Imaging of pathology involving the space around the hepatic veins: "perivenous pattern"

ABSTRACT
We aimed to illustrate diseases involving the potential space around the hepatic veins. Perivenous halo sign can be seen in patients with congestive heart failure or fluid overload. Perivenous involvement can be observed in patients with alcoholic fatty liver disease, which can be focal or diffuse. Metastasis and primary liver tumor spread can also involve this space most likely due to involvement of lymphatics around hepatic veins.

The liver may be affected by various benign and malignant disorders. The mode of spread to the liver parenchyma may include hematogenous or lymphatic routes as well as direct extension from neighboring anatomic structures. In this article, by using the term "perivenous space" we refer to the parenchymal areas surrounding the hepatic veins. Hepatic veins received little attention compared with portal veins in imaging literature (1). In the same manner, the perivenous space also gained minimal to no attention from the imaging community. Compared with several articles studying the role of imaging in the evaluation of the periportal space, not much has been written about the perivenous space. Perivenous halo sign occurs due to accumulation of fluid in perivenous space resulting from congestion in the setting of congestive heart failure or fluid overload. Fat deposition, inflammatory infiltration, and neoplastic infiltration may be seen in the perivenous space around the liver. In this article, we first describe the imaging anatomy of this space and, subsequently, the non-neoplastic and neoplastic processes involving this anatomic compartment.

Anatomy
Hepatic veins represent the main venous outflow tract of the liver parenchyma. Despite the dual vascular supply nourishing the liver parenchyma, the outflow is almost solely via the hepatic veins. They also play a major role in the anatomic segmentation of the liver, defined by French surgeon Claude Couinaud (2). Based on Couinaud’s definition, the liver is divided into eight segments with portal vein branches at the center and hepatic veins at the periphery.

In a normal liver there are 3 hepatic veins; namely, right, middle, and left hepatic veins. These hepatic veins drain into the retrohepatic portion of the inferior vena cava (IVC), approximately 2 cm caudal to the right atrium. The right hepatic vein generally joins the IVC as a separate trunk, while in 65%–85% of the patients middle and left hepatic veins form and share a common trunk before draining into IVC (3). There are several accessory hepatic vein branches described but we will not discuss them in detail for the sake of brevity of this article. Interested readers may refer to several excellent articles published in the literature regarding this topic (3–6).

Hepatic lymphatic vessels deserve attention in understanding the perivenous pattern. The hepatic lymphatic system is mainly divided into superficial and deep networks (7). The deep hepatic lymphatic system mainly surrounds the portal vein branches and is responsible for 80% of the lymphatic drainage of the liver (8). Along the portal tracts these lymphatic vessels converge into larger vessels (around 12–15 vessels) which eventually drain...
into the hepatic hilar lymph nodes. These hepatic lymph nodes are mainly located in the lesser omentum and they eventually drain into cisterna chyli, which represents the dilated origin of the thoracic duct which is the largest lymphatic vessel of the body. As mentioned above, despite the fact that the perportal compartment is where the main deep lymphatic network is located, a not insignificant portion of the deep drainage is via the perivenous lymphatic vessels which mainly reside around the hepatic veins. The perivenous lymphatic vessels finally converge into 5–6 large vessels which eventually drain into posterior mediastinal lymph nodes (7).

The superficial hepatic lymphatic system is a part of the liver surface (7). These superficial vessels originate from the convex and inferior surfaces of the liver and finally drain into several different lymph nodes.

Non-neoplastic perivenous pathologies

Lymphedema

By definition, lymphedema refers to the abnormal distention of the lymphatic vessels. The underlying etiology may be either related to overproduction of the lymphatic fluid or to the blockade of distal lymphatic flow. Lymphedema is mostly detected in the periportal space; however, perivenous lymphedema is not uncommon. Several intra and extrahepatic disorders may promote lymphedema, including, but not limited to, hepatic inflammation, trauma, overhydration, pancreatitis, pneumonia, or pyelonephritis (7). Iatrogenic causes, mainly due to extensive surgical dissection in tumor surgery as well as liver transplantation, may also represent the underlying etiology in some patients (9).

Congestive hepatopathy, which basically refers to passive hepatic congestion in congestive heart failure, is an important and relatively common cause of perivenous lymphedema. Increased hydrostatic pressure within the IVC and hepatic vein lumens subsequently gives rise to sluggish flow within the intrahepatic venous outflow network, which eventually may lead to nutmeg liver appearance and hepatocyte necrosis (10).

On imaging, perivenous lymphedema appears as a hypodense halo around the hepatic veins. On computed tomography (CT) studies, the engorged lymphatic vessels give rise to perivenous linear hypodensity, which might be reminiscent of conventional perportal halo (Fig. 1). Magnetic resonance imaging (MRI) may also be used in the evaluation of perivenous lymphedema and T2-weighted images can be especially helpful by clearly delineating the perivenous hyperintensity.

Perivenous fat deposition

Focal parenchymal fat deposition/sparing may mimic focal parenchymal liver lesions and definitive diagnosis may be difficult in some cases. Several imaging findings might be helpful for diagnosis of fatty pseudolesions over the true neoplastic/inflammatory masses. Among these findings, absence of mass effect in adjacent vascular/biliary structures, characteristic location, ill-defined lesion borders rather than round or oval shape (which are characteristic for true neoplastic lesions), contrast enhancement pattern similar to background liver parenchyma should be counted (11).

Perivascular fat deposition was first described by Hamer et al. in 2005 (12). The typical cross-sectional imaging finding of perivascular fatty infiltration is the tram-like configuration for vessel segments parallel to the imaging plane, and a ringlike or round configuration for vessel segments perpendicular to the imaging plane (12) (Fig. 2). Perivenous fatty infiltration is generally bilobar (12). The absence of mass effect is one of the key imaging features for focal fat deposition within the liver parenchyma.

Sinusoidal obstruction syndrome

Sinusoidal obstruction syndrome (SOS), also called as veno-occlusive disease, is thought to be related to chemotherapy- or radiation-induced destruction of hepatic microvasculature during cytoreductive treatment (13). Histologically, obliteration of the small hepatic venules with associated surrounding fibrosis and obstructed sinusoids from debris of necrotic endothelial cells are characteristic findings (14, 15).

SOS is a relatively common adverse effect of chemotherapy regimens and stem cell transplantation. The reported incidence of SOS in patients treated for colorectal cancer with systemic chemotherapy was reported to be between 42% and 51%. Oxaliplatin use is a well-known risk factor for SOS development with a reported incidence of 51%–79%, compared with 21%–30% with chemotherapy regimens not including oxaliplatin (16–18).

In most of the cases, SOS does not cause any detectable symptoms per se; however, its detection is important in patients undergoing evaluation for liver resection to prevent potentially mortal liver failure es-

Main points

- Perivenous space refers to the adjacent structures surrounding the hepatic veins.
- Accumulation of fluid in the perivenous space, resulting from congestion in the setting of congestive heart failure or fluid overload, presents as the perivenous halo sign.
- Fat deposition, inflammatory infiltration, and neoplastic infiltration may be seen in the perivenous space around the liver.
especially after surgery (19). Thus, the identification of SOS may be critical for optimum timing of surgery and also for the planning of further chemotherapy (20).

The typical imaging findings may not be present in all affected patients. The imaging findings are generally nonspecific; however, periporal edema, ascites, gallbladder wall thickening, heterogeneous parenchymal enhancement and hepatomegaly are suggestive imaging features when detected. Sonographic imaging findings are nonspecific, but reversal of flow in portal veins may be detected in some patients (21, 22). The presence of narrowed right hepatic vein caliber is also a reported CT finding (23).

MRI studies with the use of gadoxetic acid disodium (Gd-EOB-DTPA, Primovist or Eovist, Bayer Schering Pharma AG) appears to be a more sensitive method for detecting SOS and provided invaluable functional clues in a noninvasive manner. Gd-EOB-DTPA is a relatively new hepatocyte specific contrast agent which has recently gained wide popularity in liver imaging. Hepatobiliary phase images are generally acquired 20 minutes after contrast injection and this phase appears to be the most valuable part of the dynamic MRI of the liver. Reticular

Figure 2. a–e. A 51-year-old male with chronic steroid use was referred for evaluation of the elevated serum liver enzymes. Gray-scale US image (a) reveals increased echogenicity (arrows) around the middle hepatic vein, with no evidence of mass effect on the vessel lumen. Axial contrast-enhanced CT image (b) of the same patient shows hypoattenuating areas around the middle hepatic vein corresponding to hyperechoic areas detected in the US exam. Axial in-phase dual echo magnetic resonance image (c) reveals no abnormal signal change in the liver parenchyma. Axial out-phase dual-echo image (d) demonstrates signal loss around the hepatic veins (arrows) with fat around the middle hepatic vein. Coronal true fast imaging with steady state precession (TRUE-FISP) image (TE: 2.3 ms) (e) demonstrates perivenous low signal intensity (arrows) representing perivascular fat.

Figure 3. a–d. A 49-year-old female with known colon cancer who was referred for an abdominal CT scan for restaging purposes. Previous sonographic exam at an outside center revealed hyperechogenicity around the hepatic veins (images were not available for review). Axial T1-weighted (a) and T2-weighted (b) images reveal focal increased signal intensity (arrows) in the hepatic parenchyma surrounding the middle hepatic vein. Axial fat-suppressed T2-weighted image (c) reveals signal loss in the corresponding hyperintense areas detected on the T1- and T2-weighted images, confirming perivenous fat deposition. Diffusion-weighted image (d) demonstrates no restriction in this area.
Type hepatic parenchymal hypointensity in this phase, in patients who underwent chemotherapy for liver metastases, appears to be a sensitive imaging finding for SOS (19) (Fig. 4). Graft-versus-host disease (GVHD) may also develop in patients with a history of stem cell transplant and can manifest with symptoms similar to those of veno-occlusive disease and histopathologic evaluation may be necessary to confirm the diagnosis (23). The association of small bowel wall thickening in addition to other findings detected in SOS is more suggestive of GVHD than SOS (23).

Parasitic infection
Fascioliasis of the liver is caused by the trematode Fasciola hepatica. The life cycle of Fasciola hepatica in humans starts with ingestion of the parasite. The parasites then penetrate the duodenal wall and gain access into the peritoneal cavity with subsequent penetration into the liver parenchyma through the hepatic capsule. The spreading pattern of fascioliasis in the liver parenchyma is centripetal due to random migration of the parasites within the liver parenchyma. Intrahepatic bile ducts may be also be infiltrated which subsequently gives rise proximal bile duct dilatation (24). Imaging features of liver fascioliasis include parenchymal heterogeneity, focal irregularly distributed small parenchymal abscesses with dilatation of the bile ducts. Endoluminal filling defects within the biliary system, ductal wall enhancement and peripherally located enlarged lymph nodes may also be detected (25). Tract-like lesions might be encountered in the liver parenchyma, secondary to intraparenchymal migration of the parasites. Perivenous areas may also be affected in the course of the disease (Fig. 5).

Neoplastic perivenous pathologies
Metastases
Liver is one of the most commonly involved organs in patients with metastatic disease. Colon, breast, lung, and stomach should be counted among the most common primary tumors (26). Secondary neoplastic involvement of the liver far exceeds the incidence of primary hepatic tumors and hematologic seeding is the most common gateway to the liver parenchyma. Accurate and prompt detection of liver metastases is of critical importance for successful...
Acoustic enhancement is a useful imaging mimic cysts. The absence of posterior hypoechoic lesions which may sometimes nodules generally appear as homogeneously (30). On US images, lymphomatous nodal lesions in 90% of the cases may manifest as discrete pa.

Lymphoma

Lymphomatous involvement of the liver is a common clinical phenomenon and may be encountered in 50% of patients with non-Hodgkin lymphoma. Primary lymphoma of the liver, in contrast to the secondary involvement, is much more rare and accounts for less than 1% of all non-Hodgkin type lymphomas (28, 29).

Secondary lymphomatous involvement of the liver may manifest as discrete parenchymal focal lesions in 90% of the cases (30). On US images, lymphomatous nodules generally appear as homogeneously hypoechoic lesions which may sometimes mimic cysts. The absence of posterior acoustic enhancement is a useful imaging clue in these patients by indicating the solid nature of these lesions. Nodules may sometimes have a bull’s-eye appearance (30). CT is also a commonly utilized modality where these lymphomatous nodules generally appear as hypodense lesions, with attenuation values higher than that of water (30). On MRI, these nodules are typically hypointense compared with the background liver parenchyma on pre- and post-contrast T1-weighted images, with mild corresponding hyperintensity on T2-weighted images. Perivenous involvement may be also be seen in these patients. The piercing vessel sign, which indicates a vessel branch traversing a focal lesion, without any associated luminal narrowing or occlusion, may be an important diagnostic clue. This sign is an indirect finding of the soft consistency of these lymphomatous deposits, which is in significant contrast with the hard consistency of the metastases from primary adenocarcinoma (Fig. 7).

Hepatocellular cancer

Hepatocellular cancer (HCC) is the most common primary liver tumor with potentially grave clinical prognosis. The invasion of major hepatic venous structures is an indicator of grave clinical prognosis in major HCC staging systems, with almost no chance of complete clinical cure reported in these patients (31). There is no universal consensus on the best treatment approach to patients with macroscopic hepatic venous invasion but both surgery and systemic chemotherapy have been proposed for best outcomes (32). Portal vein and its branches are the most commonly involved vessels within the liver, and hepatic venous invasion is much more rare compared with the portal vein invasion (33). As the hepatic veins finally drain into the right atrium, potential pulmonary metastases would be expected to occur in these patients; however, it was reported that the most frequent site of recurrence in these patients was again the liver itself (32). CT and MRI are both very useful in diagnosing the hepatic vein invasion. Compared with bland thrombus, one should expect to see arterial phase enhancement within the thrombus, which basically points to the cellular nature of the tumor thrombus. The expansion of the involved hepatic vein is also a good indicator for tumor thrombus as neoplastic thrombi mostly do not respect the tissue and vessel wall boundaries (Fig. 8).

The evaluation of overall endovascular tumor load and outlining the degree of extension must be thoroughly evaluated, as these parameters have a significant potential in the selection of the optimal medical and surgical treatment approaches. Both CT and MRI may be successfully used to answer these critical questions.

Differentiation between neoplastic and non-neoplastic diseases in perivenous space

Non-neoplastic diseases involving the perivenous space perivenous space usually present with linear extension along the perivenous space. Neoplastic diseases involving the perivenous space can be differentiated from non-neoplastic diseases using the imaging features including mass effect on adjacent vascular and biliary structures, vascular invasion in hepatocellular carcinoma, contrast enhancement pattern on contrast-enhanced CT or MRI, diffusion restriction on diffusion-weighted imaging and perihepatic malignant lymph nodes if present (34, 35).
Conclusion

Perivenous space in the liver may be affected by various non-neoplastic and neoplastic conditions. Perivenous hypodensity/hypointensity is a common but nonspecific finding and may indicate edema due to various disease processes or fat infiltration. Several primary and secondary tumors may also invade perivenous space and awareness of the imaging clues may be significant help to the imaging specialists not only in narrowing the differential diagnosis list but also in making confident diagnoses.

Conflict of interest disclosure

The authors declared no conflicts of interest.

References

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