Tuberous Sclerosis Associated with Multiple Hepatic Lipomatous Tumors and Hemorrhagic Renal Angiomyolipoma

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We report a case of tuberous sclerosis associated with hepatic lipomatous tumors and renal angiomyolipomas. Abdominal ultrasonography revealed a high echoic large tumor in the left kidney. A provisional diagnosis of angiomyolipomas of the kidney was made based on computed tomography. Subsequent laparotomy revealed that the extracted tumor was renal angiomyolipoma. It was also revealed that there was an association with hepatic lipomatous tumors thought to be lipomas or angiomyolipomas by liver biopsy. Nearly half of all cases of angiomyolipoma in the kidney are reported as occasional association with tuberous sclerosis complex, but lipomatous tumors in the liver are rare.

Key words: hepatic hamartoma, hepatic angiomyolipoma, ultrasonography-guided liver biopsy, renal hamartoma, renal hemorrhage

Introduction

Tuberous sclerosis is a rare heredofamilial disease characterized by a variety of hematomatous lesions in the brain, skin, retina, and viscera. Angiomyolipoma, composed of mixed mesenchymal tissue, is not uncommon in the kidney, and many cases of renal angiomyolipoma are associated with other malformations as part of the syndrome of tuberous sclerosis. However, hepatic multiple lipomas or angiomyolipomas are rarely encountered. A diagnosis of renal angiomyolipoma or hepatic lipomatous tumor propounds considerable problems as the entity is difficult to distinguish from malignant tumor (1-3) and in some cases, it is found only after rupture, bleeding and the detection of disseminated intravascular coagulation (4,5). Herein we report the case of a Japanese woman diagnosed with hepatic multiple lipomatous tumors supposed to be lipomas or angiomyolipomas and hemorrhagic renal angiomyolipoma associated with tuberous sclerosis.

Case Report

The patient was a 30-year-old Japanese woman, 156 cm tall and weighing 53.0 kg. She was admitted to our hospital complaining of left flank pain and gross hematuria of several days duration. She was diagnosed with tuberous sclerosis at the age of 6 years. She is mentally retarded and has a long history of generalized grand mal seizures, which have been controlled with phenobarbital. A family history of a neurocutaneous syndrome could not be elicited.

The patient’s body temperature was 37.0 °C, blood pressure was 130/96 mmHg, and radial pulse rate was 78/min and regular. She was noted as having adenoma sebaceum in a butterfly paranasal distribution. She had neither anemia nor jaundice. Neurological examination revealed no abnormal findings except for mild mental retardation. Abdominal palpation revealed a mass with tenderness in the left upper quadrant.

Laboratory findings showed a red blood cell count of 384x10^4/mm^3, a white blood cell count of 5,200/mm^3, and a platelet count of 24.8x10^4/mm^3. The hemoglobin concentration was 10.0 g/dl. The liver function tests revealed: asparate aminotransferase, 12 IU/l; alanine aminotransferase, 5 IU/l; alkaline phosphatase, 234 IU/l; leucin amino peptidase, 59 IU/l; γ-glutamyltranspeptidase, 147 IU/l (normal 8-48); cholinesterase, 196 IU/l; lactate dehydrogenase, 389 IU/l; and total bilirubin, 0.4 mg/dl. Tests for C reactive protein revealed 0.11 mg/dl, and the erythrocyte sedimentation rate was 9 mm/h. With respect to renal function, blood urea nitrogen was 11.0 mg/dl and creatinine was 0.7 mg/dl. Serological studies for hepatitis B and C viruses were negative. Electroencephalogram revealed no remarkable findings and a brain computed tomography (CT) scan showed multiple calcification.

Ultrasonography (US) performed by a urologist revealed a
large, highly echoic, heterogeneous tumor around the left kidney, measuring 132×84 mm. An abdominal CT scan revealed a large, heterogeneous mass around the left kidney and small, round, low-density tumors in the right kidney (Fig. 1). An abdominal CT also showed small, round, multiple, low-density tumors in the bilateral lobes of the liver (Figs. 1, 2). The clinical diagnoses, based on these imaging examinations, were angiomyolipomas of the kidney and cysts in the liver.

The patient underwent a laparotomy because of the continuation of abdominal pain and progress of anemia after admission. During surgery, the soft tumor with yellowish-gray cut surface was found occupying the left side of the abdominal cavity. Left nephrectomy was performed and the left renal tumor was extracted at the same time. The histological diagnosis of renal tumor was angiomyolipoma. As a result of this treatment the patient’s abdominal pain and gross hematuria were resolved and anemia was improved postoperatively.

The patient visited our department after the operation for a thorough examination. An abdominal US revealed that there were multiple high echoic round tumors with acoustic shad-
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Figure 3. Images of abdominal US. Abdominal US revealed numerous multiple high echoic round tumors with acoustic shadows in the liver.

Discussion

Tuberous sclerosis is an autosomal dominant disorder characterized by adenoma sebaceum, epilepsy, and mental retardation. It is phacomatosis with a strong preponderance in females (6-8). Patients often have renal involvement with angiomyolipoma. Renal angiomyolipoma in patients with tuberous sclerosis is usually multiple, bilateral and asymptomatic, and may occur at an early age. Symptoms of renal angiomyolipoma usually result from hemorrhage in or around the tumor. Symptoms include: pain and hematuria, and a significant proportion of patients exhibit shock. A small number of patients will develop renal failure from progressive renal parenchymal replacement by tumor (9). The differential diagnosis for renal angiomyolipoma with or without the tuberous sclerosis complex includes polycystic kidney disease and renal neoplasm. If the stigmata of tuberous sclerosis are present, the diagnosis is clear. However, without the stigmata, it is difficult to distinguish the three lesions since they can present with enlarged kidneys and a benign urinalysis. The classic triad of flank pain, painless hematuria and palpable abdominal mass have been emphasized as being strongly suggestive of the presence of a renal neoplasm, though differentiation from unilateral angiomyolipomas is especially difficult (10).

Recently, preoperative diagnosis of renal angiomyolipoma has become possible with the development of various imaging modalities and the emphasis of treatments of renal angiomyolipoma has shifted to preservation of renal function through partial nephrectomy, enucleation of the tumor and arterial embolization to prevent rupture (9,11). However, a concurrence of renal angiomyolipoma and cancer in the same kidney (12) and sarcomatous changes of angiomyolipoma (13) have been reported. Therefore, a careful diagnosis is important in the conservative treatment of renal angiomyolipoma.

Lipoma or angiomyolipoma is relatively rare in the liver. More than half of all cases are asymptomatic, whereas the others have only fine clinical manifestations such as epigastric or right upper quadrant pain or discomfort (14). Hepatic involvement in tuberous sclerosis has been described in the radiographic and pathologic literature (15,16). Based on the CT findings, multiple liver cysts were suspected at first in the present case. An abdominal US performed after the operation showed hyperechoic multiple tumors in the liver, and supported the clinical diagnosis of multiple hepatic lipoma or angiomyolipoma. In our case, diagnosis of the hepatic lipomatous tumor was established by ultrasonography-guided biopsy and malignant tumor was ruled out. Angiomyolipoma generally consists of different lesions; in adipose tissue, blood vessels and smooth muscle, all of which were barely visible in the specimen obtained by ultrasonography-guided liver biopsy. Although the biopsy specimen showed adipose tissue only, hepatic angiomyolipoma was not completely ruled out in the present case.

Compton et al (15) reported that angiographically, five of eight patients with tuberous sclerosis had vascular tumors in the liver consistent with hamartomas. Roberts et al (17) reported seven cases of lipomatous masses in the liver, five of which were obtained from a retrospective review of 50 cases of renal angiomyolipoma and three of which were associated with tuberous sclerosis. The true incidence of angiomyolipomas or lipomatous tumors in the liver is not known because of the difficulty in detection. The detectability of these lesions is limited by the following facts (17): 1) fatty tumors are rare, 2) fat is difficult to detect in lesions with a low fat content, 3) the lesions are asymptomatic and hence are detected only as incidental findings, 4) small lesions can be confused for a simple cyst due to partial volume averaging, and 5) a peripheral mass or one adjacent to the fat-containing falciform ligament is difficult to appreciate. In fact, the cases of tuberous sclerosis associated with hepatic multiple lipomatous tumors are rare although nearly half of all cases of angiomyolipoma in the kidney are reported as an occasional association with tuberous sclerosis complex (11,18). However, since several cases of tuberous sclerosis associated with hepatic lipoma or angiomyolipoma have been reported (17), some relationship may exist between tuberous sclerosis and hepatic hamartoma in regard to the etiology. Further studies on the relationship between tuberous sclerosis, renal angiomyolipoma, and hepatic lipomatous tumor are required. In our patient, we do not have direct evidence that tuberous sclerosis is related to the development of hepatic lipomatous masses. However, we believed it would be valuable to report this case of tuberous sclerosis associated with renal angiomyolipomas and hepatic lipomatous tumors, since such a disease association is rare.

References

1) Wong K, Kaisary AV, Waters CM, Horner J, Hershman MJ.
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