

Imaging focal nodular hyperplasia

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The primary purpose of this brief review is to discuss the basic features of typical and atypical focal nodular hyperplasia, and its complications. This article demonstrates the full spectrum of findings and features of focal nodular hyperplasia (FNH) on different diagnostic radiological modalities. During the past few years, technical advances in CT and MR imaging have led to a marked increase in detection and characterization of FNH. MR imaging is an ideal modality to work up lesions in relatively young women with suspected FNH because radiation and iodine-based contrast media are not used in these patients. Focal nodular hyperplasia is benign, with no malignant potential and a very small risk of complications (rupture, hemorrhage); thus, it is usually treated conservatively.

Background on focal nodular hyperplasia

Focal nodular hyperplasia is defined as a nodule composed of benign-appearing hepatocytes occurring in a normal or nearly normal liver. It has a reported prevalence of 0.9% and is the second-most common benign liver tumor after hemangioma. It is more

common in young females, with a male-to-female ratio of 1:8.¹ Most FNHs (80 %) are solitary, smaller than 5 cm in diameter, and occur near the liver surface.² They are usually incidental findings at imaging. Distinguishing FNH and other hypervascular liver lesions, such as hepatic adenomas, hepatocellular carcinomas (HCC) and hypervascular metastases is critical, as their management differs considerably.

Most patients are asymptomatic and no treatment is necessary. Some patients may present with abdominal pain or a palpable mass. They typically follow a benign course and on follow-up examination remain stable or the mass decreases in size.³ Contraceptive agents have not been involved in the pathogenesis but they are associated with an increased risk of complications for patients with FNH. In symptomatic females, hemorrhagic foci or infarctions may occur within the FNH; these are aggravated by administration of contraceptive agents. Spontaneous rupture into the peritoneum is a rare complication associated with contraceptive use. FNH may be associated with hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber disease) and congenital absence of the portal vein.⁴

Focal nodular hyperplasia is subdivided into 2 types: classic (80%) and non-classic (20%). In classic FNH, all

3 characteristic features, including abnormal nodular architecture, malformed vessels and cholangiolar proliferation are present. In non-classic FNH, 2 of the 3 characteristic features are present; bile duct proliferation is always present.⁵ The classic and non-classic types contain variable amounts of Kupffer cells.⁶

Diagnostic imaging of FNH

On imaging studies, morphology, vascularity, appearance and surrounding liver architecture help to distinguish between typical and atypical lesions. They have no clinical significance, but their recognition is necessary to avoid surgery, biopsy and follow-up imaging.⁷⁻⁹

Ultrasound

On sonography, the lesion usually appears homogenous, with variable echogenicity, mostly isoechoic, however may be hypo/ hyperechoic. (Figure 1). The center of the lesion shows a scar as an echogenic and linear structure. Lesion shows a characteristic Doppler vascular pattern, including hypervascularity, centrifugal arterial flow radiating peripherally from a central vessel¹⁰ as shown in (Figure 2). On real-time contrast-enhanced ultrasound, it shows a typical spoke-wheel pattern followed by complete enhancement in the arterial phase and remains hyper/iso vascular in the portal and late phases. In general,

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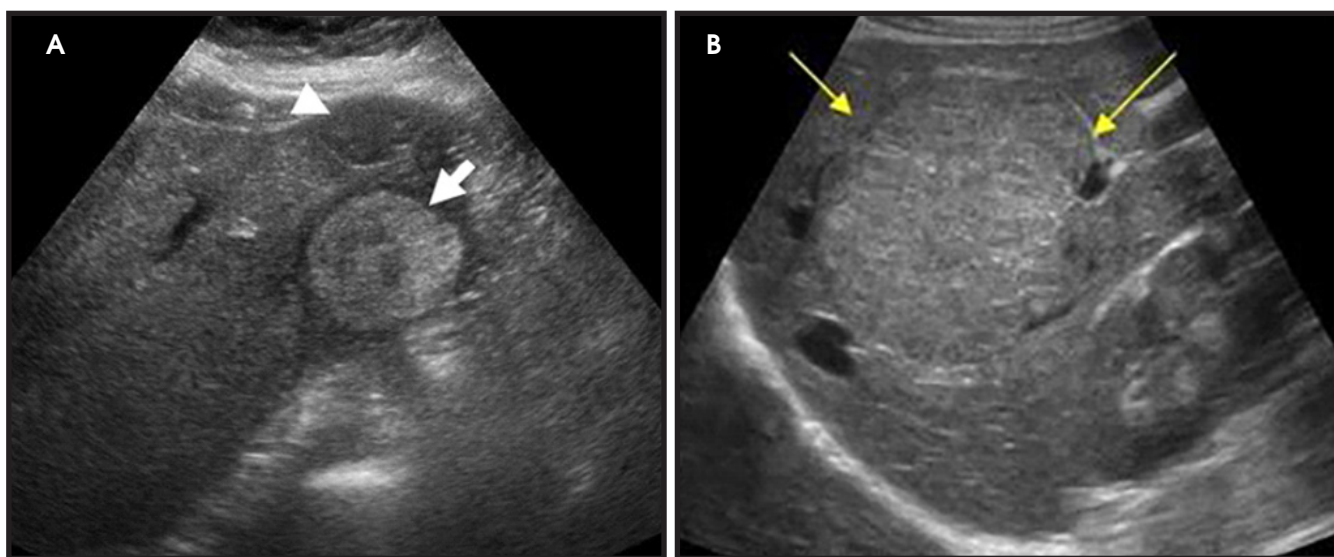


FIGURE 1. (A) A well-defined hyperechoic lesion in right lobe of liver (arrow), and a slightly hypoechoic lesion seen adjacent to it (arrowhead). (B) A large, well-defined iso- to slightly hyperechoic lesion in right lobe of liver with smooth margins. No obvious central scar is seen on ultrasonography (US).

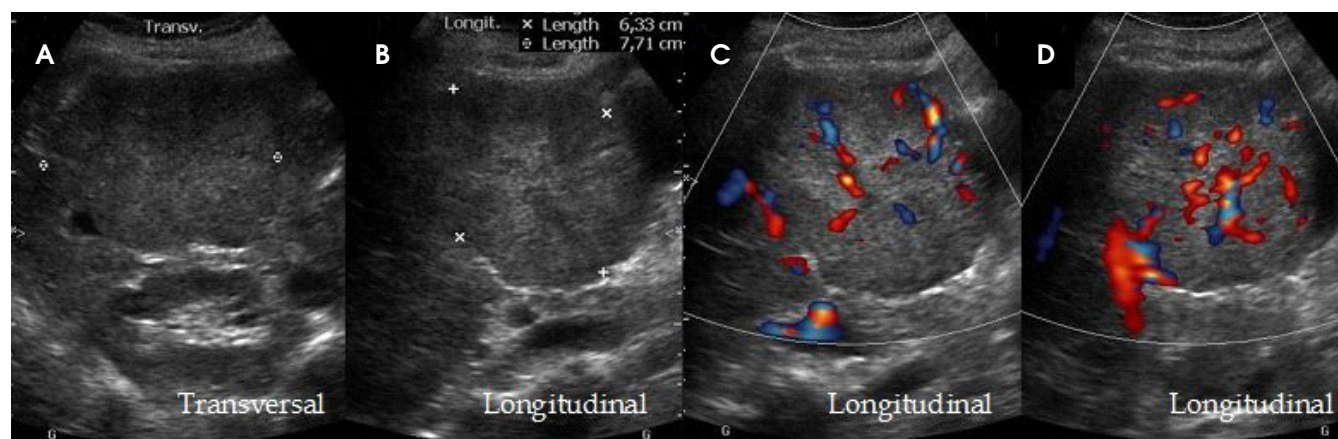


FIGURE 2. US showing a large iso- to hypoechoic lesion in right lobe showing central echogenic scar on grayscale images. On Doppler US, characteristic centrifugal flow pattern is seen from center of the lesion to the periphery.

this typical pattern has been observed in 74% to 100% of cases.¹¹

Computed tomography

A helical CT scan, 4-phase study should be mandatory for the definitive diagnosis of FNH. This evaluation should include unenhanced, hepatic arterial, portal venous and delayed-phase examinations. At CT, typical FNH may have lobulated contours.⁷⁻⁹ In the unenhanced phase, it is either hypoattenuating or isoattenuating to the surrounding liver. In the arterial phase, due to the homogeneous intense enhancement of the entire lesion, it becomes hyperattenuating except for the central scar. In

the portal and later phases, it becomes more isoattenuating; however, the central scar may show some enhancement (Figure 3).

Magnetic resonance imaging

Compared to CT and US, MRI has higher sensitivity (70%) and specificity (98%) for detecting FNH.⁹ MRI is also more accurate in detecting the central scar than CT, with a sensitivity of 78% and 60%, respectively. The reason for the higher sensitivity and specificity of MRI may be because it not only provides information regarding the soft-tissue characteristics, but also the vascularity of the lesions.

They typically appear homogeneous on MR imaging, with iso- to hypointense signal on T1-weighted images and slightly hyper- to isointense on T2-weighted images. A central hyperintense scar is seen in only 9% to 50% of cases on T2-weighted images.^{12,13} On contrast-enhanced MRI, it shows intense homogeneous enhancement in the arterial phase and enhancement of the central scar in the later phases (Figure 4). In contrast, hepatocellular adenomas show less intense enhancement and lack a central scar.

Specific super-paramagnetic iron oxide-based (eg, ferucarbotran [Resovist; Schering, Berlin, Germany]) and

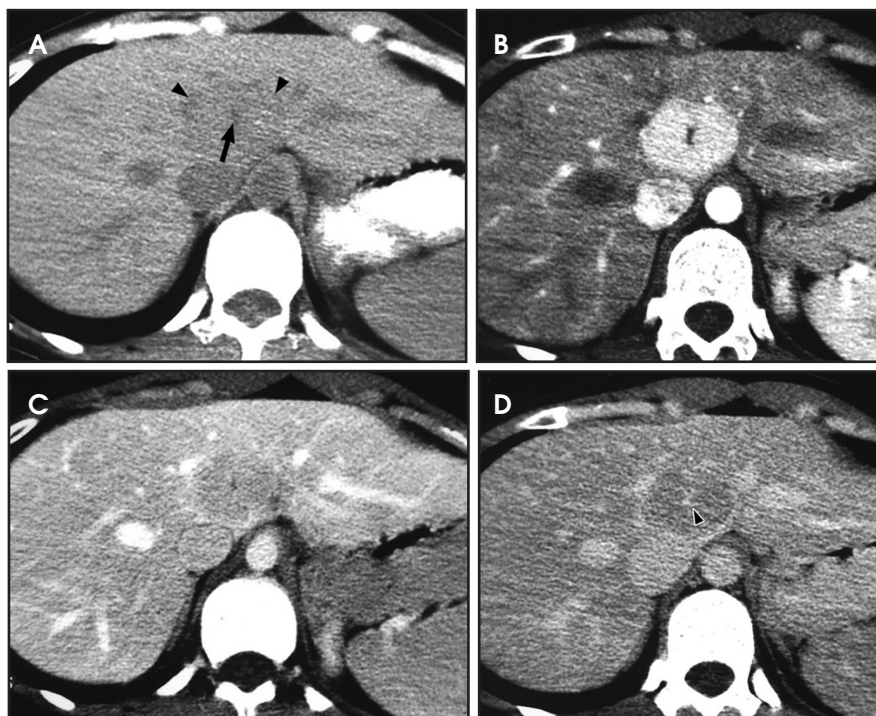


FIGURE 3. Typical CT findings of FNH in 30-year-old woman. (A) Unenhanced CT scan shows lesion in left lobe (arrowheads), which is slightly hypodense to remainder of liver. Note more hypodense central scar (arrow). (B) Arterial phase CECT scan shows strong homogeneous enhancement of lesion, caused by arterial vascular supply. Note focal central area of low attenuation, representing central scar. (C) CECT scan during the portal venous phase shows lesion being slightly hypoattenuating compared with surrounding liver tissue because of rapid contrast material washout. (D) Delayed-phase CECT scan shows persistent enhancement of central scar (arrowhead).

manganese-based (ie, mangafodipirtri-sodium [Tesla-scan; Nycomed Amer-sham, Oslo, Norway]) contrast media are targeted at the Kupffer cells and hepatocytes, respectively.¹⁴⁻¹⁷ These help to demonstrate the hepatocellular origin of the lesions. The Kupffer cells show uptake of ferucarbotran and lower the signal intensity of the lesions as well as the surrounding liver on T2- and T2*-weighted images.

A central scar is present at imaging in most patients with FNH.⁹ The size and amount of scar tissue may vary. The central scar is typically high in signal intensity on T2-weighted images and low on T1-weighted images. It shows visible enhancement on delayed contrast-enhanced images. High signal intensity of the central scar may be caused by the inflammatory reaction around the ductular proliferation as well as the vessels within the septa and central scar. The central scar is not specific for FNH and can be seen in different lesions of the liver, such as giant hemangiomas and hepatocellular carcinomas.

Various atypical features of FNH on MRI have been described, including:¹⁸

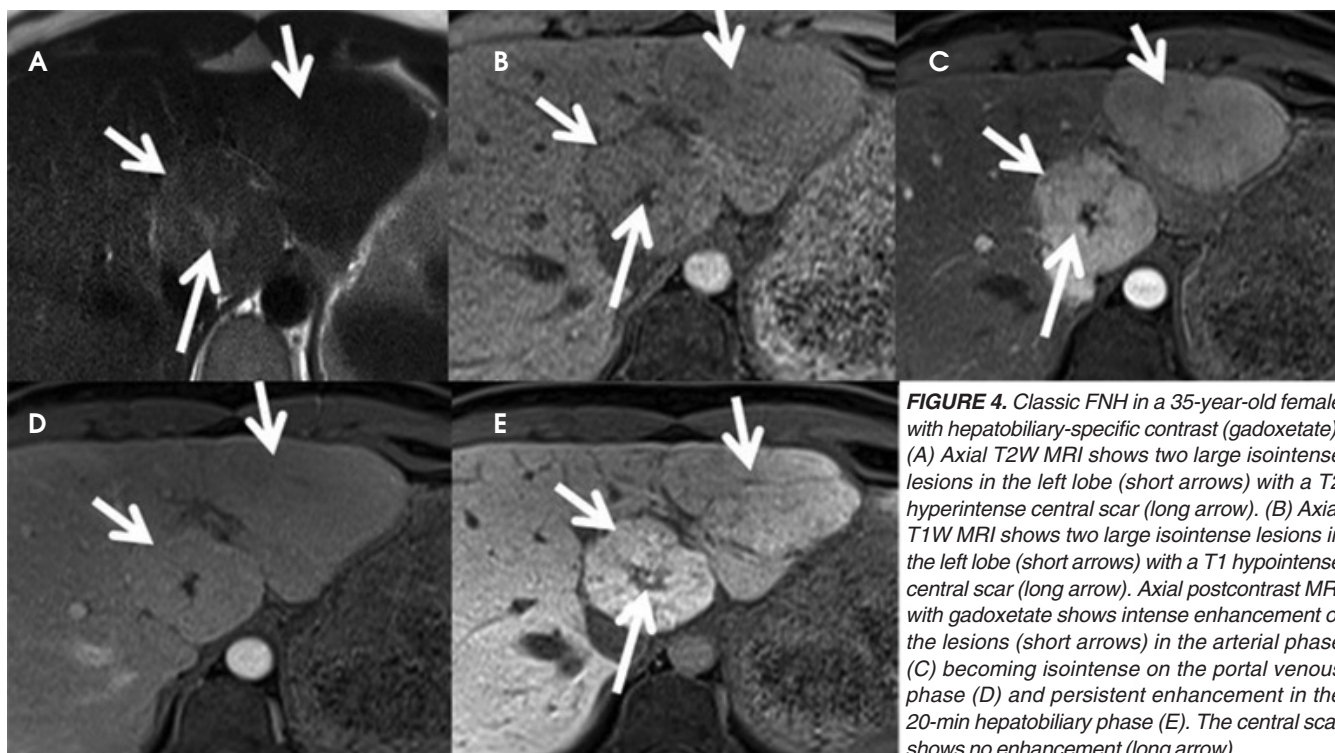


FIGURE 4. Classic FNH in a 35-year-old female with hepatobiliary-specific contrast (gadoxetate). (A) Axial T2W MRI shows two large isointense lesions in the left lobe (short arrows) with a T2 hyperintense central scar (long arrow). (B) Axial T1W MRI shows two large isointense lesions in the left lobe (short arrows) with a T1 hypointense central scar (long arrow). (C) Axial postcontrast MRI with gadoxetate shows intense enhancement of the lesions (short arrows) in the arterial phase (C) becoming isointense on the portal venous phase (D) and persistent enhancement in the 20-min hepatobiliary phase (E). The central scar shows no enhancement (long arrow).

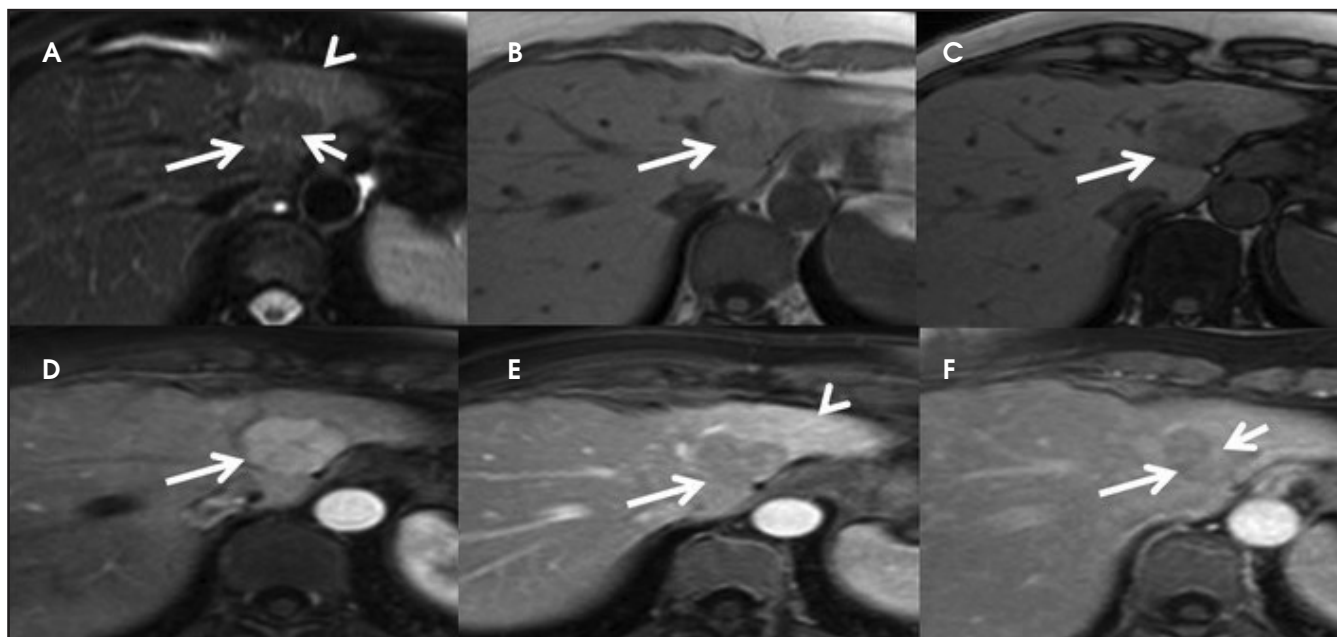


FIGURE 5. Biopsy-proven FNH with intralesional steatosis in a 46-year-old female. (A) Axial T2W MRI shows an isointense lesion (long arrow) in the left lobe with a faint hyperintense central scar (short arrow). Axial T1 in-phase (B) and out-of-phase (C) MRIs show a drop in signal in the out-of-phase images representing intralesional lipid (arrow). Axial postcontrast MRI shows an enhancing lesion (arrow) in the arterial phase (D) becoming iso- to mildly hypointense in the portal venous (E) and delayed phases (F) with delayed enhancement of the central scar (arrow). Arrowheads denote transient edema/enhancement.

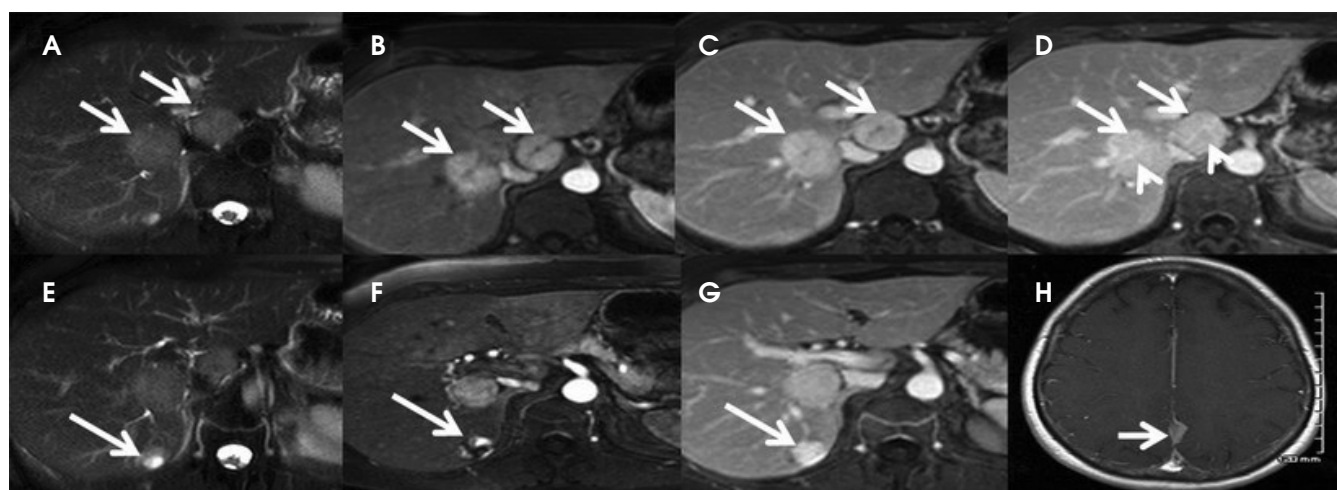


FIGURE 6. Multiple FNH syndrome in a 50-year-old female. (A) Axial T2W MRI shows two iso- to mildly hyperintense focal lesions (arrows) in segments 8 and 4 of the liver. Axial post-contrast MRI shows intense enhancement of the lesions (arrow) in the arterial phase (B) and persistent enhancement (arrow) in the portal venous (C) and delayed phases (D) with delayed enhancement of the central scar (arrowheads). (E) Axial T2W MRI in the same patient shows a small T2 hyperintense lesion in segment 7 (arrow). Axial post-contrast MRI shows peripheral nodular enhancement (arrow) in the arterial phase (F) with progressive centripetal filling (arrow) in delayed phase (G) in keeping with haemangioma. (H) Axial post-contrast MRI brain shows a small enhancing extra-axial lesion in the falx cerebri representing meningioma.

Appearing heterogeneous on both T1- and T2-weighted sequences due to the presence of small hemorrhagic foci, sinusoidal dilatation or fatty infiltration. High protein concentrations, blood degradation products or copper accumulation may result in T1 hyperintensity.

An extremely small or undetectable scar on CT (16% to 40%) and MRI

(22%). The central scar may mimic a collagenous scar seen in fibrolamellar carcinoma, hepatic adenoma, HCC or cholangiocarcinoma due to obliterative vascular hyperplasia of the central scar.

The presence of a pseudo-capsule due to compressed adjacent hepatic parenchyma, and the presence of dilated vessels and sinusoids around the lesion.

FNH rarely shows intra-lesional steatosis (Figure 5).

Telangiectatic FNH, an uncommon entity but the most common among non-classic FNHs. These lesions often show heterogeneity on pre- and post-contrast CT and MRI, and they are strongly hyperintense on T1- and T2-weighted images, often with an

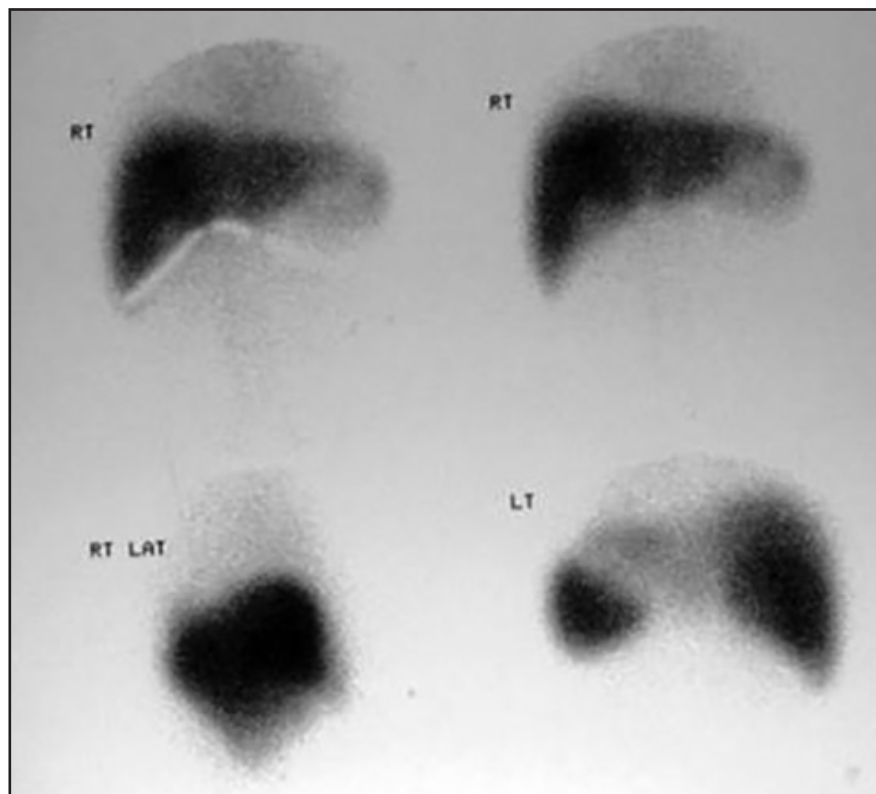


FIGURE 7. Technetium-99m sulfur colloid scans showing complete filling of the mass depicted on sonograms and CT scans.

absent central scar. Intense arterial enhancement with persistent enhancement during the hepatic venous and equilibrium phases are seen.

Multiple lesions, which are found in 20% of cases and are mostly atypical. Multiple FNH syndrome is defined as consisting of two or more FNHs in combination with hepatic liver hemangioma or vascular malformations or intracranial tumors (Figure 6).

Nuclear medicine

Radionuclide scans best demonstrate Kupffer cell activity. They historically have used technetium-99m (^{99m}Tc) sulfur colloid; normal or increased uptake of ^{99m}Tc sulfur colloid is seen in 60% to 70% of patients (Figure 7). In 30% to 40% of patients, Kupffer cells are not sufficiently concentrated and it may appear photon deficient.¹⁹

FNH Management

Focal nodular hyperplasia with typical imaging features is usually managed conservatively and does not require sur-

gical intervention. Symptomatic lesions, likely from compression of adjacent structures or hepatic capsular stretching, may warrant surgical excision. FNH with atypical imaging features requires further evaluation with additional imaging, percutaneous guided biopsy and follow-up. Suspicious lesions could be followed up or surgically excised.²⁰

Conclusion

This article demonstrates the full spectrum of findings and features of focal nodular hyperplasia in different diagnostic imaging modalities. FNH usually presents with classical imaging features, however, atypical features are important for radiologists to recognize and understand. MR imaging is an ideal modality for work-up of atypical lesions.

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