

Peritumoral Hyperplasia in Hepatic Sclerosed Hemangioma

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ABSTRACT

Peritumoral hyperplasia (PTH) is a hyperplastic lesion located around hypervascular tumors. Hepatic sclerosed hemangioma is a very rare form of hemangioma with sclerotic changes and is distinct from sclerosing hemangioma. We present a patient with non-alcoholic steatohepatitis-induced cirrhosis who presented with a hypervascular tumor. The tumor showed atypical findings of hemangioma and was treated with surgical resection because hepatic malignancy could not be ruled out. Histopathologic examination revealed the tumor was a sclerosed hemangioma with PTH. Lesions with carcinogenic potential were found in the PTH lesion. Sclerosed hemangioma should be observed and managed carefully.

INTRODUCTION

Hepatic sclerosed hemangioma (SH) is a benign tumor characterized by extensive fibrosis, hyalinization, and obliterated vessels.¹ SH is seen relatively predominantly in elderly women, although the number of cases is low.^{1,2} SH is distinct from sclerosing hemangioma, which is associated with regressive changes that are secondary to thrombosis or hemorrhage in cavernous hemangioma.¹ Ring-enhanced or not-enhanced patterns in dynamic computed tomography (CT) have been reported as findings of SH.² However, the degree of sclerotic changes such as fibrosis and hyalinization can vary, as can radiological findings, making hepatic SH difficult to diagnose, and many patients have been treated surgically.²⁻⁴ Mast cells are decreased in SH and are implicated in angiogenesis, regression, and fibrosis of SH, but the precise mechanism remains unknown.¹ Peritumoral hyperplasia (PTH) results from hyperplastic changes adjacent to tumors caused by increased blood flow.⁵ PTH has been found around hypervascular tumors and may constitute a compensatory hypervascular response to portal invasion.⁵ Recently, hyperplastic hepatocellular lesions have been reported to involve abnormal blood flow to hemangiomatous lesions.⁶

CASE REPORT

A 27-year-old Japanese man was referred for evaluation of a liver tumor that was found incidentally on follow-up. At age 23 he was diagnosed with fibromyalgia and non-alcoholic steatohepatitis (NASH). He reported only social drinking of alcohol. His body mass index was 31 kg/m², but he did not have diabetes mellitus. He had been treated over several years with opiates, laxatives, and antidepressants, which had not been changed.

The patient reported no abdominal symptoms, and physical examination revealed no abnormal findings aside from obesity. Serum biochemistry showed a slight deterioration in liver function, which was likely due to NASH, and elevated concentrations of aspartate aminotransferase (45 U/L), alanine aminotransferase (54 U/L), alkaline

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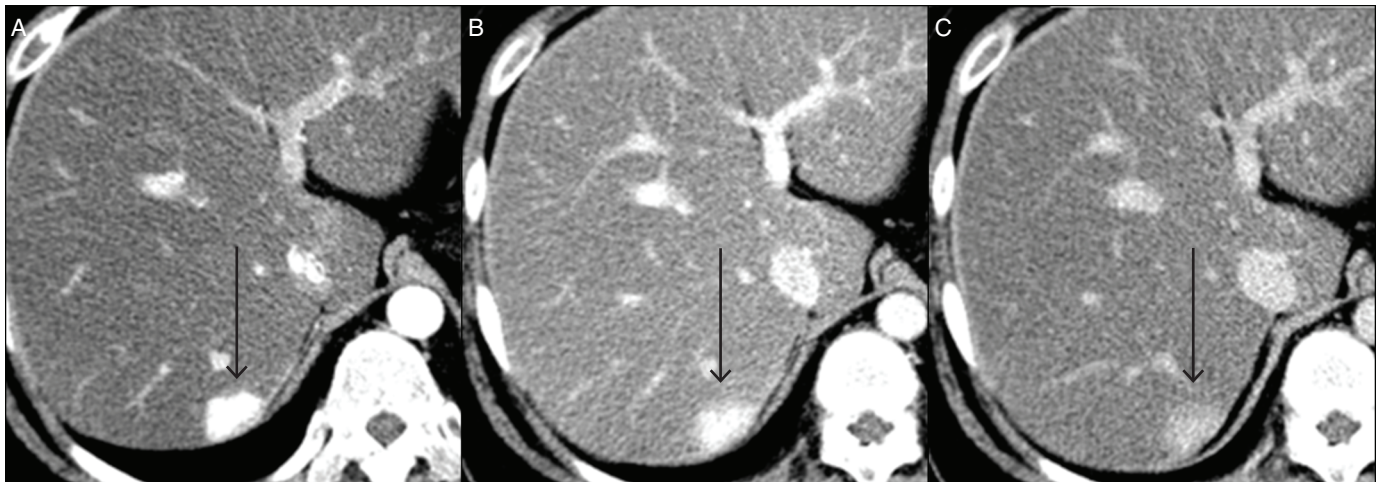


Figure 1. Dynamic CT images of the tumor with a prolonged, enhanced pattern in S7 (arrows) in the (A) arterial phase, (B) portal phase, and (C) equivalent phase.

phosphatase (433 U/L), and total bilirubin (0.4 mg/dL). His family history did not include liver disease. He was negative for hepatitis B and C infection. Serum tumor markers were all negative, with normal serum concentrations of alpha-fetoprotein (1.5 ng/mL), des-gamma-carboxy prothrombin (24 mAU/mL), carcinoembryonic antigen (1.8 ng/mL), and carbohydrate antigen 19-9 (2 U/mL). He showed no metabolic abnormality, such as hemochromatosis or Wilson's disease. Dynamic enhanced CT revealed a severe fatty liver and 22-mm tumor with prolonged hyperattenuation in the vascular phases (Figure 1). The tumor was suggested to be rich in vascular components, as with a hemangioma. Magnetic resonance imaging (MRI) using gadolinium-ethoxybenzyl-diethylenetriamine penta-acetic acid (Gd-EOB-DTPA)

showed uptake in the periphery but not the center of the tumor in the hepatobiliary phase (Figure 2). The patient was then followed-up carefully. At 6 months, the tumor extended outward, and the hepatobiliary phase of EOB-MRI showed low intensity at the periphery and iso-intensity at the center, with both showing low intensity 12 months after the initial examination (Figure 2). We could not rule out the possibility of neoplastic changes such as adenoma. Laparoscopic partial hepatectomy was performed because the tumor was small and located on the surface of the liver.

The lesion contained many dilated, blood-filled vessels, with more abundant stromal tissues with hyalinization around the vessels positive for CD34 (Figure 3). These findings were

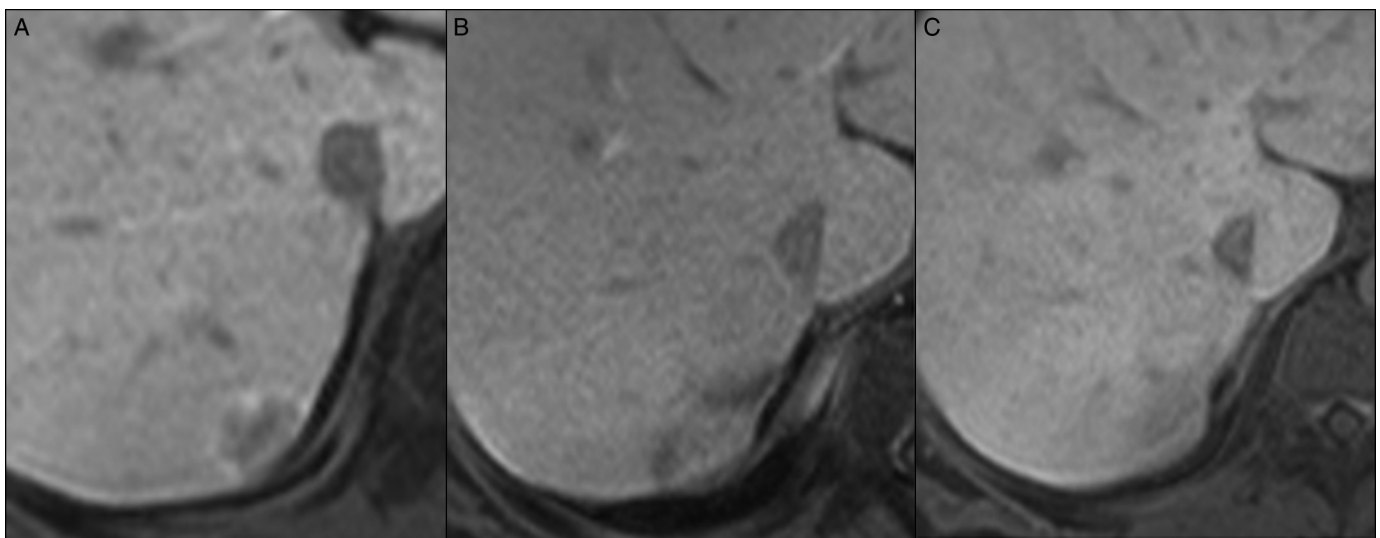


Figure 2. Hepatobiliary phase of gadolinium-ethoxybenzyl-diethylenetriamine penta-acetic acid-enhanced MRI. (A) At initial examination, the tumor showed high intensity at the periphery and low intensity at the center of the tumor. (B) After 6 months, the tumor showed low intensity at the periphery and iso-intensity at the center of the tumor. (C) After 12 months, the tumor showed low intensity at the periphery and center of the tumor.

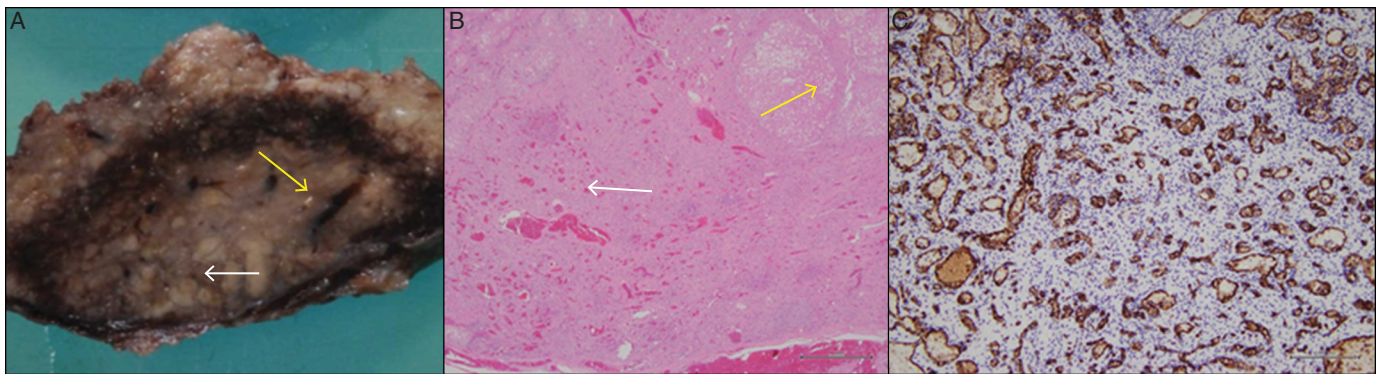


Figure 3. (A) Macroscopic finding of dilated blood vessels and interstitial tissue with sclerosis in the center of the tumor, with hyperplastic nodules around it. (B) Hematoxylin and eosin (H&E) staining (10x) showing sclerosed hemangioma (white arrow) and peritumoral hyperplasia (yellow arrow). (C) CD34 staining (40x) showing sclerosed hemangioma.

consistent with SH. Steatosis, inflammation, and bridging fibrosis were found in the background liver, compatible with NASH-cirrhosis. Hyperplastic nodules were found around SH, suggesting that the latter was caused by a mechanism similar to that of PTH. In part of the PTH-like nodules, glutamine synthetase and heat-shock protein 70 were overexpressed, and clathrin heavy chain was slightly expressed by the PTH-like lesion (Figure 4). Such phenotypical changes were not found in the surrounding liver. These observations suggested that partial hepatocarcinogenic alterations might have occurred in the PTH-like hyperplastic hepatocyte nodules. The clinical course was good, with no evidence of tumor recurrence or worsening of liver function for 3 years.

DISCUSSION

In this case, underlying complicated histological findings made the patient difficult to diagnose radiologically. Factors suggesting SH include geographic pattern, capsular retraction, reduction in size over time, and loss of contrast enhancement.^{4,7-9} Because the tumor in this patient was small and PTH was present, diagnosis was difficult. Furthermore, the radiological characteristics of PTH have yet to be fully clarified. PTH thickness was reported to be <1 cm.⁵ Consequently, accumulation of similar cases is required.

Interestingly, the PTH lesion in this patient showed characteristics similar to premalignant transformation with phenotype alterations reported in early hepatocellular carcinoma (HCC).¹⁰ NASH is a leading cause of cirrhosis and has been associated with the development of HCC.^{11,12} In this patient, the hepatocarcinogenic potential of NASH-induced cirrhosis, involving inflammatory and metabolic pathways, may have been associated with the changes found in PTH lesions. Further investigations are required.

Since SH is a very rare tumor, few cases have been reported. SH should be observed carefully with imaging studies, especially in cirrhotic livers. Surgical procedures might be considered for precise diagnosis in cases of SH with radiological alterations.

DISCLOSURES

Author contributions: S. Shimada and K. Tajiri wrote the manuscript. H. Baba, K. Tsuneyama, and M. Nakano performed the pathological evaluations. T. Sugiyama and M. Minemura reviewed the article for important intellectual content. K. Tajiri is the article guarantor.

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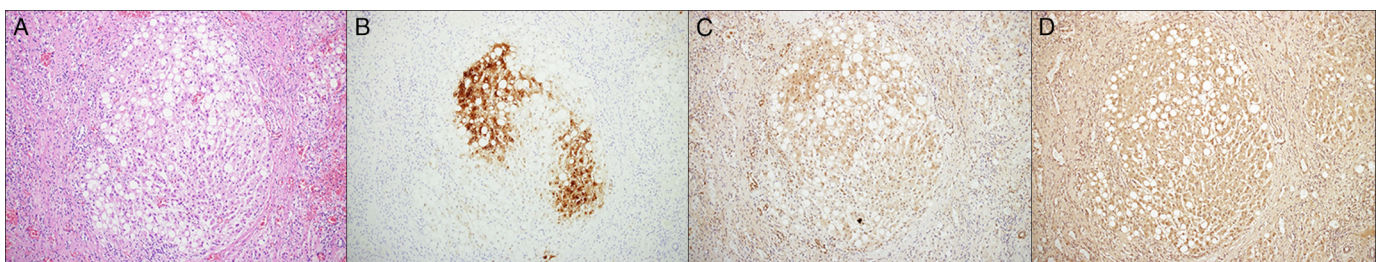


Figure 4. Premalignant potential of the peritumoral hyperplasia. (A) (H&E) staining (100x). (B) Glutamine synthetase staining (100x). (C) Heat shock protein 70 staining (100x). (D) Clathrin heavy chain staining (100x).

Informed consent was obtained for this case report.

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