



# Hepatic small vessel neoplasm: not totally benign, not yet malignant

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Hepatic small vessel neoplasm (HSVN) is a rare vascular tumor with few reports in the literature. While imaging findings may show characteristic enhancement patterns, limited available literature may not reveal the full potential for image-based diagnosis. Histologically, HSVN mimics other entities, though certain morphologic and immunohistochemical findings provide clues for diagnosis. However, HSVN still provides diagnostic challenges, especially on core biopsies with limited material for morphologic and molecular evaluation. While current recommendations are surgical resection and close observation, the long-term course of the tumor is unknown. We report a case of HSVN in a liver with additional feature of organized lymphoid aggregates necessitating additional hematopathology consultation and workup to rule out concurrent entities.

**Key Words:** Hepatic small vessel neoplasm; Liver; Vascular neoplasm

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Hepatic small vessel neoplasm (HSVN) is a recently described vascular neoplasm of the liver. Morphologically, this tumor is characterized by a mixture of benign and potentially malignant features to include bland cells lining thin-walled vascular channels, low mitotic rate, and infiltrative borders [1]. As these cases are infrequent, radiologic diagnosis is also challenging.

We report a case of liver biopsy with morphologic and immunohistochemical features characteristic of HSVN. Our case was complicated by organized lymphoid aggregates necessitating hematopathology evaluation.

## CASE REPORT

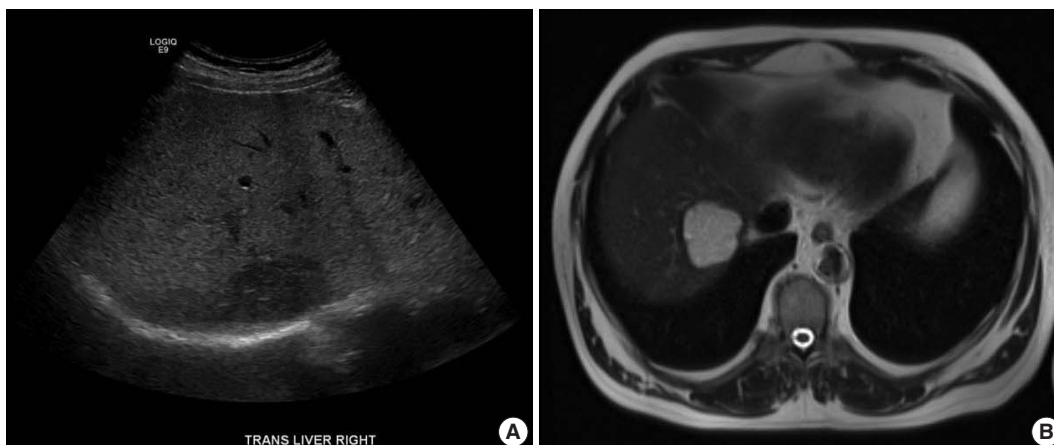
A 63-year-old asymptomatic male with a medical history of hypertension and occasional alcohol use presented for his annual exam. Routine labs demonstrated mildly elevated liver enzymes to include alanine aminotransferase 110 U/L and aspartate aminotransferase 63 U/L. Alkaline phosphatase was normal (50 U/L).

## Radiologic features

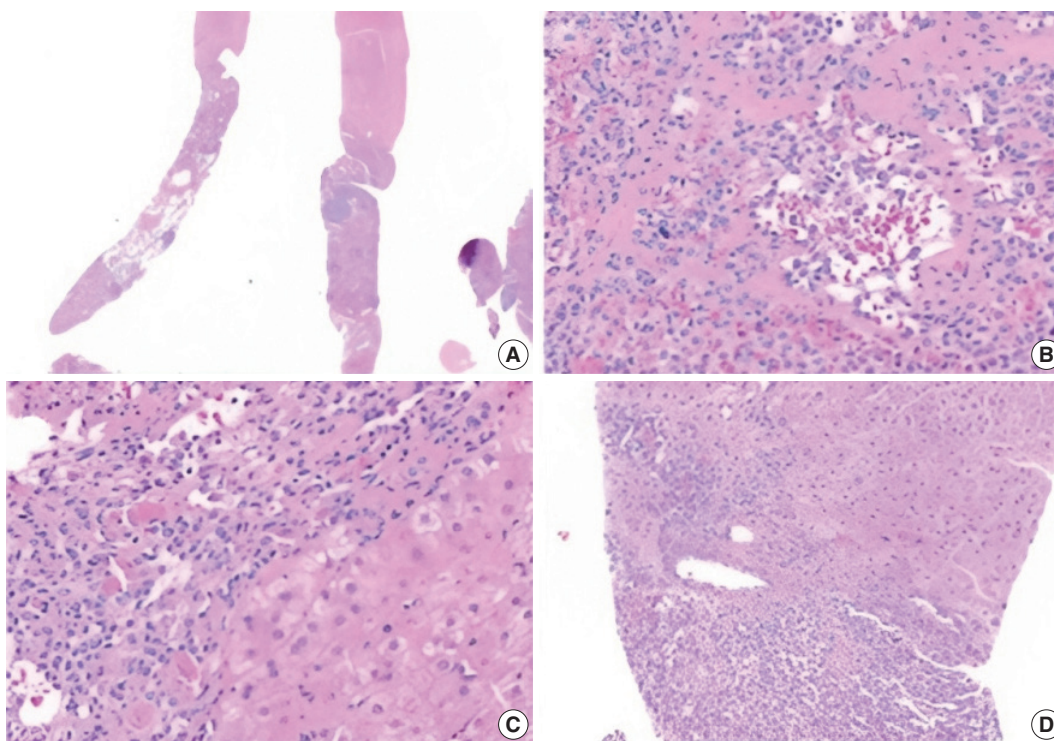
An ultrasound demonstrated a 4.7 cm hypochoic lesion in the right lobe of the liver. Liver protocol magnetic resonance imaging (MRI) with intravenous gadolinium-based contrast revealed a well-circumscribed 4.65 cm lesion that was hyperintense on T2 with prompt heterogenous contrast enhancement without washout (Fig. 1). The sonographic appearance and MRI enhancement pattern were not typical for benign lesions, so the patient subsequently underwent image-guided biopsy.

## Morphologic features

The biopsy showed a neoplasm comprised of closely packed, small, thin-walled anastomosing vascular channels lined by bland endothelial cells. The lesion was well-demarcated from adjacent parenchyma, though focally infiltrated into a portal tract. The cells had no significant nuclear atypia or mitotic activity. There was no hobnailing, papillary formation, complex architecture, or necrosis. Background liver showed mild steatosis with no other significant abnormalities. Additionally, there were various-sized aggregates of small lymphoid cells (Fig. 2).



**Fig. 1.** (A) Liver ultrasound demonstrating a hypoechoic lesion in the right lobe of the liver. (B) Liver protocol abdominal magnetic resonance imaging showing a hyperintense lesion on T2 with heterogenous contrast enhancement.



**Fig. 2.** Microscopic appearance of the biopsy specimen. (A) Multiple biopsy specimens with well-demarcated lesion. Multiple, various-sized lymphoid aggregates can be seen. (B) The lesion is composed of thin-walled small vascular channels lined by bland endothelial cells. (C) The lesion is well-demarcated from adjacent liver parenchyma in most areas. (D) Focal infiltration into portal tract.

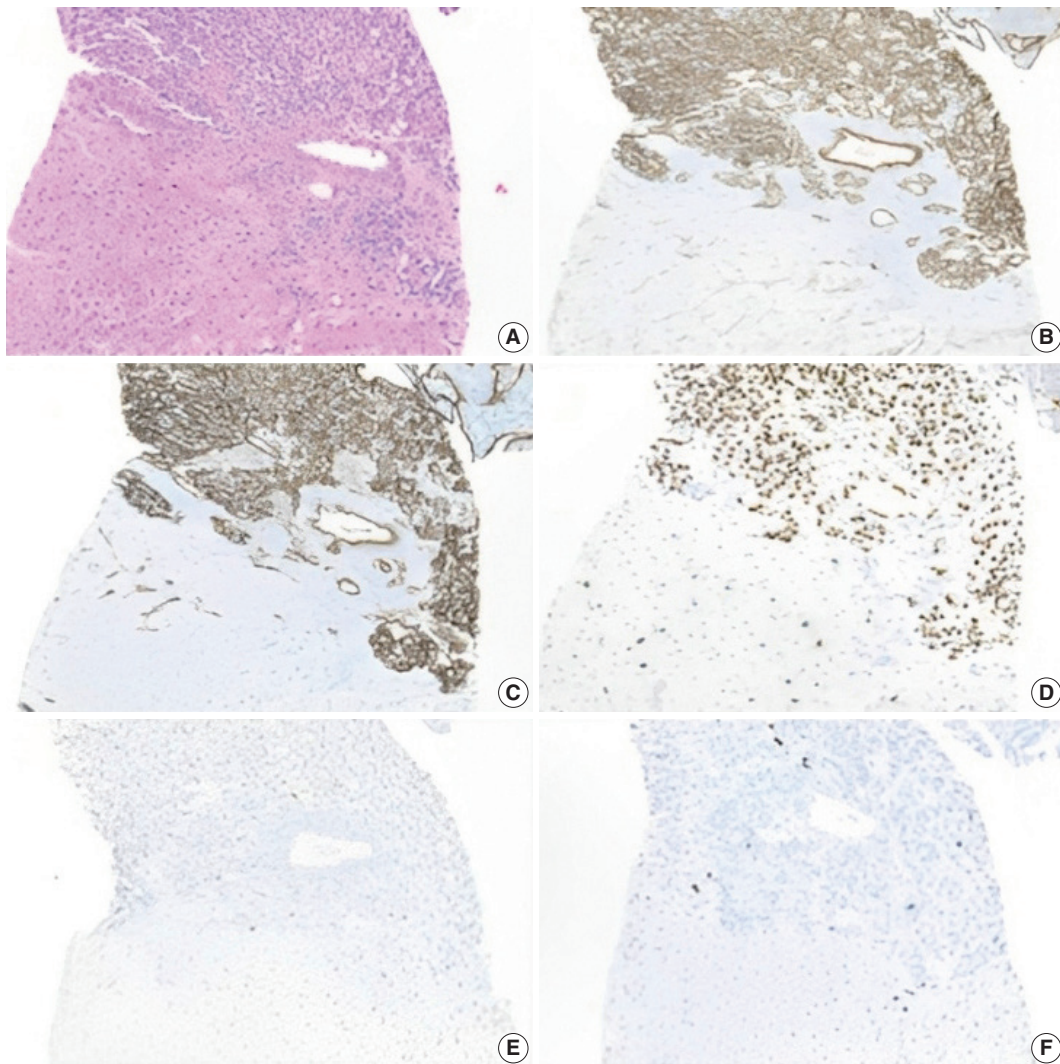
**Immunohistochemistry**

The lesion displayed diffuse positivity for vascular markers (CD34, CD31, and ERG). p53 was patchy/weak (wild type). Neoplastic cells showed Ki-67 proliferation index of 5%–10% (Fig. 3). Iron, Periodic Acid-Schiff with diastase, and copper stains were negative in the background liver.

Additional work-up was completed to exclude ectopic spleen

and/or lymphoma. CD3 and CD20 immunostains highlight mixtures of mature T cells and B cells, respectively, with a predominance of the former. CD8 stains a subset of the T cells, and no splenic sinusoidal endothelial cells are present. These findings exclude ectopic splenosis and are not compatible with a B-cell lymphoma (Fig. 4).

Morphologic and immunohistochemical findings were con-



**Fig. 3.** Immunohistochemical staining. (A) Lesion next to normal hepatic parenchyma. (B) The lesion is positive for CD31. (C) Positive for CD34. (D) Positive for ERG. (E) p53 is patchy and weak. (F) Ki-67 proliferation index is 5%–10%.

sistent with HSVN. Though most of the biopsy specimen showed a well-demarcated neoplasm, focal infiltration into a portal tract favored this diagnosis. The case was sent to an expert with special interest in HSVN, who agreed with our assessment [1].

#### Follow-up

The patient was seen by the hepatobiliary surgical team. Treatment options were discussed, including surgical resection, yttrium radioembolization, or observation with serial imaging. The patient opted for observation.

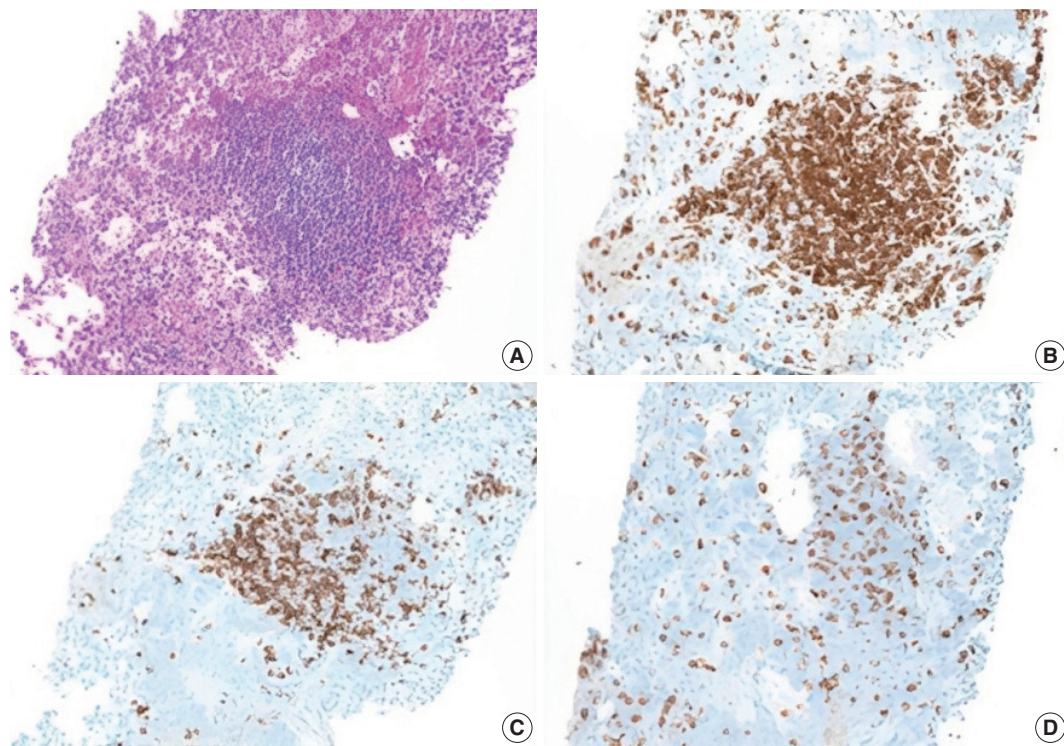
## DISCUSSION

HSVN is a rare vascular neoplasm of the liver with morpho-

logic features that make diagnosis challenging. HSVN is usually incidentally found, and ranges in size from 0.2 to 16 cm [1-3]. It is characterized by strong expression of vascular markers (CD31, CD34, FLI-1, and ERG) and is pancytokeratin negative. All cases have a low Ki-67 proliferation index (<10%) [4]. Next-generation sequencing has shown activating hotspot mutations in the alpha subfamily of G-proteins (*GNAQ*, *GNA11*, and *GNA14*) [5]. In one particular case, foci of high-grade transformation were noticed microscopically while *RAF1* and *GNA11* concurrent mutations were detected at the molecular level. A link between these unique morphology and molecular profile was hypothesized [6].

Anastomosing hemangioma (AH), another rare vascular neoplasm, was at the top of our differential diagnosis list. It is char-





**Fig. 4.** Immunohistochemical staining of lymphoid aggregate. (A) Varying sized aggregates of small lymphoid cells were present in the lesion. (B) CD3 stains a moderate number of small T cells. (C) CD20 stains a small number of small B cells. (D) CD8 did not demonstrate organized lymphoid tissue.

acterized by anastomosing vascular spaces lined by bland, round-to-oval endothelial cells with scattered hobnail morphology. While cases have been reported in many organs, the kidney is most frequently affected [7]. AH is immunoreactive for CD34 and CD31 and negative for keratin [8]. AH shares many morphologic features as HSVN including the characteristic mutations in the G-protein subfamily [5]. However, AH is well-demarcated with no infiltrative growth.

Hepatic angiosarcoma (HAS) is the most common malignant mesenchymal liver tumor and is highly aggressive, with survival less than 6 months at time of diagnosis. Histologically, HAS displays infiltrating anastomosing vascular channels with tumor cells alongside dilated sinusoids. Endothelial cells may be round or spindle-shaped and exhibit severe nuclear atypia with frequent mitotic activity [9]. CD31 and CD34 are positive. Ki-67 levels are higher with a mean of 42.8% [3,4]. Thus, the Ki-67 proliferation index can be a useful distinction in differentiating these two neoplasms. Furthermore, the G-protein mutations seen in HSVN and AH are not found in HAS, which often has *TP53* or *KDR* mutations [6].

Different imaging modalities have been used in the workup of HSVN. Paisant et al. [2] reported possible characteristic imag-

ing findings in a case series involving four patients who underwent contrast-enhanced ultrasound (CEUS), computed tomography, and MRI. All modalities demonstrated similar enhancement patterns on arterial phase imaging with early, irregularly thick peripheral and continuous enhancement. The appearance at arterial phase on larger lesions was described as “flower petal shaped” due to early septa enhancement. Imaging-specific characteristics include persistent thick rim enhancement with mild central washout on CEUS and heterogenous hyperintensity on T2-weighted imaging [2]. However, there has been a case with innumerable enhancing lesions that were only visualized on the arterial phase [6].

While these radiological features are not totally diagnostic, they may be used to distinguish HSVN from other vascular hepatic lesions. For example, in classic hemangioma, there is peripheral, globular discontinuous enhancement as opposed to the thick rim, continuous enhancement seen in HSVN [2]. Hemangiomas also frequently display homogenous hyperintense T2 signal. AH shows nonspecific heterogenous, nodular enhancement [10]. HAS commonly shows heterogenous centripetal enhancement. It is also more likely to be poorly-circumscribed with a higher likelihood of intratumoral hemorrhage [11].

Unique to our case was the concern for hepatic splenosis or lymphoma. Splenosis is one type of ectopic spleen tissue, that typically occurs following abdominal trauma or splenectomy. Viable splenic tissue is autotransplanted in the abdominal cavity or more rarely in the thoracic cavity or brain. Hepatic splenosis is exceedingly rare and often asymptomatic with nonspecific imaging that can mimic other hepatic lesions [12]. CD8 stains a subset of T cells, and is useful for identifying splenic tissue because the endothelial cells lining the splenic sinuses are positive for CD8, a finding that is unique to those endothelial cells (littoral cells). In addition, there are case reports of contiguous primary marginal zone B-cell lymphoma and hemangioma [13]. The presumed T-cell predominant lymphoid aggregate in our HSVN case is not consistent with a marginal zone B-cell lymphoma and are more typical of reactive lymphoid aggregates.

Currently there are no treatment guidelines. While HSVN is considered a benign lesion, its full course is not understood, and the current recommendation is complete resection and close observation. The reported follow-up period is variable, with a mean of seven months. Both those with complete resection and those with positive margins showed no evidence of disease recurrence [14]. Long-term data is still needed to understand the disease course and guide definitive management.

### Ethics Statement

Institutional Review Board approval was waived due to the use of retrospective, de-identified data. This study adhered to the guidelines enacted by the Office of Human Research Protection that is supported by the U.S. Department of Health & Human Services. All information included in this report is de-identified and no personal details that may be used to identify the patient are included in this report. Written informed consent for the publication of this report was obtained from the patient.

### Availability of Data and Material

Data sharing not applicable to this article as no datasets were generated or analyzed during the study.

### Code Availability

Not applicable.

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Conceptualization: TEJ. Investigation: MM. Supervision: TEJ. Writing—original draft: MM. Writing—review & editing: MM, DH, TEJ. Approval of final manuscript: all authors.

### Conflicts of Interest

The authors declare that they have no potential conflicts of interest.

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