There is a known female preponderance, and compared with men, women tend to develop larger FNH lesions that present earlier (95). Because of these epidemiologic characteristics, it has been believed that there may be a causative role for sex hormones in FNH development; however, over time, this has been disproven because of lack of correlation between OCP use and FNH growth or prevalence and lack of evidence of change in FNH during pregnancy (98,99). Importantly, unlike adenomas, FNH do not need to be treated differently in men as compared to women and do not require monitoring during pregnancy.

Imaging most often allows the definitive diagnosis of FNH vs adenoma, which is important because management differs between the 2 lesions. An MRI with a hepatobiliary contrast agent, such as gadoxetic acid, is the preferred imaging modality of choice because it can correctly classify FNH from adenoma with an accuracy of over 90% (100–102). MRI has a specificity of almost 100% for diagnosis of an FNH (103). If the patient has a contraindication to MRI, then multiphase CT can be performed. CEUS can be used for diagnosis of FNH, with increased diagnostic accuracy in lesions measuring <3 cm in size (104–107).

On postcontrast CT or MRI, FNH usually appears as a well-circumscribed homogeneously arterial hyperenhancing mass, which becomes isoenhancing on portal venous and delayed phase of imaging (Figure 6) (108). Classically, there is a central scar, which is usually hypodense/hypointense on noncontrast imaging CT/MRI, respectively, demonstrates delayed enhancement on portal venous and delayed phase of imaging, and is isointense to hyperintense on T2-weighted imaging.

Because FNH contains hepatocyte-specific membrane transport proteins, they almost always show hyperintense signal on the 20-minute HBP of imaging, rendering the diagnosis of FNH with nearly 100% confidence (108,109) (Figure 6). In fact, studies show that only 2% of FNH are hypointense on 20-minute HBP of imaging (110).

Of note, with increasing use of biopsy for hepatic adenomas and newer stains allowing improved subtype classification, there is emerging evidence that 11% of inflammatory and 59% of β-catenin mutated adenomas demonstrate OETP1B3 receptor expression and therefore can demonstrate hyperintense signal on HBP of imaging. Therefore, any lesion that has atypical imaging appearance for FNH on dynamic imaging that demonstrates HBP hyperintense signal should be closely followed (111).

In the rare case that a diagnosis of FNH cannot be made by imaging, then a biopsy may be considered after discussion at multidisciplinary tumor board. Biopsy can sometimes be difficult to interpret, with some case series reporting diagnosis as low as 58%, although the interpretation can be aided with the addition of immunohistochemistry (112,113).

Once the diagnosis of FNH is confidently made, a conservative approach with no further follow-up is recommended. Given the little to no change over time in most cases, there is no benefit to continued imaging, and those lesions that do grow do not cause life-threatening complications (114). Current evidence suggests no indication that patients should avoid or discontinue OCPs or hormonal therapy, and that FNH does not need to be followed during pregnancy (115,116).

In the rare case of symptoms such as pain, surgical resection may be considered, but most FNH lesions are incidental to symptoms rather than the cause of symptoms and patients should be educated that their symptoms may not improve after surgery (117). Even in the setting of growth of an FNH, there is an extremely slim chance of malignancy, and therefore, resection is not recommended (117). Because FNH is usually supplied by a single artery, TAE seems like a logical minimally invasive method for treatment in cases that require treatment. There remains much debate, however, as to which embolic agent is best used for TAE of FNH. A few small case series suggest that TAE with bleomycin for symptomatic FNH can result in decrease in tumor size by 50%, but bland embolization is often used (80,118,119).

Key concepts

19. Advanced imaging techniques (e.g., contrast-enhanced multiphase MRI with hepatobiliary-specific contrast) can accurately diagnose FNH in most cases, and biopsy is not routinely needed.
20. In a patient with an FNH confirmed on imaging, no further follow-up is required.
21. If the diagnosis of FNH is confirmed, then even in the case of growth, resection is not required. If resection is being considered because of symptoms, then patients must be counseled that their symptoms may not improve after surgery as FNH rarely causes symptoms.
22. If FNH lesions are symptomatic and surgery is not an option because of comorbidities or anatomic considerations, then TAE with or without bleomycin may be considered to decrease size.
23. Men with FNH do not need to have any different evaluation, monitoring, or treatment compared with women.

Recommendations

9. We suggest evaluating patients with FLLs that are suspicious for FNH using multiphase MRI with hepatobiliary-specific contrast agents to distinguish FNH from HCA (conditional recommendation, low quality of evidence).
10. We do not suggest routinely discontinuing OCPs in patients diagnosed with FNH (conditional recommendation, very low quality of evidence).

Hemangioma

Hemangiomas are the most common benign noncystic liver lesions, occurring in up to 20% of the population, with a reported preponderance in women at a 4:1 ratio (120). They are benign mesenchymal vascular lesions consisting of clusters of blood-filled cavities lined by endothelial cells, ranging in size from a few millimeters to greater than 20 cm (121). Hemangiomas are believed to arise from a congenital abnormality in vasculogenesis, growing slowly from birth. Increase in size of hemangiomas can occur and is favored to be due to progressive ectasia of the vasculature and not related to hypertrophy of the lesion (122). Hemangiomas are usually asymptomatic lesions, which are incidentally detected on imaging studies, although larger lesions can result in pain, poor appetite, or abdominal fullness (122). Rarely, hemangiomas can result in a consumptive coagulopathy known as Kasabach–Merritt syndrome, which can present as thrombocytopenia, systemic bleeding, and disseminated intravascular coagulation, usually seen in giant cavernous hemangiomas (123,124).

There has been no clear causative link between hemangiomas and female sex hormones, and thus, it is not recommended to avoid OCP or pregnancy in patients with hemangiomas