>

*F: Female; M: Male; **Age at the moment of diagnosis.
DISCUSSION

Patients with chronic liver disease represent a high-risk group regarding the development of malignant liver lesions, which on occasion exhibit a sonographic appearance indistinguishable from that of hepatic angioma. In our healthcare area we demonstrated the malignant origin of chronic liver disease and of lesions originally described as angiomas in 3% of patients. Specifically, it is cirrhotic patients who are at a greatest risk for malignant liver lesions. That was the case in our series – in the two cases in which we confirmed that lesions were in fact malignant, patients were cirrhotic. Thus, in 15% of cirrhotic patients in our series we demonstrated the malignant nature of lesions originally interpreted as angiomas. In other series, it has been demonstrated that up to 50% of angioma-like liver lesions in cirrhotic patients are in fact hyperechoic hepatocarcinomas or preneoplastic lesions (5). It is generally accepted that low-risk patients with hepatic focal lesions sonographically identified, and with typical signs of angioma do not require any complementary explorations (6). However, in patients with liver cirrhosis (considered to be high-risk) it is recommendable that other imaging techniques be performed to confirm the diagnosis (4). The choice of one technique or another will be influenced by experience and availability in each center. Despite the high diagnostic efficacy of abdominal CT in terms of diagnosis of focal liver lesions (7,8), in our healthcare area CT turned out an unwise technique in this indication, probably due to the high proportion of small lesions (< 1 cm) sonographically seen, which limits this technique as shown in other studies (3,4,9-11). The recent development of contrast sonography will allow a better characterization of this type of liver lesion, and a more accurate sonography-related differential diagnosis (12-14).

In four of all thirteen cirrhotic patients, we performed a sonographically guided fine-needle biopsy of the lesion to obtain a cytological diagnosis. This technique is safe and profitable even in the diagnosis of small lesions (15,16), but as often happens in these cases a negative result does not excludes a diagnosis of malignancy (3,4). Hence, in 9 cirrhotic patients, we decided not to carry out a cytological study. These cases included elderly patients, patients who did not give their consent, and those who had lesions smaller than 10 mm, in which case we proceeded to conduct a trimestral sonographic follow-up (3,4,9). Traditionally, fine-needle biopsy is not recommended for angioma lesions. However, it does result in a safe and recommendable procedure for patients with an atypical image and/or a high risk of malignant neoplasm (17,18).

The risk for malignant lesions seems greater when an angioma-like liver lesion is detected during follow-up or in cases where sonographic characteristics change (5).
Special attention needs to be paid to lesions increasing in size, since it is unlikely that a congenital tumor, such as liver angioma, would significantly increase in size at least enough to be sonographically identified. Angioma reduction or disappearance during follow-up in patients with chronic liver disease is a well known feature of these tumors (19) that has been related to not only to explorer-dependant factors, but also to changes in the echogenicity of hepatic parenchyma and lesions themselves, due to an increase in fibrous contents that impairs identification (19). It can also be a sign suggesting the malignant nature of lesions, as was the case in our patients. In this patient, after 35 months of follow-up, a lesion smaller than 10 mm had disappeared, in one of the trimestral sonographies; however, this lesion reappeared afterward in the same location and as a larger lesion suggestive of hepatocarcinoma.

In conclusion, in patients with chronic liver disease, and above all in cirrhotic patients, a considerable percentage of sonographic lesions initially interpreted as angiomas are in fact malignant lesions. Thus, close sonographic follow-up and complementary studies seem advisable in these patients, and most particularly in cirrhotic patients and in those in whom sonographic characteristics change during follow-up.

REFERENCES