Focal Nodular Hyperplasia and Hepatic Adenoma

Evaluation and Management

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KEYWORDS

• Focal nodular hyperplasia • Hepatic adenoma • Hepatocellular adenoma
• Liver lesion

KEY POINTS

- Focal nodular hyperplasia (FNH) is a common benign liver lesion that rarely requires intervention.
- Hepatocellular adenomas (HCAs) are benign lesions commonly associated with obesity and oral contraceptive use in women.
- HCAs may be at risk for malignant transformation to hepatocellular carcinoma; risk of rupture is greatest in lesions over 5 cm in size.
- Molecular subtyping may be helpful to characterize and guide treatment decisions in HCA lesions.

FOCAL NODULAR HYPERPLASIA

Focal nodular hyperplasia (FNH) is the second most common benign hepatic lesion seen with a previously reported prevalence on ultrasound of 0.03%.[1] FNH lesions are typically discovered incidentally, and 74% of cases are asymptomatic. Those who present with symptoms may have mild epigastric abdominal pain or discomfort.[2] FNH may be seen in conjunction with elevations in alkaline phosphatase and/or gamma-glutamyl transferase (GGT) levels, or no abnormalities in liver biochemistries.[3] These lesions are most commonly seen in young and middle-aged women (ages 20–50 years) with a prevalence ratio of 8 women to every man diagnosed.[4–7] FNH lesions are generally solitary but may be associated with hepatic hemangiomas in about 20% of cases.[8]

Focal nodular hyperplasia are characterized by densely packed functioning hepatocytes fed by an enlarged artery with a central scar of fibrous tissue and malformed bile ductules. These are thought to reflect a hyperplastic response to a congenital or

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acquired vascular abnormality. The background liver histology is otherwise normal.[9] It has been hypothesized there is a genetic component to their formation with noted activation of genes seen in vascular remodeling.[9] When FNH lesions are sampled, they are noted to have a characteristic map-like pattern of glutamine synthetase staining.[10,11]

Occasionally, FNH lesions are seen in an atypical form such as without a central scar (in which lesions are usually <3 cm in size), or associated with significant steatosis, intralesional fat; these constitute about 85% of atypical FNH lesions.[12,13] Multiple FNH lesions may be seen in patients with vascular disease such as Budd-Chiari syndrome or obliterative portal venopathy. In rare cases, FNH has been reported to cause Budd-Chiari.[12]

Because of the high prevalence of FNH lesions in women, it was initially thought there was a link between FNH and female hormones. Several studies have looked into both exogenous hormone administration and pregnancy. Neither oral contraceptive pills (OCPs) nor pregnancy were associated with FNH prevalence nor FNH progression.[14,15] As such, it is felt that FNH lesions are not hormonally sensitive.

Recently there have been studies of the possible association of FNH with prior chemotherapy exposure. Benign regenerative lesions have been noted in children with a history of malignancy receiving high-dose chemotherapy or a hematopoietic stem cell transplant. This is thought to be potentially a late manifestation of prior injury from chemotherapy or radiation therapy.[16,17] In adults, a case series identified 14 patients previously treated with oxaliplatin who developed new FNH lesions. The pathogenesis of this remains unknown.[18]

Diagnosis of Focal Nodular Hyperplasia

FNH lesions seen on ultrasound imaging appear slightly hypoechoic or isoechoic to the background liver tissue (**Table 1**). The surrounding liver tissue may often be seen as steatotic.[12,19,20] With Doppler ultrasound, there may be the presence of multiple well-defined arterial vessels originating from the center of the lesion traveling to the periphery and the presence of feeding vessels from the hepatic arterial tree.[12,21]

Table 1
Imaging characteristics of focal nodular hyperplasia lesions

	Ultrasound	CEUS	CT	MRI
FNH	Homogenous mostly isoechoic	Spoke wheel centrifugal pattern enhancement	Unenhanced phase: hypointense/ isointense with surrounding liver	Iso/hypointense in T1 weighted
	On Doppler: centrifugal arterial flow, radiating central vessel	Enhancement in arterial phase	Homogenous enhancement of lesion on arterial phase, hyperintense except central scar	Hyper/isointense Central hyperintense scar on T2 weighted
		Remaining hyper/isointense in portal and late phases	Isointense on portal and late phases	Homogenous -enhancement arterial phase
				Enhancement of lesion in later phase with hepatobiliary gadolinium

Contrast-enhanced ultrasound (CEUS) may be helpful in diagnosing small FNH lesions (Fig. 1). The use of intravenous microbubbles in the early arterial phase gives an enhancement in a centrifugal appearance in FNH lesions that closely corresponds with lesion size.[12,22] CEUS has a reported 93% sensitivity and 100% specificity in diagnosing FNH lesions smaller than 35 mm in size. MRI is less accurate in diagnosing small FNH lesions, and as such, it is has been recommended that CEUS, where available, be used to diagnose FNH lesions less than 3 cm.[23,24]

Cross-sectional imaging including computed tomography (CT) and MRI with the addition of extracellular contrast may be used to noninvasively diagnose FNH. Five imaging criteria may be used to guide diagnosis:

1. Signal intensity of the lesion is similar to surrounding liver tissue
2. Homogeneity of the lesion.
3. Strong enhancement in the arterial phase without washout
4. Presence of a central scar
5. Lesion may be lobulated but lacks a capsule

In the absence of abnormal liver biochemistries, chronic liver disease, and extrahepatic malignancy, this is 98% specific and 70% sensitive to diagnose FNH.[2,12,24]

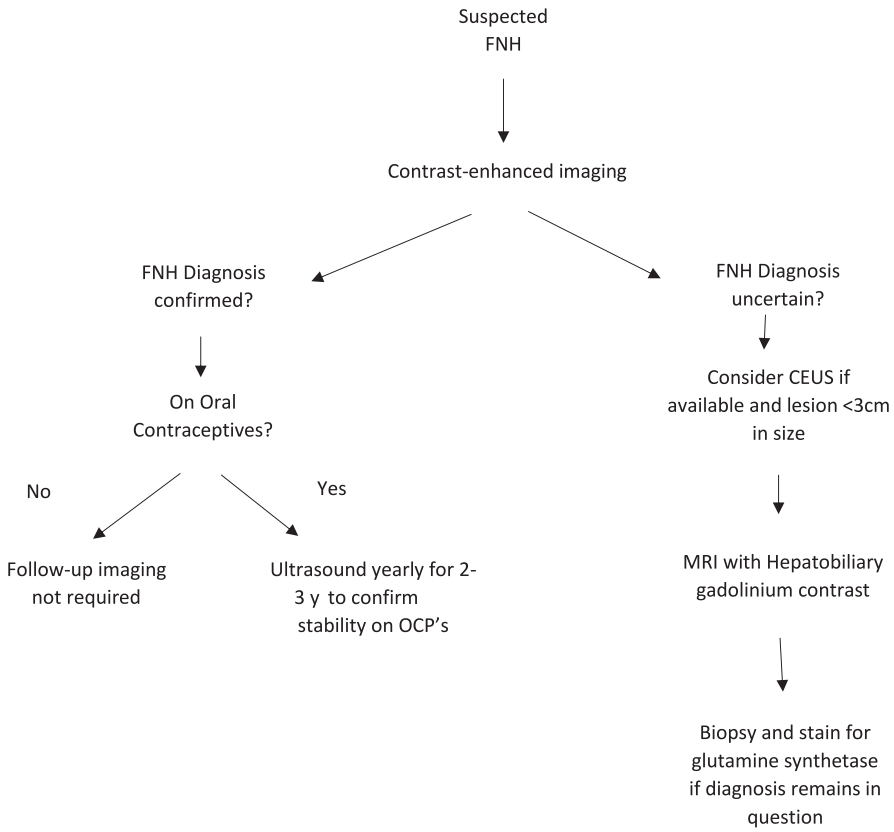

Fig. 1. Diagnosis and management of FNH.

MRI with extracellular contrast utilizes gadolinium-based chelate agents that shorten the longitudinal relaxation time (T1) and have similar pharmacokinetics of iodinated contrast for CT that rely on differential blood flow between liver and lesion for lesion detection.[25] FNH lesions are best seen on MRI in the arterial phase in which the lesion is noted to have intense enhancement given its predominant arterial blood supply. The FNH lesion appears consistent with background liver in post-contrast imaging, and its characteristic central scar is T2 hyperintense. For lesions smaller than 3 cm, 40% of FNH lesions are inconclusive on standard MRI.[26] MRI is felt to be less accurate in diagnosing small FNH lesions because of the lack of central stellate scarring seen.[23] On standard extracellular contrast MRI, hepatocellular adenoma (HCA) and FNH may both have overlapping imaging features with arterial enhancement.[27] As management of these lesions is distinct, further differentiation of these lesions is crucial. The addition of specific MR hepatobiliary gadolinium contrast agent increases the ability to differentiate these lesions. Hepatobiliary gadolinium agents gadoxetate disodium and gadobenate dimeglumine have selective uptake in functioning hepatocytes and are secreted in bile in the hepatobiliary phase. Gadoxetate disodium is most commonly used in clinical practice, as it has a higher percentage of excretion of the agent into the biliary system and a faster time for accumulation of contrast agent into hepatocytes over gadobenate dimeglumine.[26] FNH lesions are thought to have abnormal drainage from bile calculi because of ductular reaction along the septa, while an HCA lesion has few to no bile ducts, resulting in increased accumulation of hepatobiliary gadolinium contrast agent in FNH lesions during hepatobiliary phase of MRI.[26,28] With the addition of hepatobiliary gadolinium, over 90% of FNH lesions are noted to be either hyperintense or isointense on the hepatobiliary phase, while solid components of most HCA lesions appear hypointense.[29,30] In cases where FNH cannot be distinguished from HCA, the lesion should be biopsied and stained for glutamine synthetase to improve diagnostic certainty.[31]

Management of Focal Nodular Hyperplasia

Approximately 70% of cases of FNH are asymptomatic and do not require intervention. There is no malignant transformation potential. Several case reports have been published highlighting the spontaneous rupture of larger FNH lesions.[32,33] However, most FNH lesions followed over time were either stable or found to have regressed in size.[34]

Symptoms can occur in approximately 20% of patients with FNH thought caused by the increased size of the mass causing liver capsular stretch. Surgical resection may be a consideration for symptomatic individuals unresponsive to analgesia.[2,35–37] The most common indications for resection were symptoms or diagnostic uncertainty and suspicion for cancer.[38] Surgery for FNH lesions was more frequently performed in men, for smaller lesions and for atypical FNH lesions.[5] For minimally invasive treatment approaches for FNH, there are limited data, but studies are predominantly focused on transarterial embolization.[39] This is predominantly considered for individuals who are not surgical candidates or if the resection site is difficult.[40] Overall, there is poor correlation between FNH lesions and symptoms, and even if a patient is symptomatic, treatment is rarely recommended.[24]

For those individuals with a firm diagnosis of FNH and who are not on OCPs, ongoing follow-up imaging is not recommended. There is no indication to discontinue OCPs or discourage pregnancy in individuals with FNH. Ongoing follow-up for FNH lesions is not necessary in pregnancy, but it has been recommended for those who continue OCPs to have an ultrasound annually for 2 to 3 years to ensure stability.[4,24]

Focal nodular hyperplasia features

- 8:1 young female predominance
- Typically, not clinically significant
- Common imaging characteristics include a homogenous, hypervascular lesion with a central scar
- Map-like pattern of glutamine synthetase staining on biopsy
- Not hormonally sensitive
- Ongoing imaging surveillance is not recommended in the absence of OCP use with the firm diagnosis FNH

HEPATOCELLULAR ADENOMA

HCA is seen 10 times less frequently than FNH, with a prevalence of 0.001% to 0.004% in the general population. On ultrasound studies, the prevalence has been noted to be 7 cases per 100,000 populuation.[1,24,41] HCA has a female-to-male ratio 10:1, with the most common presentation in women of child-bearing age in their third and fourth decade.[24,41] HCAs are most often a solitary lesion in the right hepatic lobe found as an incidental finding in 12% to 25% of cases. In cases that present with symptoms, they may range from chronic right upper quadrant pain/epigastric pain to acute pain associated with anemia or even circulatory collapse in settings of acute HCA rupture or hemorrhage.[41]

Historically, HCAs were identified in women of childbearing age with approximately 1 case per 100,000 population without the use of OCPs. With the increasing utilization of early generation OCPs in the 1960s and 1970s, there was an increase in prevalence to 3 to 4 cases per 100,000 population in women who used OCPs.[42] The risks of HCAs are increased 30- to 40-fold for those on OCPs.[24] This hormonal association is seen also in the setting of HCA enlargement during pregnancy.[41] It has been noted that lesion size can regress with the removal of exogenous hormones/OCPs.[43] Additionally, there is an increased association of HCA lesions with androgenic steroid use. The risk of androgen-associated lesions correlates with cumulative androgen dosing, and those who are suspected for abusing androgenic steroids should be monitored for liver risks.[44] In cases of endogenously increased androgens or sex hormone imbalances such as polycystic ovarian syndrome (PCOS) or Klinefelter syndrome, HCA prevalence is also increased.[24]

Obesity, along with the associated risk factors of the metabolic syndrome, has been found to be linked with the development and progression of HCAs.[45,46] Increased levels of adipokines circulating in obesity trigger the release of interleukin (IL)-6 by adiopocytes. IL-6 has been previously identified as a risk factor for malignant transformation[47]

Glycogen storage disease (GSD) is linked with an increased prevalence of HCAs and greater risk of malignant transformation to hepatocellular carcinoma (HCC), particularly with GSD types Ia, III, and IV. The frequency of reported HCA in this population is 16% to 74%, with HCA typically occurring in the second and third decade of life with a male predominance. Hepatomegaly in these cases is near universal, and the presence of bilobar HCA lesions is seen more commonly than in the general population. There is a 50% risk of developing at least 1 HCA lesion by age 25 in GSD with an associated increased risk of HCC. At least half of GSD-associated HCAs tend to be of the inflammatory subtype. Management with frequent ultrasound surveillance and early consideration of surgical resection is recommended in this population.[41,48]

The complications arising from the presence of HCA lesions are risk of hemorrhage of the lesion and malignant transformation to HCC. The risk of hemorrhage occurs in

11% to 29% of cases, but it typically occurs in lesions larger than 5 cm.[41] Over 50% of histologically examined HCA lesions were noted to have bleeding, but the cases of symptomatic bleeding were again associated with lesion size greater than 5 cm.[49,50] The risk of malignant transformation of HCA is 5% to 10% overall and also increases with lesion size.[47] Thus with increased risk of these complications, resection is recommended for lesions over 5 cm in size.

Molecular Subtypes of Hepatocellular Adenoma

HCA is a benign neoplasm of hepatocyte proliferation in response to a hormonal or metabolic abnormality.[41] These lesions may be further classified by molecular subtypes to describe disease risk factors and associated complications.

Hepatocyte nuclear factor 1α

Hepatocyte nuclear factor 1α (HNF1α) inactivating mutation account for 34% to 46% of all HCAs.[49,51] Most of these lesions are highly steatotic because of the biallelic inactivating mutations of the HNF1α gene. This abnormal HNF1α gene silences expression of liver fatty acid binding protein (LAFBP), which impairs fatty acid movement in the hepatocytes leading to intracellular fat deposition.[10,51,52] Ninety percent of HCA lesions with HNF1α inactivating mutation are found in women who use OCPs. Hormones are felt to act as endogenous genotoxic agents that may partly be responsible for somatic mutations in HNF1α- mutated HCA.[51,53] Familial hepatic adenomatosis with multiple lesions and maturity-onset diabetes mellitus of the young (MODY) have been associated with this molecular subtype.[54] Malignant transformation of these lesions is rare.[24,52]

Inflammatory

The inflammatory subtype of HCA lesions is seen in approximately 18% to 44% of cases and is typically asymptomatic.[49,51] This subtype arises from the sustained activation of the Janus Kinase (JAK) signal transducer and activation transcription (STAT) pathway, resulting in hepatocellular proliferation.[49,51] On histopathology, the inflammatory subtype is noted to have inflammatory infiltrates, sinusoidal dilatation, and dystrophic vessels with immunostaining noting the expression of serum amyloid protein (SAA) and C-reactive protein (CRP).[52,53] These lesions are prone to bleeding because of their dilated sinusoids and abnormal arteries. They tend to be more subcapsular in location and larger in size..[52] Inflammatory HCAs are associated with a high body mass index (BMI) and excessive alcohol consumption.[10] They may be associated with chronic anemia, elevated CRP, or alkaline phosphatase/GGT elevations.[49]

Telangiectatic hepatocellular adenoma

Telangiectatic HCA (formerly known as telangiectatic FNH) has been reclassified under the inflammatory hepatocellular adenoma subtype based on molecular similarities. These lesions have been associated with OCP/hormonal therapy, and patients are more likely to be overweight, with 15%–40% of cases presenting with another benign liver lesion.[55,56] Telangiectatic HCAs are also more likely to be symptomatic because of increased risks of intralesional hemorrhage and necrosis.[56,57]

β-catenin

The sustained activation of β-catenin gene leads to uncontrolled hepatocyte formation and constitutes a molecular subtype classification of HCAs. β-catenin activation is noted with cytologic abnormalities of increased nuclear cytoplasmic ratio, nuclear atypia and an acinar pattern of staining.[52] This subtype of HCA is more frequently found in men, associated with GSD, male hormone administration, and familial adenomatous

polyposis. β-catenin is the most frequently activated oncogene in HCCs, and this subtype has a greater likelihood of malignant transformation to HCC.[10,51,53] Recently, β-catenin associated HCAs have been further divided into 2 subtypes: mutations of cadherin-associated protein β1 (CTNNB1) exon 3 activating β-catenin and mutations of CTNNB1 exon 7 or 8, which mildly activate the Wnt/β-catenin pathway. Clinically, these 2 subtypes differ in their risk of HCC malignant transformation. CTNNB1 mutations exon 7 and 8 account for approximately 3% of HCAs, are found at a young age, and are not associated with an increased risk of malignant transformation. Conversely, CTNNB1 mutations exon 3 are approximately 7% of lesions and have the highest risk of malignant transformation because of the full β-catenin pathway activation. These are associated with androgens and vascular liver disease and have a 10% malignant/premalignant risk.[49]

Mixed inflammatory and β-catenin

Upon review of HCA lesions, 2 additional subtypes have been noted to share both the inflammatory and either CTNNB1 exon 3 or CTNNB1 exon 7,8 β-catenin phenotypes.[49] Although β-catenin and inflammatory pathways may be found in mixed HCA lesions, β-catenin and the biallelic inactivation of HNF1α pathways are mutually exclusive.[53] In cases of mixed and multiple lesions, β-catenin and exon 3 were associated with the largest nodule.[49]

Sonic hedgehog

Activation of the sonic hedgehog pathway leads to benign hepatocyte proliferation and has been newly characterized as a subtype of hepatocellular adenoma accounting for approximately 4% of lesions in the study population. This has been associated with higher BMI and OCP use in the population. The sonic hedgehog subtype was more frequently associated with symptomatic bleeding.[49]

Unclassified

There are 7% to 23% of hepatocellular adenoma lesions that remain unclassified without specific genetic or pathologic abnormalities found at this time.[49,53]

Diagnosis of Hepatocellular Ademona

HCAs may be seen as a heterogenous lesion on ultrasound that may be hyperechoic if steatotic, with an anechoic center if any prior hemorrhage. CEUS may note hyperenhancement with the arterial phase, hypoenhancement in the portal phase, and no enhancement in late phase. The diagnosis of HCA may be made by CT imaging, noting that if a lesion is more often homogenous than heterogenous, it may be hypodense appearing if steatotic or hyperdense in the presence of hemorrhage.[41]

Although MRI is helpful in diagnosing HCA, it may also be useful in identifying different subtypes of HCA lesions. Inflammatory HCA lesions appear hyperintense on T2 weighted MR images with arterial hyperenhancement that persists into the portal venous phase. With the high T2 signal intensity, there is increased T2 signal along the peripheral rim noted as the atoll sign.[52,53,58,59] HNF1α HCA lesions are noted by their diffuse intralesional fat deposition diagnosed on in- and opposed-phase imaging. They have a nonpersistent arterial enhancement.[58] β-catenin has been found to activate the organic anion transporting polypeptide (OATP) B1/B3 and as a consequence allows for uptake of the hepatobiliary contrast gadolinium. β-catenin HCA, particularly CTNNB1 exon 3 subtype lesions have been found to uptake contrast and are iso- to hyperintense relative to liver parenchyma in the hepatobiliary phase of MRI. Caution should be used in interpreting this, as both FNH lesions and some HCC lesions enhance in the presence of hepatobiliary contrast agent.[59,60] Sonic hedgehog HCA

lesions have not been associated with particular MRI characteristics; however, it is hypothesized this subtype may be characterized by the presence of hemorrhage on imaging.[59]

At this time, there are no recommendations for histopathology or molecular subtyping of HCA in routine clinical practice. The identification of subtypes on imaging is not currently a driving factor in HCA management.[24,59] It has been proposed, however, that molecular classification may be most helpful in women, particularly those with small lesions (<5 cm) to help guide treatment and surveillance[49] (**Table 2**).

The most common differential diagnosis for HCA is FNH; however, HCA may share imaging characteristics with HCC such as washout or the presence of a capsule. The clinical context in which these lesions occur is important to consider: the presence of underlying liver disease, postmenopausal state, or use of anabolic steroids, all of which may increase the potential of malignancy.[61,62] As the management for HCA, FNH, and HCC differs significantly, in cases for which imaging is inconclusive and further data will have an impact on treatment, a biopsy can be obtained.[4]

Management of Hepatocellular Ademona

Upon the diagnosis of HCA, all OCPs and other forms of exogenous hormones (ie, intrauterine device [IUD], androgens) should be stopped (**Fig. 2**). Regardless of size, all HCA lesions diagnosed in men are recommended to be surgically resected or treated with a curative intent because of the increased risk of malignancy.[4,24] Weight reduction should be encouraged, as weight loss has demonstrated lesion stability and/or reduction in the size of HCA lesions.[45,63]

Women who are diagnosed with HCA lesions smaller than 5 cm may be managed conservatively. Follow-up imaging is recommended every 6 months (for a 1 year based on European guidelines, for 2 years based on US guidelines) to establish growth patterns and monitor for malignant transformation.[4,24] Alpha-fetoprotein (AFP) may be trended but has not been found to be a reliable marker for malignant transformation, as it is often normal even in cases of transformation.[64] Long-term observation of HCA lesions suggests that most lesions are stable (58%) or decrease in size (37%). Fat-containing lesions are significantly less likely to decrease in size than lesions without fat. After an initial size decrease was seen within 5 years, no further changes in size were seen beyond 5 years, suggestive that lesions typically remain stable beyond a 5-year timeframe.[65]

Surgical resection

Given the increased risk of rupture and risks of malignancy associated with growing size, HCA lesions greater than 5 cm are recommended to be surgically resected.[4] Additionally, growth seen on surveillance of an HCA lesion of at least 20% would prompt recommendation for surgical excision.[24] Laparoscopic excision of the HCA is ideal if lesion location and patient comorbidities permit. In cases of hemodynamic instability associated with HCA hemorrhage/rupture, transarterial embolization and abdominal packing with initial laparotomy are recommended to stop hemorrhage and allow for stabilization. A plan for more definitive resection is then recommended 24 to 48 hours later.[66] For adenomas seen in GSD patients, surgical resection is an effective step in HCC prevention until consideration for definitive liver transplant. However, partial hepatectomy is more morbid in GSD than the general population.[48]

Indications for surgical resection in hepatocellular adenomas include lesion size of at least 5 cm, HCAs in males, HCAs that grow at least 20% on surveillance, any instance of biopsy-proven β-catenin mutation, HCAs associated with GSD.

Table 2
Hepatocellular ademona molecular classifications

		Mixed Inflammatory/B-catenin				
			B-Catenin			
	HNF1A	**Inflammatory**	**b-catenin Exon 3**	**b-catenin Exon 7,8**	**Sonic Hedgehog**	**Unclassified**
	HNF1A mutations	Sustained JAK/STAT pathway activation	Mutation CTNNB1 exon 3	Mutation CTNNB1 exon 7,8	Activation Sonic Hedgehog pathway	Unknown
Prevalence of lesions	~34%–46%	~18%–44%	~7%	~3%	~4%	~7%–23%
OCP association?	Yes	Yes			Yes	
Risk associations	MODY	Alcohol, elevated BMI	Androgen use, GSD, familial adenomatous polyposis, vascular liver disease		Elevated BMI	
Presentation	Female, hepatic adenomatosis	Elevated alk phos/GGT/CRP, anemia	Male, malignant transformation	Young patient	Symptomatic bleeding	
Risk of malignancy	Rare		High risk	Less risk		
Histology	Intracellular fat deposits	Inflammatory infiltrates, sinusoidal dilatation, abnormal vessels	Increased nuclear ratio, nuclear atypia, large lesions	Nuclear atypia		
MRI characteristics	Intralesional fat deposition, nonpersistent arterial enhancement	Hyperintense on T2 weighted, increased T2 signal along rim of lesion atoll sign	Uptake gadolinium contrast, iso- or hyperintense on hepatobiliary phase		Possible findings of hemorrhage	

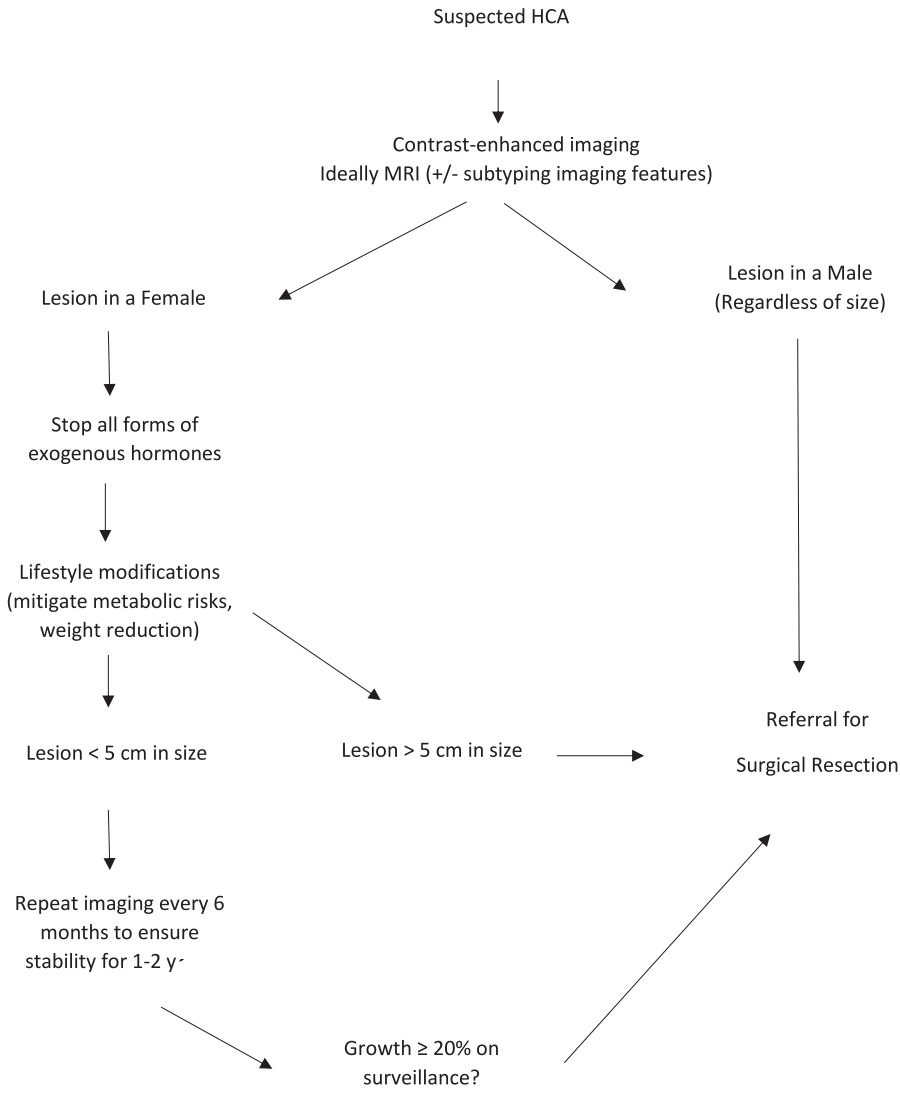

Fig. 2. Management of HCA.

Minimally Invasive Treatments

Transarterial embolization and ablation may be pursued in settings of poor surgical candidacy, in cases of acute hemorrhage, or as a bridge to surgical resection to decrease the size and bleeding potential of HCA lesions. Embolization monotherapy may be limited in treatment of HCA as it may not eradicate all the cells in adenoma and has been found to require retreatment in 25% of cases. There are limited data on the use of microwave ablation in the treatment of HCA. Radiofrequency ablation (RFA) has been used in small unresectable HCA and may impede growth in settings of pregnancy or hormones when a patient may be unable to stop therapy. RFA is mostly used in lesions less than 5 cm, and decreased effectiveness is seen with increasing lesion size.[67–69]

Liver Transplantation

Liver transplantation may be considered in the treatment of HCAs, and transplantation has been performed for the presence of multiple adenoma lesions, suspicious or biopsy-proven malignant transformation, or the presence of portosystemic venous shunts. Specifically, criteria have been proposed for transplant for HCA that include histologic proof of malignant transformation or the presence of 3 of the 5 minor criteria:

More than 2 previous life-threatening hemorrhage
More than 2 prior hepatectomies
β-catenin mutated/inflammatory adenoma
Underlying liver disease such as major steatosis or vascular abnormalities
Age greater than 30 years old[70]

Liver transplantation may be considered in patients with multifocal, growing HCA lesions that do not regress with dietary improvements in GSD and as such would be curative of the underlying enzymatic defect in GSD.[48]

Pregnancy

Managing pregnant women with HCA should be individualized. Ideally there would be prepregnancy intervention (such as resection, ablation, or embolization) of large lesions or for lesions with complications during prior pregnancy.[71] Pregnancy is not contraindicated for those lesions less than 5 cm, and it is recommended to monitor for the potential of growth with ultrasound every 6 to 12 weeks during pregnancy.[4,24] Because of elevated levels of circulating estrogens, hyperdynamic circulation, and increased vascularity of the liver, the greatest risk of rupture is in the third trimester of pregnancy. Women with HCA can deliver vaginally in lieu of cesarean section if there are no other complicating factors. Surgical resection of HCA lesions may be considered in pregnant women who are under 24 weeks of pregnancy; however, general anesthesia risks are greatest in the second trimester, and abdominal surgery becomes more difficult in late second trimester because of the gravid uterus; thus it is generally avoided. Selective arterial embolization is only recommended if needed for lifesaving purposes during pregnancy because of increased risk of radiation exposure to the fetus (particularly before 26 weeks of gestation).[71]

Liver Adenomatosis

Liver adenomatosis is recognized as its own entity and characterized as the presence of multiple HCAs with more than 3 to 10 lesions present in normal liver parenchyma.[72] These lesions are associated with the metabolic syndrome hepatic steatosis and are thought to be as a result of congenital or acquired hepatic vascular abnormalities and mutations in the HNF1α germline.[49,51,73] Upon retrospective analysis, liver adenomatosis was found to be stable or regress in size of lesions with weight loss.[45] Because of the presence of multiple lesions, partial resection is challenging; thus liver adenomatosis is managed based on targeting the largest/dominant lesion.[24] Liver transplantation may be considered in select cases of liver adenomatosis.

SUMMARY

FNH and HCA lesions continue to pose diagnostic and management challenges despite improvements in imaging and refinements in therapeutic approaches. Given that focal liver lesions continue to evoke fear and uncertainty regarding the possibility of malignancy in patients and providers, it is important to understand the advances made in diagnostic and management approaches of FNH and HCA as outlined in

this article. Clear understanding of FNH and HCA imaging features and molecular subtyping will prove useful in alleviating uncertainty and reducing fear in the practical care of these patients seen commonly in clinical practice. Finally, a more precise risk stratification of HCA lesions for progression to HCC will allow a more nuanced approach to refined management with more definitive decision making toward surgical or radiological therapy.

DISCLOSURE

The authors have nothing to disclose.

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