Hepatic Angiomyolipoma Associated with Splenic Hamartoma

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Abstract

A 52-year-old woman was admitted to our hospital with thrombophlebitis of the internal jugular vein. Abdominal ultrasonography demonstrated a high echogenic mass measuring 4.5 cm in diameter in the liver, and abdominal CT revealed another liver tumor and an isodensity mass in the spleen. Abdominal MRI and angiography were performed and we presumed the tumors to be two hepatic angiomyolipoma and a splenic hamartoma. As an abdominal CT 21 months later revealed that all tumors were growing, these tumors were surgically resected. The histological diagnoses were hepatic angiomyolipoma and splenic hamartoma. (Internal Medicine 41: 191-198, 2002)

Key words: hepatic tumor, HMB-45, splenic tumor, pulposal type, tuberous sclerosis

Introduction

Angiomyolipoma is not uncommon in the kidney and many cases of renal angiomyolipoma are associated with tuberous sclerosis (1). However, hepatic angiomyolipoma is very rare, splenic tumors are relatively rare and splenic hamartoma is very rare. We describe the rare case of a hepatic angiomyolipoma associated with a splenic hamartoma.

Case Report

A 52-year-old woman visited our hospital in September 1998 with right neck swelling. Right internal jugular vein thrombophlebitis was diagnosed. A liver tumor and a splenic tumor were discovered by chance following abdominal ultrasonography. Following computed tomography (CT), magnetic resonance imaging (MRI) and angiography, we presumed the tumors to be two hepatic angiomyolipoma and a splenic hamartoma. The idiopathic venous thrombosis was treated with warfarin and the tumors were treated conservatively by observing them over time. In June 2000, abdominal CT revealed apparent growth of the tumors and she was admitted to our hospital for further investigation and treatment. Her medical history consisted of hypertension, myoma uteri and ventricular septum defect. Her family history was unremarkable. On admission, physical examination revealed a grade 2 systolic murmur at the third intercostal space at the left sternal border. No other abnormal findings were identified. Laboratory investigations on admission revealed a slight elevation of γ-GTP, blood sugar, and Hb A1c (Table 1). Abdominal ultrasonography, performed in September 1998, revealed a round and well demarcated 4.5 cm mass with homogeneous hyper-echogenicity in the right hepatic lobe (Fig. 1). The tumor appeared as a well-demarcated markedly hypodense mass on precontrast CT with slight enhancement following intravenous administration of contrast medium. A small, hypodense 0.2 cm nodule in the left hepatic lobe (S2) and a 2 cm isodense splenic tumor which demonstrated no enhancement following intravenous administration of contrast medium were also found (Fig. 2). The tumor in the right hepatic lobe (S7) was visualized as a hyperintense mass on both T1- and T2-weighted MRIs, but the tumor in the left

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<td>WBC (-)</td>
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hepatic lobe (S2) was not visualized on either T1- or T2-weighted MRIs. The splenic tumor was visualized as a hypointense mass on T1- and T2-weighted MRIs and was not enhanced after administration of Gd-DTPA (Fig. 3). Angiography showed a circumscribed hypervascular mass in the right hepatic lobe (S7) and an avascular mass in the spleen. The tumor in the left hepatic lobe (S2) was not visualized on angiography. In the early phase, the hypervascular mass in the liver was devoid of neovascularity. In the late phase, pooling of the contrast medium was noted within the hepatic tumor (Fig. 4).

Figure 1. Abdominal ultrasonography performed in September 1998 revealed a round and well demarcated 4.5 cm mass with homogeneous hyperechoic patterns in the right hepatic lobe (S7).

Figure 2. Tumor presented as a well demarcated 4.5 cm hypodense mass on precontrast computed tomography performed in September 1998 with slight enhancement following intravenous administration of contrast medium (A, B). A small, hypodense mass measuring 0.2 cm in diameter was found in the left hepatic lobe (S2) on abdominal computed tomography (arrow) (C, D). An abdominal precontrast CT also revealed a 2 cm isodense splenic tumor which was demonstrated no enhancement following intravenous administration of contrast medium (E, F).
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Figure 3. The tumor in the right hepatic lobe (S7) was visualized as a hyperintense mass on both T1 and T2-weighted magnetic resonance imaging (MRI) in September 1998 (A, B). The splenic tumor was visualized as a hypointense mass on T1 and T2 weighted MRI (C, D).

These imaging findings suggested the liver tumors were angiomyolipoma and the splenic tumor was a hamartoma. An abdominal CT performed in June 2000 revealed growth in all 3 tumors (Fig. 5). MRI performed in June 2000, also revealed growth of tumors in the right hepatic lobe (S7) and spleen. The tumor in the hepatic lobe (S2) which was not detected in the MRI performed in September 1998, was visualized as a hypointense mass on the T1-weighted images and a hyperintense mass on the T2-weighted images (Fig. 6).

Resection of the posterior segment of the right lobe in addition to enucleation of the tumor in the left lobe (S2) and splenectomy were performed on June 8, 2000. The resected liver tumors of the right lobe (S7) and left lobe (S2) measured 5.5 cm and 0.8 cm in diameter, respectively. Both tumors appeared well demarcated and the cut surface of both tumors was yellow and soft in consistency. Histologically, the majority of cells in both tumors were fat cells with a smaller number of smooth muscle cells and blood vessels also present. The S7 tumor consisted of a greater proportion of adipose tissue, with less blood vessels and smooth muscle cells than in the S2 tumor. Immunohistochemical staining revealed that the smooth muscle cells were positive for HMB-45, a monoclonal antibody for melanoma, and thus we could make a definite diagnosis of hepatic angiomyolipoma (Fig. 7). On the other hand, the splenic tumor measured 4 cm in diameter and presented as a well-demarcated mass. The cut surface of the tumor was normal splenic pulp with a central whitish area. Histologically, the tumor was composed of multiple nodules surrounded by fibrous connective tissue. The nodules were composed of red pulp-like areas and the diagnosis of hamartoma, predominantly pulposal type, was made (Fig. 8).

Discussion

Angiomyolipoma is a kind of hamartoma and commonly consists of different components, such as adipose tissue, blood vessels and smooth muscle cells. This tumor was first reported by Ishak (2) and occurs more frequently in the kidney than in the liver. Hepatic angiomyolipoma is fundamentally a benign tumor and patients can be treated conservatively if spontaneous hemorrhage (3) or malignant change does not occur as an associated complication. However, diagnosis may be difficult when the various imaging modalities yield little information about the radiological features of the tumors. Consequently, surgical resection is performed in many cases.

In the diagnostic images of the 78 cases of hepatic angiomyolipoma collected from the Japanese literature, ultrasonography showed the hepatic angiomyolipoma to be a well-
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Figure 4. Early phase angiography demonstrated a circumscribed hypervascular mass in the liver (A). Late phase angiography demonstrated pooling of the contrast medium (B). Early phase angiography demonstrated an avascular mass in the spleen (C). Late phase angiography demonstrated no pooling of the contrast medium (D).

circumscribed, solid, hyperechoic and homogeneous mass in 63 cases and as a hypoechoic mass in 3 cases. CT demonstrated a low-density lesions in 67 cases and a high-density lesion in one case. On administration of contrast, enhancement was observed in 39 of 45 lesions. T1-weighted MRI imaging demonstrated the hepatic angiomyolipoma as an area of high-intensity in 20 lesions, iso-intensity in 3 lesions, and low-intensity in 11 lesions. T2-weighted MRI imaging demonstrated the hepatic angiomyolipoma as an area of highintensity in 35 lesions. However, there were no lesions with an area of lowintensity or iso-intensity on T2-weighted MRI imaging. Angiography in 56 lesions demonstrated hypervascularity in 52 lesions and hypovascularity in 3 lesions.

The variations in these imaging modalities are due to variations in the proportion of the three tissue components. The present case had two angiomyolipoma which demonstrated differing radiological features. The large tumor demonstrated highintensity on T1-weighted MRI imaging and the small tumor demonstrated lowintensity on T1-weighted MRI imaging. Histologically, the former consists of more adipose tissue and less blood vessels and smooth muscle cells than the latter. Probably, the difference in MRI imaging is due to this histological
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Figure 5. An abdominal CT performed in June 2000 revealed growth of the tumors (A, B).

variation. Differential diagnoses are hepatoma with a high fat content or other fat-containing lesions including hepatic adenoma and liver metastases from fatty tumors, such as liposarcoma and malignant teratoma. The 3 components of the angiomyolipoma are often not present in ultrasound-guided biopsies and this often leads to errors in the pre-operative diagnosis. Of the 22 cases in the Japanese literature, ultrasound-guided biopsy revealed HCC in 2 cases, angiomyolipoma in 10 cases, focal nodular hyperplasia in one case and in the other cases, a diagnosis could not be made. In the Japanese literature, only 6 patients did not have the tumors surgically resected. It was recently revealed that smooth muscle cells of angiomyolipoma stain positively for HMB-45, a monoclonal antibody for melanoma (7). The present case was also positive for HMB-45. Since no other tumors of the liver are positive for HMB-45, this stain is very useful in confirming the diagnosis of hepatic angiomyolipoma.

Splenic hamartoma however, is a rare benign tumor composed of an abnormal mixture of normal splenic elements and was first described by Rokitansky in 1861 as “splenoma” (8).

In Japan, the first case was reported in 1973 by Hisano et al (9). To our knowledge, 61 cases have been reported in the Japanese literature. Because of its rarity, there is no established policy for treating patients with splenic hamartoma. However, as imaging procedures, such as ultrasonography and computed tomography, are becoming more prevalent, the rarity of this tumor will probably decrease. In the Japanese literature, ultrasonography showed the splenic hamartoma as a hyperechoic mass in 8 cases, an isoechoic mass in 4 cases, and a hypoechoic mass in 24 cases. The border was clear in 20 cases and unclear in 5 cases. The echogenic pattern was homogenous in 13 cases and heterogeneous in 9 cases. CT scan demonstrated isodense lesions in 10 cases and low-density lesions in 34 cases. There were no high-density lesions demonstrated. On administration of contrast, enhancement was observed in 30 lesions of 37 lesions. T1-weighted MRI imaging demonstrated the splenic hamartoma as an area of highintensity in 2 lesions, isointensity in 11 lesions, and lowintensity in 5 lesions. T2-weighted MRI imaging demonstrated the splenic hamartoma as an area of highintensity in 8 lesions, isointensity in 3 lesions, and lowintensity in 11 lesions. Angiography showed hypervascularity in 28 lesions and hypovascularity in 11 lesions.

Histologically, Berge classified the splenic hamartoma into four types: follicular, pulposal, fibrous and mixed (10). The pulposal type seems to be the most common. We found no consistent relationship between the pathological classification of the splenic hamartoma and their characteristic appearance using different imaging modalities. This lack of consistency in appearance may be due to differing proportions of tissue components or the presence of tumor hemorrhage, cyst, calcification and/or degenerative change.

The splenic hamartoma is fundamentally a benign tumor and we can treat patients conservatively if spontaneous rupture (11) or hypersplenism (12) does not occur as an associated complication. However, in the Japanese literature, only 2 patients did not undergo surgical resection. One case was diagnosed correctly by needle biopsy (13) and in the other case a probable diagnosis was made because the tumor revealed splenic-like function using 99mTc-Sn colloid scintigraphy (14). However, sometimes needle biopsy is misleading (15, 16) and in many cases surgical resection is performed to exclude other possible diagnoses. In the Japanese literature, pre-operative diagnoses were splenic hamartoma in 12 cases, splenic hemangiosarcoma in two cases (9, 17), splenic capillary hemangiomata in one case (18), plasmacytoma in one case (19), metastatic tumor in one case (20) and inflammatory pseudotumor in one case (21). In many of the cases diagnosed as splenic hamartoma the diagnosis of some kind of malignant tumor could not be ruled out. We think it is necessary to establish a protocol for the investigation of suspected splenic hamartoma.

Both hepatic angiomyolipoma and splenic hamartoma are
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very rare diseases; in the Japanese literature, these two diseases occurred together in only one report in a patient suffering from tuberous sclerosis (22). Tuberous sclerosis is an autosomal-dominant disorder characterized by three clinical features: adenoma sebaceum, epilepsy and mental retardation. Patients also develop hamartomatous lesions in many different organs, most commonly in the brain, heart, kidney and skin.

Angiomyolipoma, composed of mixed mesenchymal tissue, is common in the kidney but uncommon in the liver. Many cases of renal angiomyolipoma are associated with other malformations as part of tuberous sclerosis complex.

In the present case, adenoma sebaceum, epilepsy, mental retardation, lung disease and cardiac rhabdomyosarcoma did not exist. However, it is unlikely that hepatic angiomyolipoma and splenic hamartoma exist simultaneously in one person by chance. There is a possibility of some disorder in the pluripotent cells with differentiation occurring along multiple pathways leading to the development of hepatic angiomyolipoma and splenic hamartoma. We assume that our patient is suffering from some kind of atypical tuberous sclerosis.

Tuberous sclerosis complex-determining loci have been mapped to the tumor-suppressor chromosomes 9q34 (TSC1) and to 16p13.3 (TSC2) (23). We are now investigating as to whether our patient has these genes or not.

Figure 6. The tumor in the left hepatic lobe (S2), not detected on MRI performed in September 1998, was visualized as a hypointense mass on T1-weighted MRI and a hyperintense mass on T2-weighted MRI (arrow) (A, B) performed in June 2000. A MRI revealed enlarging tumors of the right hepatic lobe (S7) and spleen (C, D, E, F).
Figure 7. The resected liver tumors of right lobe (S7) and left lobe (S2) measured 5.5 cm and 0.8 cm in diameter, respectively. Both tumors presented as a well demarcated masses and the cut surface of both tumors was yellow and soft in consistency (A, B). Histologically, both tumors were mainly composed of fat cells with smooth muscle cells and blood vessels also present. Tumors of right lobe (S7) (HE stain, x10; C) consist of relatively more adipose tissue and less smooth muscle and blood vessels than the tumor in the left lobe (S2) (HE stain, x10; D). The smooth muscle cell element was positive for HMB-45, a monoclonal antibody for melanoma (x25; E).

References


Figure 8. The splenic tumor measured 4 cm in diameter and presented as a well-demarcated mass. The cut surface of tumor was normal splenic pulp with a central whitish area (A). Microscopically, the tumor was composed of multiple nodules surrounded by fibrous connective tissue. The nodules were composed of red pulp-like areas (HE stain, x40; B).