Pitfalls in Gd-EOB-DTPA-Enhanced Liver Magnetic Resonance Imaging With an Emphasis on Nontumorous Lesions

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Gd-EOB-DTPA (gadoxetic acid; Eovist in the United States and Primovist in Europe and Asia; Bayer HealthCare) is a widely used magnetic resonance (MR) contrast agent for liver imaging. After intravenous injection, Gd-EOB-DTPA is distributed throughout the vascular and extra-vascular spaces presenting in the arterial, portal venous, and late dynamic phases, and progressively into the hepatocytes and bile ducts during the hepatobiliary phase.¹ Gd-EOB-DTPA achieves its popularity by providing both hemodynamic and cellular information regarding focal hepatic lesions. It can also provide excellent lesion-to-liver contrast during the hepatobiliary phase.¹

Hypointensity on the hepatobiliary phase of Gd-EOB-DTPA–enhanced MR imaging is usually considered a typical imaging finding for tumors. Lesions with no hepatocytes, such as metastases or cholangiocarcinoma, or those with less functioning hepatocytes, such as hepatocellular carcinoma (HCC) or adenoma, are unable to accumulate and excrete Gd-EOB-DTPA. Therefore, they usually appear hypointense compared with the normal liver parenchyma.² However, various nontumorous lesions may also appear hypointense during the hepatobiliary phase because of hepatocyte dysfunction or a decreased number of functioning hepatocytes in the area where nontumorous lesions are located. Nontumorous hypointensity may, therefore, make it possible to make a misdiagnosis.

In this article, we show various nontumorous lesions with hypointensity seen on the hepatobiliary phase of
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Gd-EOB-DTPA–enhanced MR imaging and highlight the clues for an accurate diagnosis of nontumorous hypointensity.

ARTERIOPORTAL SHUNTS

An arteriportal shunt is a communication between the hepatic artery and the portal vein that results in the redistribution of arterial flow into a focal region of the portal venous flow. It appears as transient hepatic intensity differences (THIDs) on contrast-enhanced MR imaging, that is, focal arterial enhancement that faded on the portal and venous phases. Typically, an arteriportal shunt is not accompanied by signal intensity changes on T₁- or T₂-weighted images. It is generally undetectable on the hepatobiliary phase of Gd-EOB-DTPA–enhanced MR imaging. However, approximately 3.8% to 15% of arteriportal shunts are visualized as a defect on the hepatobiliary phase, and they can mimic small nodular HCCs (Fig. 1).

The typical wedge shape and peripheral location of arteriportal shunts distinguish them from HCCs. Other features, such as a lack of washout on the portal phase, no restriction on diffusion-weighted images, and lower liver-to-lesion contrast on the hepatobiliary phase, could be helpful in diagnosing nontumorous arteriportal shunts.

PORTAL VENOUS OBSTRUCTION

If the portal venous flow is decreased or absent and the hepatic arterial flow is insufficiently compensated, liver parenchyma could be injured in numerous ways, including sinusoidal congestion, hepatocyte depletion, and fibrosis. These histological changes are reflected on MR imaging.

**FIG 1** Arteriportal shunt in a patient with HCC. (A) In the peripheral portion of the right lobe of the liver, an ill-defined, wedge-shaped, arterial-enhancing nodule (arrow) is noted. In the left lobe of the liver, a nodular lesion (arrowheads) with arterial hyperenhancement is also seen. (B) On a hepatobiliary-phase image of Gd-EOB-DTPA–enhanced MR imaging, the lesion in the right lobe (arrow) shows subtle hypointensity. The lesion was confirmed as an arteriportal shunt on serial follow-up images. The lesion in the left lobe (arrowheads) appears hypointense with a well-defined, nodular shape. This lesion was confirmed as HCC by surgery.

**FIG 2** Portal venous obstruction. (A) A portal-phase image depicts thrombi in portal vein branches in segment VIII (arrowheads) with hypointensity in the corresponding hepatic parenchyma (arrows). (B) On a hepatobiliary-phase image, the area shows hypointensity (arrows) with a vertex of the wedge-shaped defects pointing to the hepatic hilum.
as hyperintensity on T$_2$-weighted images and as a defect on hepatobiliary-phase images. The area supplied by the occluded portal vein shows wedge- or geographic-shaped enhancement on the arterial phase, known as THID, and appears as a defect on the hepatobiliary phase (Fig. 2).

Portal venous obstruction has a typical distribution, with a straight border of the involved parenchyma that intersects with the corresponding branch of the hepatic veins, and the vertex of the wedge-shaped defect points to the hepatic hilum. These characteristic findings can provide a clue for distinguishing this lesion from tumor infiltration.

**BILE DUCT OBSTRUCTION**

Sustained biliary obstruction can lead to hepatocellular edema and hepatocyte dysfunction and, consequently, result in diminished Gd-EOB-DTPA uptake and secretion. On MR imaging, segmental hypointensity during the hepatobiliary phase can be seen in the affected liver segment (Fig. 3). The corresponding area appears hyperintense on both T$_1$- and T$_2$-weighted images because of the accumulation of paramagnetic materials (e.g., iron, copper, and manganese ions). Arterial enhancement can be accompanied in the corresponding area of bile duct obstruction.

**STEREOTACTIC BODY RADIATION THERAPY**

Stereotactic body radiation therapy (SBRT) is an emerging treatment option for patients with inoperable HCC. It is a 3-dimensional, conformal radiation therapy with multiple, noncoplanar portals with various directions. Irradiated liver shows hypervascularity with an irregular border on the arterial phase of contrast-enhanced computed tomography or MR imaging. This finding can be explained by a compensatory increase in the hepatic arterial flow secondary to veno-occlusive disease induced by radiation. The area shows hypointensity on the hepatobiliary phase of Gd-EOB-DTPA–enhanced MR imaging caused by hepatic edema and hepatocyte dysfunction (Fig. 4). Ablation zones can also be hypointense on postcontrast and the hepatobiliary phase, although typically this is localized to the area of the lesion and often round with less surrounding hepatocyte dysfunction.

The lack of washout on the portal phase, no diffusion restriction on apparent diffusion coefficient maps, volume loss on follow-up images, and no mass effect on the adjacent vessels or bile ducts are helpful features for differentiating the radiation change after SBRT for residual or recurrent HCC.

**PERITUMORAL HYPOINTENSITY**

An irregular, wedge-shaped or flame-like, hypointense area outside the tumor margin can be seen on the hepatobiliary phase of Gd-EOB-DTPA–enhanced MR imaging (Fig. 5). Peritumoral hypointensity is known to be a predictive factor for microvascular invasion of HCC. This may be explained by the decreased uptake of Gd-EOB-DTPA by hepatocytes as a result of the invasion of minute portal branches by tumor thrombi that result in perfusion changes. Peritumoral hypointensity appears relatively hypointense to surrounding parenchyma but less hypointense than the tumor itself.
Sinusoidal obstruction syndrome (SOS) is a form of hepatic injury that occurs in patients undergoing cytoreductive therapy before hematopoietic stem cell transplantation or chemotherapy with oxaliplatin. In SOS, damage to endothelial cells leads to sinusoidal dilatation, marked sinusoidal fibrosis, necrosis of pericentral hepatocytes, and narrowing of the central vein with fibrosis. On hepatobiliary-phase images, SOS frequently manifests diffuse hypointensity with a characteristic reticular pattern. Occasionally, SOS can be seen as a focal lesion mimicking metastasis, especially in patients undergoing treatment for cancer (Fig. 6).

Focal SOSs have nonspherical and ill-defined margins with heterogeneous internal signal intensity. The lack of
rim enhancement seen on dynamic enhanced images and less diffusion restriction can be clues for SOS.

FOCAL EOSINOPHILIC INFILTRATION

Focal eosinophilic infiltration in the liver is an intermingled focus of coagulation necrosis and inflammatory cell infiltration with a large proportion of eosinophils commonly associated with peripheral eosinophilia. This has commonly been reported in Asian countries. On Gd-EOB-DTPA–enhanced MR images, eosinophilic infiltration shows heterogeneous hypointensity during the hepatobiliary phase and with an irregular, fuzzy margin and a nonspherical shape (Fig. 7).

The nonspherical shape and indistinct margin, together with peripheral eosinophilia, could be helpful in

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**FIG 5** Peritumoral hypointensity in a patient with HCC. (A) An arterial-phase image identifies a hypervascular HCC (arrows) in the right lobe of the liver. (B) During the hepatobiliary phase, irregular, flame-like hypointensity (arrowheads) is seen adjacent to the tumor (arrow). (C) Microscopic evaluation reveals a tumor thrombus (asterisk) within the small vessel adjacent to the tumor (T) (hematoxylin and eosin stain, x40).

**FIG 6** Focal SOS in a patient who underwent chemotherapy using oxaliplatin. (A) A T₂-weighted image depicts a round, hyperintense lesion (arrow) in the peripheral portion of the right lobe of the liver. (B) The lesion appears almost indiscernible on the portal-phase image. (C) A hepatobiliary-phase image depicts the ill-defined margin as well as the heterogeneous texture of the lesion (arrows).
differentiating eosinophilic infiltration from hepatic metastasis. The changes in tumor location seen on follow-up imaging favor the possibility of focal eosinophilic infiltration. Eosinophil infiltration can be diagnosed when a lesion shows a typical imaging appearance in a patient with peripheral eosinophilia; imaging follow-up would be appropriate management. However, if the diagnosis is uncertain, especially in a patient with malignant disease, biopsy could be an option.

**PELIOSIS HEPATIS**

Peliosis hepatitis is pathologically characterized by sinusoidal dilatation and the presence of multiple blood-filled, lacunar spaces of variable size in the liver. MR imaging of peliosis shows various findings on T₁-weighted, T₂-weighted, and dynamic enhanced images, depending on the age and the statue of the blood component filling cavity.
the hepatobiliary phase of Gd-EOB-DTPA–enhanced MR, peliosis hepatis appears hypointense because it is a blood-filled cavity that lacks functioning hepatocytes (Fig. 8).

The differential diagnosis should include primary or metastatic neoplasm, hematological disorders, and hepatic abscess. Although peliosis hepatis is often a diagnosis of exclusion, a clinical history such as drug use (including anabolic steroids, oral contraceptives, and corticosteroids) or chronic wasting disease (e.g., tuberculosis, leprosy, and various malignancies) could be useful, particularly if a patient has long-standing human immunodeficiency virus infection. Ill-defined margins and the paucity of a mass effect could be helpful in the diagnosis of peliosis hepatis.
FOCAL CONFLUENT FIBROSIS

Focal confluent fibrosis is the process of hepatic parenchymal collapse and its replacement with a focal fibrotic mass in patients with liver cirrhosis. It has a wedge-shaped appearance radiating from the porta hepatis and retraction or flattening of the overlying hepatic capsule. It shows progressive volume loss in follow-up images, and it shows hypointensity on hepatobiliary-phase images because of the replacement of hepatocytes by fibrosis (Fig. 9). Its typical location in the anterior segment of the right liver lobe and the medial segment of the left lobe, as well as its wedge shape, may allow the correct diagnosis.

FOCAL FAT DEPOSITION

Focal fat deposition usually occurs in specific areas in the anterior and posterior portions of hepatic segment IV. Focal...
Fat deposition can be differentiated from tumors on the basis of their characteristic location, the absence of a mass effect on vessels, or poorly delineated margins. In general, focal fat deposition appears isointense on Gd-EOB-DTPA–enhanced MR imaging. Some focal fat deposition can be seen as hypointense because of the unexpected hepatocyte dysfunction induced by fat deposition (Fig. 10). Moreover, fat deposition can be seen to have a nodular appearance masquerading as fat-containing hepatic tumors.

**CONCLUSION**

Even though hypointensity on the hepatobiliary phase of Gd-EOB-DTPA–enhanced liver MR imaging is generally considered a sign of a tumor, it occurs in various nontumorous conditions that compromise the delivery and uptake of Gd-EOB-DTPA to the hepatocytes. Recognition of the patterns and causes of nontumorous defects on the hepatobiliary phase of Gd-EOB-DTPA–enhanced MR imaging would therefore help to avoid their false-positive diagnosis as tumors.

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