Management of Hepatic Hemangiomas: A 14-Year Experience

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Hemangioma is the most common primary tumor of the liver and its diagnosis has become increasingly prevalent. Most of these lesions are asymptomatic and are managed conservatively. Large hemangiomas are often symptomatic and reports of surgical intervention are becoming increasingly frequent. We present our experience, over the last 14 years, with diagnosis and management of 249 liver hemangiomas, with special attention to a conservative strategy. Clinical presentation, diagnosis, treatment, and long-term outcome are analyzed. Of 249 patients, 77 (30.9%) were symptomatic, usually with right abdominal upper quadrant pain. Diagnosis was based on a radiologic algorithm according to the size and characteristics of the tumor; diagnosis by this method was not possible in only one case (0.4 %). Giant hemangiomas (>4 cm) were found in 68 patients (27.3%) and in 16 were larger than 10 cm. Eight patients (3.2%) underwent surgical treatment; indications were incapacitating pain in 6, diagnostic doubt in 1, and stomach compression in 1. No postoperative complications or mortality were observed in this series. Patients who did not undergo surgery (n = 241) did not present any complication related to the hemangioma during long-term follow-up (mean = 78 months). Hemangioma is a benign course disease with easy diagnosis and management. We propose a conservative approach for these lesions. Resection, which can be safely performed, should be reserved for the rare situations such as untreatable pain, diagnostic uncertainty, or compression of adjacent organs. (J GASTROINTEST SURG 2005;9: 853–859)

KEY WORDS: Surgery for hepatic hemangiomas

Hemangiomas are the most common primary liver tumor, with a prevalence in the general population estimated to range between 0.4% and 7.3%.[1,2] These vascular tumors have an unknown etiology; however, some studies have suggested a possible relationship with the intake of steroid hormones.[3,4] Hepatic hemangiomas are usually diagnosed unexpectedly during routine abdominal ultrasound and generally present as small-sized, asymptomatic nodules, although they may eventually reach large volumes. Their finding has become increasingly prevalent, becoming a frequent issue in specialized day-to-day clinical practice. Much has been discussed about the natural history of these lesions. Their benign clinical course and rarity of complications, such as rupture and bleeding, are well recognized.[5–7]

In recent years, there has been an increasing enthusiasm with surgical therapy, and some recent publications have shown excellent results after operative treatment.[8–16] However, based on their benign clinical course, we believe that liver hemangiomas should be conservatively managed. Liver resection, although a relatively safe procedure in specialized centers, should be reserved for rare circumstances such as incapacitating pain, compression of adjacent organs, Kasabach-Merritt syndrome, or diagnostic doubt (suspected malignancy).

The aim of this paper is to present our experience with 249 patients with hepatic hemangiomas referred to our institution. We will discuss the diagnostic process, clinical behavior, and management of this highly prevalent liver tumor, with special attention to our conservative strategy.

PATIENTS AND METHODS

From March 1988 to March 2002, 249 patients diagnosed with hepatic hemangiomas were prospectively followed in our unit. Ages ranged between 23

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and 79 years (median = 49 years) with a female predominance of 67.5%. Location, size of the hemangiomas, and the patient's characteristics (e.g., age, sex, and symptoms) were recorded.

Diagnosis was based on a radiologic algorithm as shown in Figure 1. All patients underwent ultrasound liver evaluation. For small lesions (≤1 cm), diagnosis was based solely on ultrasound and patients were observed. In patients with larger nodules, where ultrasound evaluation was not able to establish the diagnosis, the investigation proceeded. Patients with tumors between 1 and 3 cm were submitted to magnetic resonance imaging and those with tumors larger than 3 cm to CT scan, red blood cell scintigraphy, or magnetic resonance imaging. Diagnostic laparoscopy or biopsies from the lesions were not performed in this series.

Surgical treatment was indicated in eight patients of this series (3.2%), for the following reasons: untreatable pain in six, diagnostic uncertainty in one, and tumor growth with compression of the stomach in one. Surgical interventions are shown on Table 1.

Patients were evaluated by liver ultrasonography every 6 months for the first 2 years and annually thereafter. The follow-up period ranged from 12 months to 14 years (mean = 78 months).

The variables were compared by χ^2 test and the statistical significance level was set at 5%.

RESULTS

Solitary nodules were present in 195 patients (78.3%), 32 had two lesions, and 22 presented with three or more lesions. Lesion sizes ranged from 0.2 to 35 cm in diameter (mean = 3.7 cm), and in 152 cases (61%), the hemangioma was located on the right lobe of the liver. Giant hemangiomas, previously defined as lesions larger than 4 cm,[17] were found in 68 cases (27.3%). In 16 patients (6.4%) hemangiomas were larger than 10 cm in diameter. Seventy-nine patients (31.7%) were symptomatic, and the most frequent complaints were right upper quadrant abdominal pain and nonspecific dyspeptic symptoms. Abdominal pain was present in 44.1% (n = 30) of the patients with giant hemangiomas, whereas 27.0% (n = 49) of those with lesions smaller than 4 cm presented with pain. Pain as well as refractory pain were significantly more frequent in patients with lesions larger than 10 cm (Tables 2 and 3). Six patients, all with tumors larger than 14 cm, presented with refractory pain and underwent surgical resection as shown on Table 1.

Abdominal ultrasound was performed in all patients, with an overall diagnostic sensibility of 67.4%. CT scan was performed in 162 patients, defining the diagnosis in 122 (75.3%), and magnetic resonance imaging, indicated in 50 patients, was able to define the diagnosis in 46 (92.0%). Red blood cell scintigraphy was performed in 24 patients with lesions larger than 5 cm, with the results positive in 22 (91.6%).

A diagnosis based on imaging modalities was possible in 248 patients (99.6%). One patient, with an uncharacteristic heterogeneous 18 cm in diameter liver mass was submitted to right hepatectomy and the diagnosis of hemangioma was confirmed by histologic evaluation.

All symptomatic patients, excluding those undergoing surgical treatment, who presented pain were efficiently treated with analgesics, and the ones who had dyspeptic symptoms were investigated with upper digestive endoscopy and then managed according to endoscopic findings. In 20 patients (8%), associated gallstones were found, and all underwent laparoscopic cholecystectomy with further complete relief of the symptoms.

Eight patients (3.2%), all with lesions larger than 14 cm in diameter, underwent surgery: six with

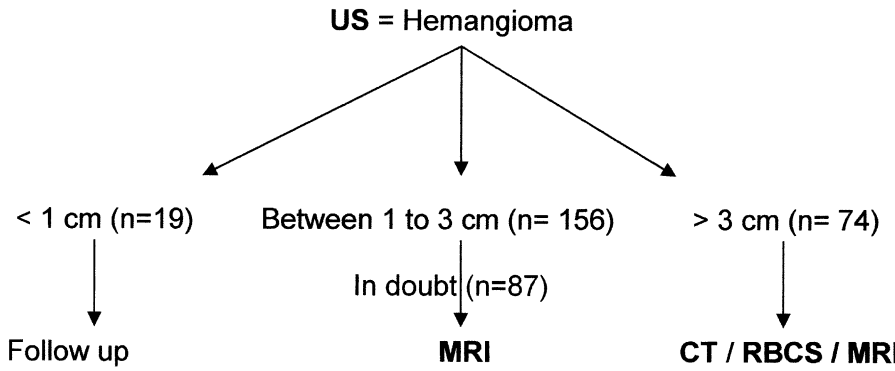

Fig. 1. Diagnostic algorithm for liver hemangiomas. US = ultrasonography; MRI = magnetic resonance imaging; CT = computed tomography; RBCS = red blood cell scintigraphy.

Table 1. Indications, patient characteristics, size of hemangioma, surgical procedure, and follow-up in patients undergoing liver resection

Indication	Gender/Age	Size (cm)	Surgery	Follow-up (months)
Untreatable pain	M / 43	30	Segmentectomy V, VI	Asymptomatic (52)
Untreatable pain	M / 41	24	Left lobectomy	Asymptomatic (28)
Untreatable pain	F / 40	18	Left lobectomy	Asymptomatic (60)
Untreatable pain	F / 39	14	Right hepatectomy	Asymptomatic (72)
Diagnostic doubt	F / 32	18	Right hepatectomy	Asymptomatic (48)
Untreatable pain	M / 47	20	Right hepatectomy	Symptomatic (18)
Untreatable pain	F / 38	16	Segmentectomy V, VI	Asymptomatic (12)
Stomach compression	F / 30	20	Left lobectomy	Asymptomatic (24)

untreatable pain, one with a large tumor of uncertain etiology, and one with tumor enlargement and consequent compression of the stomach. Only one patient (12.5%) required blood transfusion and received 2 units of packed red blood cells during surgery. There were no postoperative complications, and all patients had an uneventful postoperative recovery with a mean hospitalization period of 7 days. The other 10 patients with lesions larger than 10 cm were observed and did not develop any complications.

Among the six patients with incapacitating pain who underwent surgery, five (83.3%) experienced an improvement in symptoms but one had persistent abdominal pain after surgery.

During long-term follow-up (mean = 78 months), none of the 241 patients who had not been surgically treated developed any complication related to the hemangioma. Liver ultrasound follow-up did not show any significant change in the size or characteristics of the lesions.

DISCUSSION

Hepatic hemangiomas are the most frequent hepatic tumors, usually found incidentally during abdominal imaging procedures, laparoscopies, or laparotomies. They are more frequently found in women, usually in the fifth decade, being rare in children. Most of the lesions are asymptomatic, but abdominal pain may be present, especially in patients with large lesions. Pain is the most frequent symptom, usually intermittent and easily controlled with common analgesics, but the investigation of concomitant disorders such as gastritis or biliary stone diseases are sometimes necessary. In our series, biliary stone disease was present in 20 patients (8%).

Lesions larger than 4 cm have been defined as giant hemangiomas,[18] and some authors believe that these lesions are more frequently symptomatic and carry a greater risk of rupture.[5,12,17–19] In our series, pain was reported by 30.9% of the patients, being most commonly seen in those with giant hemangiomas (44.2%), and all patients with untreatable pain had lesions larger than 14 cm in diameter, showing a direct relationship between pain and the size of the hemangioma, as also shown by others.[5,12,17–19] Rupture was not observed in this series. Rarely, large hemangiomas can be responsible for the Kasabach-Merritt syndrome, which is characterized by a consumptive coagulopathy.

Many imaging methods have been employed for suspected hepatic hemangioma investigation. Ultrasound (US) is particularly useful in the identification of small lesions, usually demonstrating a homogeneous, well-delimited hyperechoic lesion (Fig. 2). The accuracy of US depends on the experience of the radiologist; it can reach up to 80% in experienced hands. In this series, typical US findings of hemangiomas were observed in 67.4% of the cases. Larger lesions are usually heterogeneous as the result of intratumoral hemorrhage or thrombosis, and thus lack the typical ultrasonographic characteristics. In these

Table 2. Incidence of symptoms (pain) according to size of hemangioma

Size	Patients (n)	Symptoms
<10 cm	233	63 (27%)
>10 cm	16	16 (100%)*

*$P = 0.0046$

Table 3. Incidence of refractory pain according to size of hemangioma

Size	Patients (n)	Refractory pain
<10 cm	233	0
>10 cm	16	6 (37.5%)*

*$P < 0.0001$

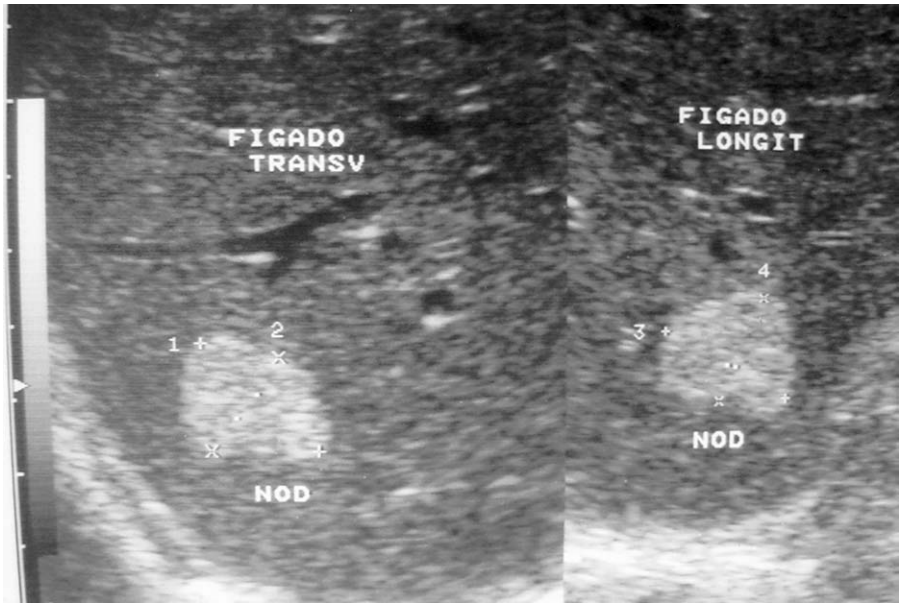

Fig. 2. Liver ultrasound showing a small (1.2 cm in diameter) homogeneous, hyperechoic well-delimited nodule.

cases investigation should be carried out with other methods, such as CT scan or MRI.[20]

On CT, hemangiomas are sharply defined masses, and are usually hypoattenuating compared with the adjacent hepatic parenchyma on unenhanced scans. After intravenous contrast administration, there is a distinctive pattern of enhancement characterized by peripheral nodular opacification proceeding with centripetal filling toward the center of the lesion (Fig. 3). CT scan sensitivity ranges between 75% and 90%[20] and, in our series, confirmed the diagnosis in 75.3% of the cases.

Red blood cell scintigraphy is an excellent diagnostic tool for tumors larger than 3 cm, with a typical radioactive pooling inside the tumor (Fig. 4). Recently, the employment of single photon emission computed tomography (SPECT) has enhanced the diagnostic sensitivity of scintigraphy[21,22] and, in our series, the former was able to establish diagnosis in up to 91.6% of the patients.

MRI has a sensitivity of up to 90%, and is considered by many authors to be the gold standard diagnostic method. On the other hand, it is the most expensive diagnostic tool and should be reserved for small lesions or diagnostic doubt after CT or scintigraphy. In this series, MRI established the diagnosis in 92% of the cases in which it was employed. Hemangiomas appear with low signal on T1 and high-intensity signal on T2 (Fig. 5), demonstrating a relative increase in signal on heavily T2-weighted images.[20,21]

In doubtful cases, some authors indicate a percutaneous needle biopsy.[14,19,23,24] This procedure is hazardous and should not be employed because of the high risk of bleeding.[5,15,25] Fine-needle aspiration may considerably reduce bleeding rates but, on the other hand, provides scarce material for histologic examination. Thus, for undetermined diagnosis, a conventional operative procedure with tumor resection is indicated and, for superficial lesions, a diagnostic laparoscopy could be carried out. Fortunately, with the continuous improvement in diagnostic imaging modalities, these situations are becoming the exceptions.

The natural history of hepatic hemangiomas is sometimes misunderstood. Iwatsuki et al. suggested that lesions larger than 10 cm with central necrosis carry a greater risk of rupture.[19] The risk of spontaneous rupture and bleeding, which is a frequent concern, is actually very low. In an extensive review of the literature published in 1991, only 28 well-documented cases of spontaneous rupture had been reported[7,15]; this is an extremely rare situation taking into account the high prevalence of these tumors. Rapid growth of lesion, which is considered an indication for resection, rarely occurs; some authors report an increase in tumor size in approximately 5% of the patients.[5,14,16,17,26] Nevertheless, in our series, only one patient (0.4%) presented significant growth of the lesion with consequent stomach compression. No other lesion showed any significant change in its dimensions during long-term follow-up.

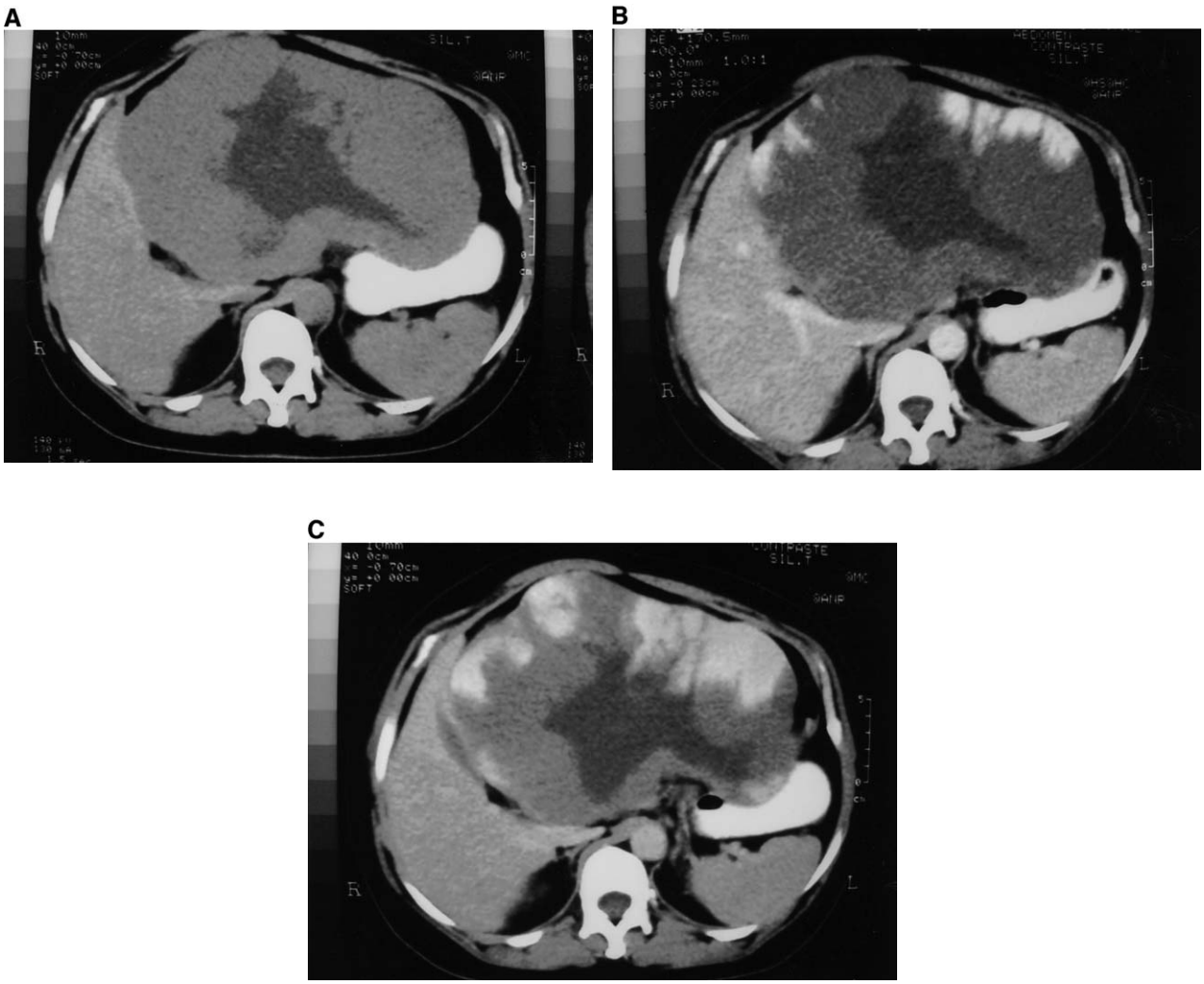

Fig. 3. CT scan disclosing (**A**) a large hypoattenuating mass (20 cm in diameter) in the left lobe of the liver. (**B**) Peripheral nodular opacification. (**C**) Centripetal filling and compression of the stomach.

Pain, the most common indication for resection, should be conservatively treated with analgesics after a thorough search for other concomitant gastrointestinal disorders. Farges et al. reported that, in their experience, pain typically waxes and wanes and, in many cases, may even disappear.[5] In the series from Farges et al. and Terkivatan et al., some patients persisted with symptoms in spite of the hepatic resection.[5,24] In our series, of six patients undergoing resection for untreatable pain, five (83.3%) had complete relief of the symptoms and one had persistent right quadrant abdominal pain after surgery.

Surgical resection is considered the definitive treatment; however, its indications are quite restricted and resection must, indeed, be reserved for situations such as incapacitating pain, compression of adjacent organs, diagnostic uncertainty, and the extremely rare Kasabach-Merritt syndrome. Ozden et al. support operative treatment for patients whose hobby or occupation carry a risk of hepatic trauma, such as football players and boxers, but the validity of this interesting rationale has never been established.[16]

Iwatsuki et al. emphasize that large hemangiomas (>10 cm in diameter) may rupture or bleed and should be resected.[17,19] Tumor size is not a formal indication for resection, although in our patients, pain was more frequently observed than in those with smaller lesions. When pain control is possible with analgesics we, as other authors,[5,24] adopt a conservative approach. In our experience, no patient presented with tumor rupture, and refractory pain was present in 37.5% of the patients with large tumors (>10 cm), which led us to conclude that resection should be indicated only in a selected group of patients with large hemangiomas.

In most of the publications showing the efficacy of hemangiomas resection, surgery was performed based on the following criteria: (1) risk of rupture;

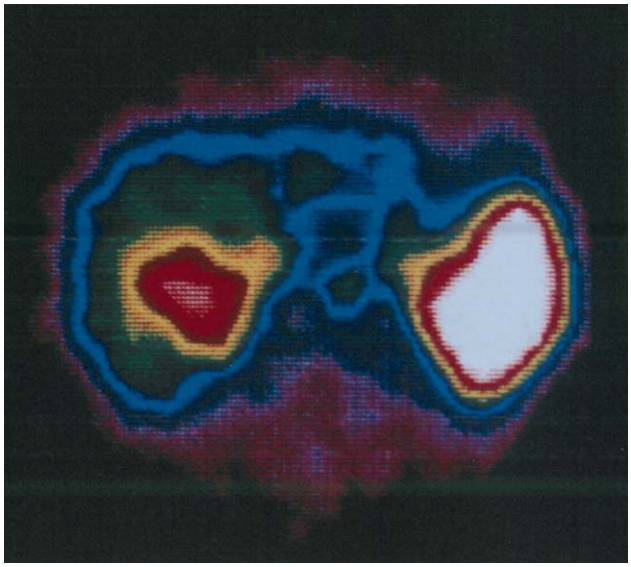

Fig. 4. Red blood cell scintigraphy showing a radioactive pooling area (red) in the right lobe of the liver.

(2) patient's willingness because of the undesirable feeling of living with a hepatic tumor, even if asymptomatic; and (3) the simple presence of a hepatic lesion. In specialized centers, liver resection mortality has dramatically declined lately to rates lower than 3%, and this may explain the enthusiasm with operative treatment of this benign condition. Nevertheless, it is noteworthy that there is a significant risk of intraoperative bleeding, and postoperative complications such as biliary fistula and abscess may follow any hepatic resection, even in experienced hands.[5,24] In Iwatsuki's series of 114 resections of benign liver tumors, there was no mortality[19] but, in other series, mortality rates of up to 2.4% were reported,[16] which should be considered unacceptable considering the benign nature of these lesions.

When surgery is indicated, hemangioma enucleation should be the procedure of choice, even though sometimes it is difficult to find a cleavage plane between the nodule and the surrounding liver parenchyma, which may cause significant bleeding. In Belli et al.'s report,[12] patients submitted to enucleation received an average of 2.8 packs of red blood cell units. In our series we favored classic resections because lesions were larger than 14 cm in diameter, considerably increasing the chance of bleeding, leading us to prefer anatomical resections. Among operated patients, only one (12.5%) required blood transfusion and all had uneventful postoperative recoveries.

Liver transplantation has already been employed for the treatment of the extremely rare cases of diffuse hepatic hemangiomatosis and in patients with the Kasabach-Merritt syndrome, with good postoperative results.[15,27]

A conservative nonsurgical approach is always advised considering that although hepatic hemangiomas are highly prevalent, complications are extremely rare. Surgery should be avoided even in the presence of symptoms like pain, which should be treated with analgesics, because liver resection presents higher morbidity and mortality rates when compared to the natural course of the disease. Special attention should be given to patients with hemangiomas larger than 10 cm in whom refractory pain is significantly more prevalent (37.5%), but the size of the lesion should not be the sole indication for resection. Patients who require surgical treatment should be referred to specialized centers, where resection can be safely performed.

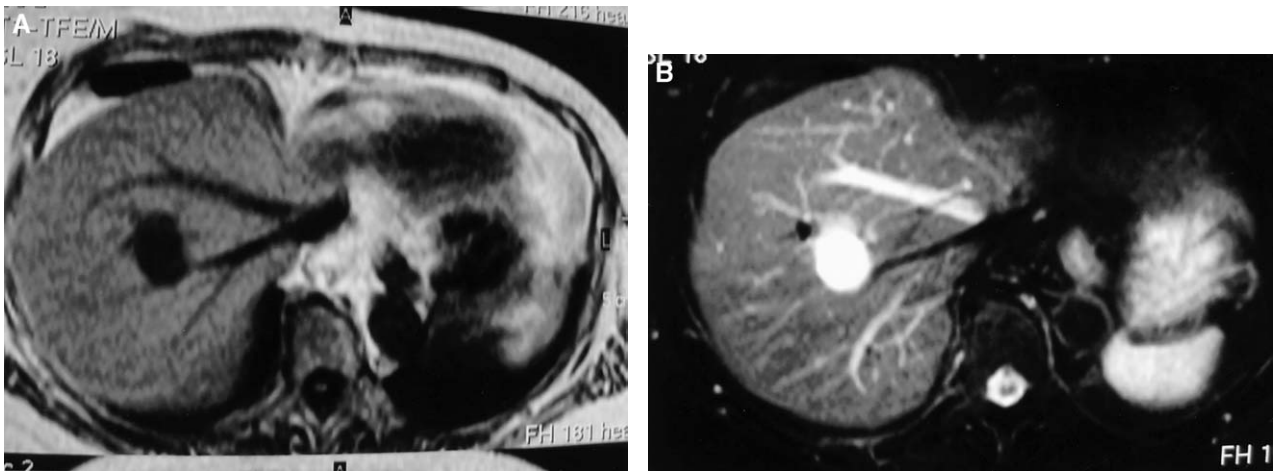

Fig. 5. Magnetic resonance imaging shows (**A**) a low-signal lesion between the middle and right hepatic veins on T1 and (**B**) a high-intensity signal on T2.

REFERENCES

1. Ochsner JL, Halpert B. Cavernous hemangioma of the liver. Surgery 1958;43:577–582.
2. Ishak KG, Robin L. Benign tumors of the liver. Med Clin North Am 1975;59:995–1013.
3. Conter RL, Longmire WP. Recurrent hepatic hemangiomas: Possible association with estrogen therapy. Ann Surg 1988; 207:115.
4. Zafrani ES. Update on vascular tumours of the liver. J Hepatology 1989;8:125–130.
5. Farges O, Daradkeh S, Bismuth H. Cavernous hemangiomas of the liver: Are there any indications for resection? World J Surg 1995;19:19–24.
6. Baer HU, Dennison AR, Mouton W, Stain SC, Zimmermann A, Blumgart LH. Enucleation of giant hemangiomas of the liver. Ann Surg 1992;216:673–676.
7. Yamamoto T, Kawarada Y, Yano T, Noguchi T, Mizumoto R. Spontaneous rupture of hemangioma of the liver: Treatment with transcatheter hepatic arterial embolization. Am J Gastroenterol 1991;86:1645.
8. Starzl TE, Koep LJ, Weil R III, et al. Excisional treatment of cavernous hemangioma of the liver. Ann Surg 1980;192: 25–27.
9. Schwartz SI, Hessere WC. Cavernous hemangioma of the liver: A single institution report of 16 resections. Ann Surg 1987;205:456–465.
10. Tsai MK, Lee PH, Tung BS, Yu Sc, Lee CS, Wei TC. Experiences in surgical management of cavernous hemangioma of the liver. Hepatogastroenterology 1995;42:988–992.
11. Kuo PC, Lewis WD, Jenkins RL. Treatment of giant hemangiomas of the liver by enucleation. J Am Coll Surg 1994;178: 49–53.
12. Belli L, DeCarlis L, Beati C, Rondinara G, Sansalona V, Brambilla G. Surgical treatment of symptomatic giant hemangiomas of the liver. Surg Gynecol Obstet 1992;174:474–478.
13. Borgonovo G, Razzetta F, Arezzo A, Torre G, Mattioli F. Giant hemangiomas of the liver: Surgical treatment by liver resection. Hepatogastroenterology 1997;44:231–234.
14. Pietrabissa A, Giulianotti P, Campatelli A, et al. Management and follow-up of 78 giant haemangiomas of the liver. Br J Surg 1996;83:915–918.
15. Browers MAM, Peeters PMJG, De Jong KP, et al. Surgical treatment of giant haemangioma of the liver. Br J Surg 1997; 84:314–316.
16. Ozden I, Emre A, Alper A, et al. Long-term results of surgery for liver hemangiomas. Arch Surg 2000;135:978–981.
17. Iwatsuki S, Starzl TE. Personal experience with 411 hepatic resections. Ann Surg 1988;208:412–434.
18. Adam YG, Huvos AG, Fortner JG. Giant hemangiomas of the liver. Ann Surg 1970;172:239–245.
19. Iwatsuki S, Todo S, Starzl TE. Excisional therapy for benign hepatic lesions. Surg Gynecol Obstet 1990;171:240–246.
20. Freeny PC, Vimont TR, Barnett DC. Cavernous hemangiomas of the liver: ultrasonography, arteriography and computed tomography. Radiology 1979;132:143–148.
21. Birnbaum BA, Weinreb JC, Megibow AJ. Definitive diagnosis of hepatic hemangiomas: MR imaging versus Tc-99m-labeled cell SPECT. Radiology 1990;176:95–101.
22. Jacobson AF, Teefey SA. Cavernous hemangiomas of the liver: Association of sonographic appearance and results of Tc-99m labeled red blood cell SPECT. Clin Nucl Med 1994; 19:96–99.
23. Solbiati L, Livraghi T, De Pra L. Fine needle biopsy of hepatic hemangioma with sonographic guidance. AJR Am J Roentgenol 1985;144:471–474.
24. Terkivatan T, Vrijland WW, den Hoed PT, et al. Size of lesion is not a criterion for resection during management of giant liver haemangioma. Br J Surg 2002;89:1240–1244.
25. Kato M, Sugawara I, Okada A, et al. Hemangioma of the liver. Diagnosis with combined use of laparoscopy and hepatic arteriography. Am J Surg 1975;129:698–704.
26. Gandolfi L, Leo P, Vitelli E, Verros G, Colecchia A. Natural history of hepatic haemangiomas: Clinical and ultrasound study. Gut 1991;32:677–680.
27. Tapetes K, Selby R, Webb M, Madariaga JR, Iwatsuki S, Starzl TE. Orthotopic liver transplantation for benign hepatic neoplasms. Arch Surg 1995;130:153–156.