

# Giant cavernous hemangioma coexistent with diffuse hepatic hemangiomatosis presenting as portal vein thrombosis and hepatic lobar atrophy

## ULTRASONOGRAPHY

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### CASE REPORT

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A combination of giant hepatic hemangioma and diffuse hemangiomatosis is extremely rare in adults. Even when they are large, hemangiomas are soft and rarely compress adjacent structures. A 78-year-old man presented with abdominal pain and distension. Ultrasonography, computed tomography, and magnetic resonance imaging demonstrated a large expansile mass replacing the medial segment and caudate lobe with diffusely scattered nodules in the entire liver. The large hilar mass contained a central nonenhancing area and had a mass effect, leading to left portal vein occlusion. The image findings also revealed two unprecedented findings: left lateral segmental atrophy of the liver and recent portomesenteric vein thrombosis. The hepatic lesions were confirmed with hemangiomas by ultrasonography-guided biopsy. We diagnosed intrahepatic portal vein obstruction caused by a mass effect of giant hepatic hemangioma coexistent with diffuse hemangiomatosis, resulting in hepatic segmental atrophy and extrahepatic portal vein thrombosis.

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## Introduction

Hepatic hemangiomas are soft tumors that usually do not compress bile ducts, the portal vein, or the inferior vena cava. In rare cases, these can be large (giant hemangioma) and eventually compress the biliary or vascular structures [1]. However, no cases have been reported in the literature in which hepatic lobar atrophy and portal vein thrombosis developed as a result of hepatic hemangioma compression. Isolated diffuse hepatic hemangiomatosis without extrahepatic lesions is extremely rare in adults [2]. Furthermore, giant hepatic hemangioma coexistent with diffuse hepatic hemangiomatosis is even more uncommon, although an association exists between hemangiomatosis and giant hepatic hemangiomas [3]. Here, we describe a pathologically proven giant hepatic hemangioma coexistent with diffuse hepatic hemangiomatosis that presented as intrahepatic portal vein obstruction with subsequent hepatic segmental atrophy and extrahepatic portal vein thrombosis.

## Case Report

A 78-year-old man was admitted to our hospital with a two-week history of abdominal pain and

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distension. The patient had been taking medicine for hypertension but denied a prior history of using other drugs. The laboratory findings revealed abnormalities such as decreased hemoglobin (11.4 g/dL), and slightly elevated levels of serum alanine aminotransferase (41 IU/L), aspartate aminotransferase (41 IU/L), and alkaline phosphatase (161 IU/L). Alpha-fetoprotein was not increased and the Child-Pugh score classification was A; total bilirubin, serum albumin, and platelet count were within normal limits, there was no evidence of hepatic encephalopathy, and a small amount of ascites was observed on the initial abdominal computed tomography (CT) scan. On physical examination, the patient showed no hemangiomas on the skin.

At the first appearance of symptoms, an initial abdominal CT scan was performed at an outside clinic. The CT demonstrated diffuse hepatic nodules involving the entire liver and a large heterogeneous mass replacing the left medial segment and caudate lobe (Fig. 1). Because ascites, colonic edema, and gallbladder edema accompanied the diffuse hepatic lesions, diffuse hepatocellular carcinoma was suggested, and the patient underwent chemotherapy



**Fig. 1.** Initial abdominal computed tomography (CT) of diffuse hepatic hemangiomas and coexistent giant cavernous hemangioma in a 78-year-old man. Axial contrast-enhanced CT image during the arterial phase shows heterogeneous nodular enhancement in both hemilivers and a contour-bulging mass with a central markedly low density area involving the caudate lobe. The expansile mass (arrowheads) protruded anteriorly, and the horizontal portion of the left portal vein was invisible, suggesting left portal vein occlusion by the mass effect of the caudate lobe lesion. The umbilical portion of the left portal vein was also invisible along the fissure for ligamentum teres (white arrow). Ascites in the right subphrenic space and dilated hepatic artery (long arrows) measuring 10-mm can be noted. There was no portomesenteric vein thrombosis (not shown).

(sorafenib, 400 mg/day) for 12 days. He complained of a newly developed headache and general weakness, so chemotherapy was stopped immediately. However, he continued to suffer from the abdominal pain and distension that he had previously reported. Two months after the symptoms had begun, ultrasonography (US; iU22 system, Philips, Bothell, WA, USA), CT (Somatom AS+, Siemens, Forchheim, Germany), and magnetic resonance imaging (MRI; Magnetom Skyra 3.0T, Siemens, Erlangen, Germany) were performed for a further work-up.

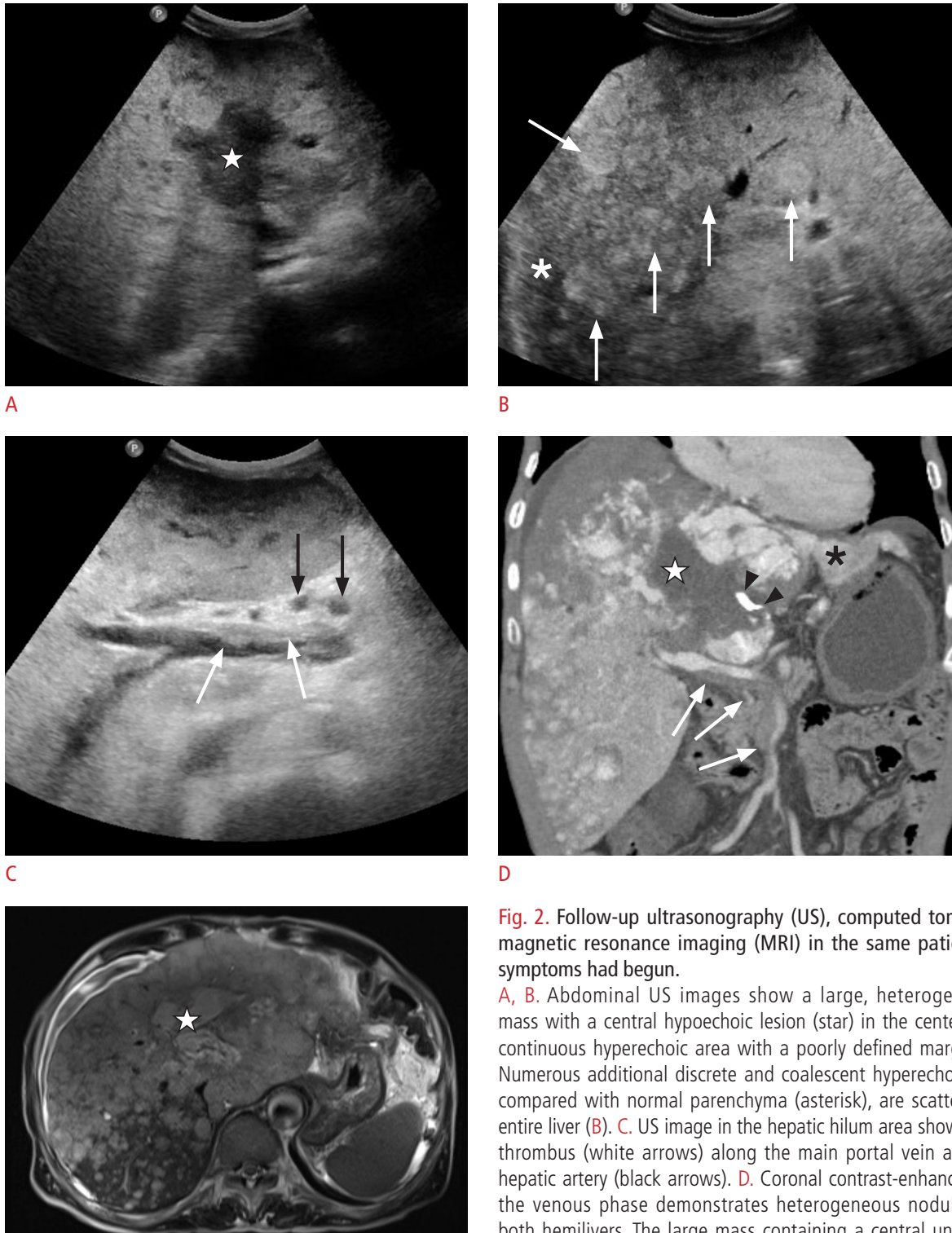
On abdominal US, a large heterogeneous hyperechoic mass with a central hypoechoic portion was observed in the central hilus of the liver and the outer margin of the hyperechoic mass was not well defined (Fig. 2A). Numerous discrete and coalescent hyperechoic nodules, relative to the normal liver parenchyma, were scattered throughout the liver (Fig. 2B). In addition, hyperechoic bland portal vein thrombosis and dilated hepatic arteries were noted at the hepatic hilus level (Fig. 2C).

Both initial and follow-up abdominal contrast-enhanced CT images demonstrated heterogeneous nodular enhancement in the entire liver with a large central mass containing an unenhanced, central, markedly hypodense area in the medial segment and caudate lobe. It also showed peripheral punctate calcifications in the central hypodense area, suggesting phleboliths (Figs. 1, 2D).

On T2-weighted MR images, numerous nodular hyperintense lesions were scattered throughout the liver. A central markedly hyperintense area was suspected to be a different histologic region, compared with the adjacent nodular lesions (Fig. 2E). Dynamic MR axial images revealed discontinuous nodular enhancement with gradually filled nodules that turned more homogeneous, but with some remaining unfilled portions. These findings were consistent with diffuse hepatic hemangiomas. The central unenhanced, hypointense area did not change without enhancement, corresponding to a degenerative change of a giant hemangioma. Similar to the US images, there was no distinct margin between the giant hemangioma and the adjacent hemangiomas (Fig. 2F, G).

CT and MRI images clearly revealed the mass effect of the central hepatic lesion. The medial segment and caudate lobe were replaced by a large mass with an anteriorly bulging appearance. Furthermore, the horizontal and umbilical portions of the left portal vein could not be traced, suggesting left portal vein occlusion by central mass compression (Figs. 1, 2D). The mass also compressed the intrahepatic inferior vena cava (not shown in figure).

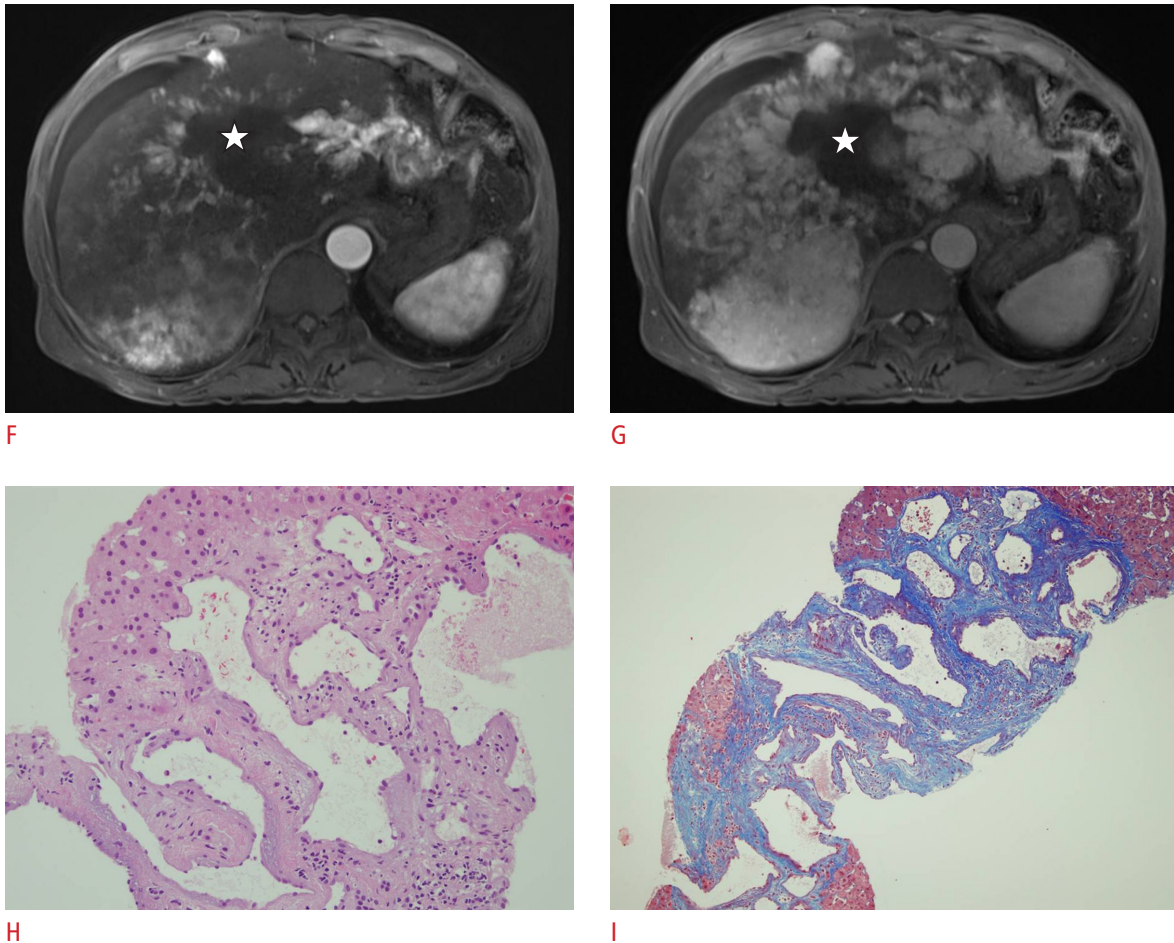
Further, they showed two unique findings consequential of the mass effect. First, left lateral segmental atrophy of the liver was evident, suggesting a result of left portal vein occlusion. Second, similar to the US findings, portomesenteric vein bland thrombosis was observed from the superior mesenteric vein to the main portal



**Fig. 2.** Follow-up ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI) in the same patient 2 months after symptoms had begun.

**A, B.** Abdominal US images show a large, heterogeneous hyperechoic mass with a central hypoechoic lesion (star) in the center of the liver, and a continuous hyperechoic area with a poorly defined margin of the mass (**A**). Numerous additional discrete and coalescent hyperechoic nodules (arrows), compared with normal parenchyma (asterisk), are scattered throughout the entire liver (**B**). **C.** US image in the hepatic hilum area shows hyperechoic bland thrombus (white arrows) along the main portal vein and dilated common hepatic artery (black arrows). **D.** Coronal contrast-enhanced CT image during the venous phase demonstrates heterogeneous nodular enhancement in both hemilivers. The large mass containing a central unenhanced, markedly hypodense area (star) replaces the medial segment with a bulging contour. There is portomesenteric bland thrombosis from the superior mesenteric vein

to the main portal vein, part of the right portal vein (white arrows). Furthermore, the volume of the left lateral segment of the liver (asterisk) was decreased, suggesting hepatic lobar atrophy. It also shows calcification (black arrowheads) in the central large mass. The remaining ascites should be noted in both subphrenic spaces. **E.** T2-weighted MR image using half-Fourier single-shot turbo spin echo sequence (TR/TE infinite/103 ms, flip angle 107°) demonstrates diffusely scattered nodular lesions with hyperintensity relative to the unaffected liver parenchyma (segment 7). This also shows marked hyperintensity of the central area (star).



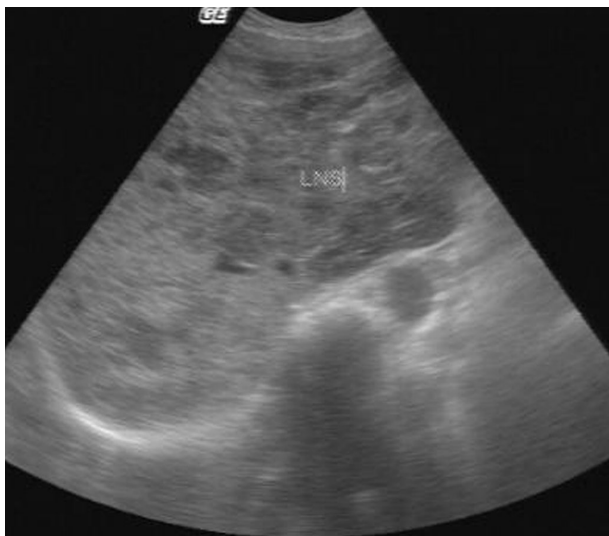
**Fig. 2.** F, G. Serial gadolinium-enhanced T1-weighted MR axial images using a fat-suppressed, 3-dimensional volumetric interpolated breath-hold examination sequence (TR/TE 3.5/1.5 ms, flip angle 9°) show discontinuous nodular enhancement on the arterial phase (F) and gradual fill-in enhancing nodules turning more homogeneous but some remaining unfilled portions during the delayed phase (G), consistent with diffuse hepatic hemangiomas. The central markedly hypointense area (star) did not change without enhancement, corresponding to a degenerative change of the giant hemangioma. There was no distinct margin between giant hemangioma and adjacent diffuse hemangiomas. H, I. Histological findings reveal large, dilated vessels of varying size lined by flattened endothelium and arranged in a haphazard pattern (H; H&E, ×200), and they are separated by fibrous septa of various thicknesses (I; Masson's trichrome stain, ×100).

vein, and in part of the right portal vein (Fig. 2D). In addition, ascites, colonic edema, and gallbladder edema appeared consistent with the findings of an earlier CT performed at an outside clinic (not shown in figure), suggesting more associated evidence of portal vein obstruction.

To rule out other hepatic malignant tumors, an US-guided gun biopsy was performed in the right hemiliver using an 18-gauge core needle (Acecut, TSK Laboratory, Tochigi, Japan). The histological analysis revealed a typical cavernous hemangioma that had irregularly dilated nonanastomotic vascular spaces lined with flat endothelial cells alternating with normal hepatic parenchyma, without cellular atypia (Fig. 2H, I). During a further work-up, we obtained previous outside abdominal US images taken 8 years earlier, and they showed diffuse and inhomogeneous

echogenicity throughout the liver, suggesting pre-existing diffuse hemangiomas (Fig. 3). Hence, we finally diagnosed the patient with intrahepatic left portal vein obstruction caused by a giant hepatic hemangioma coexistent with diffuse hepatic hemangiomas, resulting in development of left hepatic lobar atrophy and extrahepatic portal vein thrombosis.

There were no significant complications (high-output heart failure, liver failure, or thrombocytopenia) caused by the hepatic hemangiomas. Surgery was not performed, and the patient was observed with follow-up. Over a 9-month follow-up period, abdominal discomfort was reduced and quality of life improved. The blood chemistry, including liver enzymes, improved to within normal limits.



**Fig. 3.** Previous abdominal ultrasonography of the same patient, taken 8 years before diagnosis of diffuse hepatic hemangiomatosis and coexistent giant cavernous hemangioma. Diffuse and inhomogeneous echogenicity is located in the center of the liver.

## Discussion

Cavernous hemangiomas are the most common type of hepatic benign tumors and are most frequently observed in women between the third and fifth decade of life [2]. These tumors are soft and usually do not compress or invade adjacent structures. However, they may cause a mass effect when they attain substantial dimensions or have a modified internal component, such as a thrombosis or hemorrhage, transforming the lesion into a firm solid mass [1,4]. Some reports have described a mass effect on the bile duct, inferior vena cava, or portal vein in giant hepatic hemangioma (>4 cm in diameter) [1,4–6]. These mass effects manifest as displacement or compression of the intrahepatic vein or inferior vena cava without associated complications. In three cases, portal vein obstruction was described, two of which presented on imaging as a perfusion abnormality in the adjacent liver parenchyma [1]. In the other case, a significant portal vein obstruction was observed with a cavernous transformation [5]. However, none of them showed portal vein thrombosis or hepatic lobar atrophy as sequential findings of portal vein obstruction.

Hepatic lobar atrophy is mostly caused by a hepatic hilar malignant tumor or iatrogenic damage of the biliary duct and portal vein, and there is a strong correlation between lobar atrophy and ipsilateral portal vein obstruction [7]. In our case, the giant hemangioma was located in the medial segment and caudate lobe of the liver and protruded anteriorly. Therefore, this compressed the horizontal portion of the left portal vein and had a possibility of long-standing

compression due to benignness of the mass. Therefore, we suggest that the hilar giant hemangioma caused the left portal vein obstruction, leading to ipsilateral hepatic lobar atrophy.

Sorafenib (BAY 43–9006, Nexavar; Bayer, Leverkusen, Germany) is an oral multikinase inhibitor with antiangiogenic and antiproliferative effects. This could exert a beneficial effect on portal vein thrombosis by the inhibition of the vascular endothelial growth factor receptor pathway, which may play a pivotal role in portal vein thrombosis onset and evolution, as well as in hepatocellular carcinoma angiogenesis [8]. A portal vein thrombosis is found in 0.18% of patients with hepatocellular carcinoma when using sorafenib [9]. This is a much lower incidence than that of native hepatocellular carcinoma (neoplastic thrombosis, 6.5%–44%; bland thrombosis, 42%) [10], and could show that sorafenib actually reduces the risk of development of portal vein thrombosis. Thus, although portal vein thrombosis was found after sorafenib monotherapy in our case, there is a low possibility of chemotherapy-induced portal vein thrombosis. Furthermore, ascites, colonic congestion, and gallbladder edema were already present in the initial abdominal CT without evidence for other causes such as liver cirrhosis or inflammatory lesions. Therefore, we came to the conclusion that all of the imaging findings, including portomesenteric vein thrombosis, were caused by intrahepatic portal vein obstruction, resulting from the mass effect of the giant hepatic hemangioma. Prothrombotic states, local factor causing vessel wall injury, venous stasis contribute to mesenteric vein thrombosis. The latter is more frequently associated with combined mesenteric and portal vein thrombosis, whereas the former manifests as isolated mesenteric vein thrombosis [11]. Because superior mesenteric vein thrombosis was combined with portal vein thrombosis in our case, we suggested that this was also a sequential finding of the intrahepatic portal vein obstruction.

Our case showed typical imaging findings for giant cavernous hemangioma—[HC1] early discontinuous peripheral nodular enhancement with progressive centripetal enhancement to uniform fill-in but a persistent, markedly hypodense central area in the medial segment and caudate lobe of the liver. Some studies have demonstrated that marked hyperintensity of the central area on a T2-weighted image corresponds to hypocellular myxoid tissue and may represent an intermediate stage in the evolution from thrombosis to the final well-formed fibrous scar [1,4]. Our case also showed a central area with marked hyperintensity on the T2-weighted image, suggesting the possibility of myxoid change. Based on the above-mentioned references, we assumed that hemorrhage might have occurred in the central area of the giant hemangioma just before the onset of symptoms and that this aggravated the mass effect by increasing the volume and making the tumor firmer. Accordingly, this probably evoked development of recent portal vein thrombosis,

as well as ascites, colonic congestion, and gallbladder edema, which were acute manifestations of the portal vein obstruction.

Diffuse hepatic hemangiomatosis usually presents in infancy, with Rendu-Osler-Weber disease or skeletal hemangiomatosis. Isolated diffuse hepatic hemangiomatosis without extrahepatic lesions is extremely rare in adults [2]. Jhaveri et al. [3] argued for a significant association between giant hepatic hemangioma and hepatic hemangiomatosis. They found a hemangiomatosis pattern adjacent to the giant hemangioma in 18 of 41 patients (44%) with giant cavernous hemangiomas (>8 cm in diameter). In most cases, hemangiomatosis involved the adjacent margin of the giant hemangioma, without normal liver tissue separating them. The enhancement pattern of hepatic hemangiomatosis is similar to those of common hepatic hemangiomas. Our case showed multiple small discrete and coalescent nodules with a uniformly filled-in enhancement pattern in both hemilivers without a definitive separation from the giant hemangioma. They also described US findings of hemangiomatosis as heterogeneous echo patterns with multiple discrete or small coalescent hypoechoic nodules on a hyperechoic background [3]. In our patient, the US findings were somewhat different from those of previous reports and showed mainly hyperechoic nodules with confluent to hyperechoic giant hepatic hemangioma, containing a markedly hypoechoic central area. Hepatic artery dilatation can be seen in patients with diffuse hepatic hemangioma and giant hepatic hemangioma [3]. Our case also showed diffuse dilatation of the common hepatic artery and its branches.

Hepatic angiosarcoma can mimic diffuse hepatic hemangiomatosis or giant hemangioma because this shows the image findings of an increased signal on the T2-weighted image, heterogeneous centripetal enhancement, and occasionally a central nonenhancing hypodense area, similar to that of giant cavernous hemangioma. However, this is rapidly progressive vascular tumor and most patients die within a year of diagnosis [12]. In our case, the hepatic lesions already existed 8 years earlier and were pathologically proven to be hemangiomas, so we could exclude angiosarcoma from the differential diagnosis.

In conclusion, giant hepatic hemangioma can cause significant portal vein obstruction by its mass effect. This, in turn, can cause hepatic lobar atrophy and portal vein thrombosis. Despite its rarity and these atypical features, a diagnosis of diffuse hepatic hemangioma coexistent with giant hepatic hemangioma in adults can be suggested based on the distinctive CT, MR, and US findings.

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### Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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