

Liver Masses in Women

Zunirah Ahmed MD

Assistant Professor

Internal Medicine, Gastroenterology and Transplant Hepatology

The University of Kansas Health Systems

Case 1

- 54 yrs old female present to primary care office with complaints of intermittent epigastric pain and nausea. She denies any other associated symptoms.
- PMH- HTN, Obesity, DM
- PSH – None.
- Medications – Lisinopril, Metformin.

AST- 27

US Abdomen – 5 cm hyperechoic lesion in right lobe

ALT- 16

Diagnosis ?

AP- 57

TB- 0.9

Hemangiomas

- Hepatic hemangiomas are the most common benign liver lesion.
- Hemangiomas are characterized by clusters of blood-filled cavities lined by a single layer of endothelial cells and are fed by the hepatic arterial circulation.
- Prevalence ranges from 3%–20%, with the highest incidence rate in adults between 30 and 50 years.
- Women are more commonly affected with a female-to-male ratio of 4.5:1 to 5:1.

Aziz H, Brown ZJ, Baghdadi A, Kamel IR, Pawlik TM. A comprehensive review of hepatic hemangioma management. J Gastrointest Surg. 2022;26:1998–200

Hasan HY, Hinshaw JL, Borman EJ, Gegios A, Levenson G, Winslow ER. Assessing normal growth of hepatic hemangiomas during long-term follow-up. JAMA Surg. 2014;

Clinical Presentation

- Most hemangiomas are <5 cm in diameter, and they usually remain stable and asymptomatic
- Giant hemangiomas (variable definition from 5-10 cm) can cause symptoms like abdominal discomfort, nausea, early satiety and rarely jaundice, or high output cardiac failure.
- Kasabach-Merritt syndrome – giant hemangioma leading to hemolytic anemia, thrombocytopenia, prolonged prothrombin time, and hypofibrinogenemia.

Di Carlo I, Koshy R, Al Mudares S, Ardiri A, Bertino G, Toro A. Giant cavernous liver hemangiomas: Is it the time to change the size categories? Hepatobiliary Pancreat Dis Int. 2016;

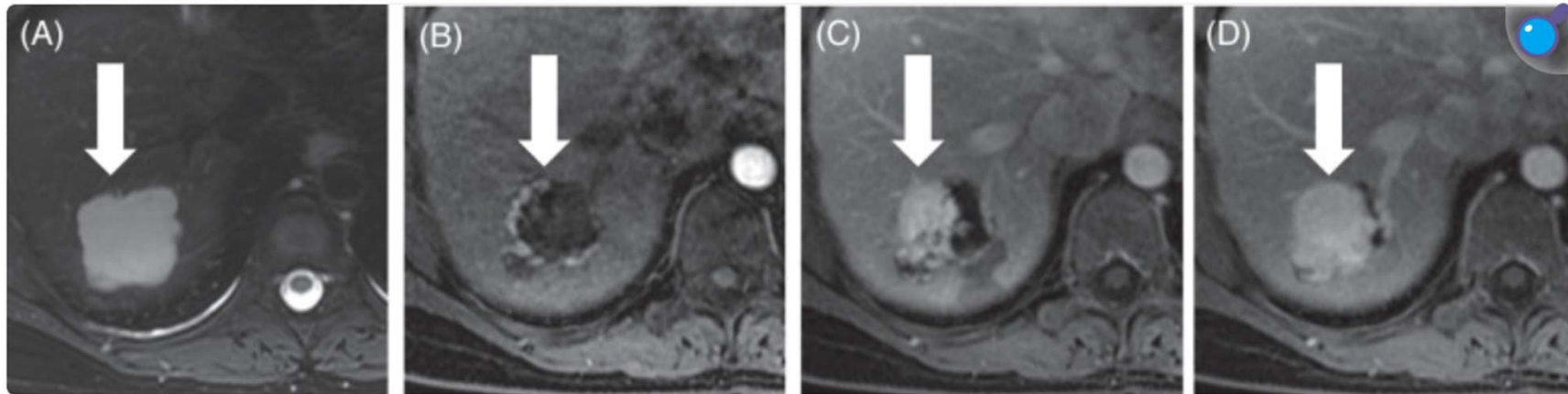
Albitar HAH, Iyer V. Giant liver hemangioma with Kasabach-Merritt syndrome. Am J Med. 2020

Diagnosis

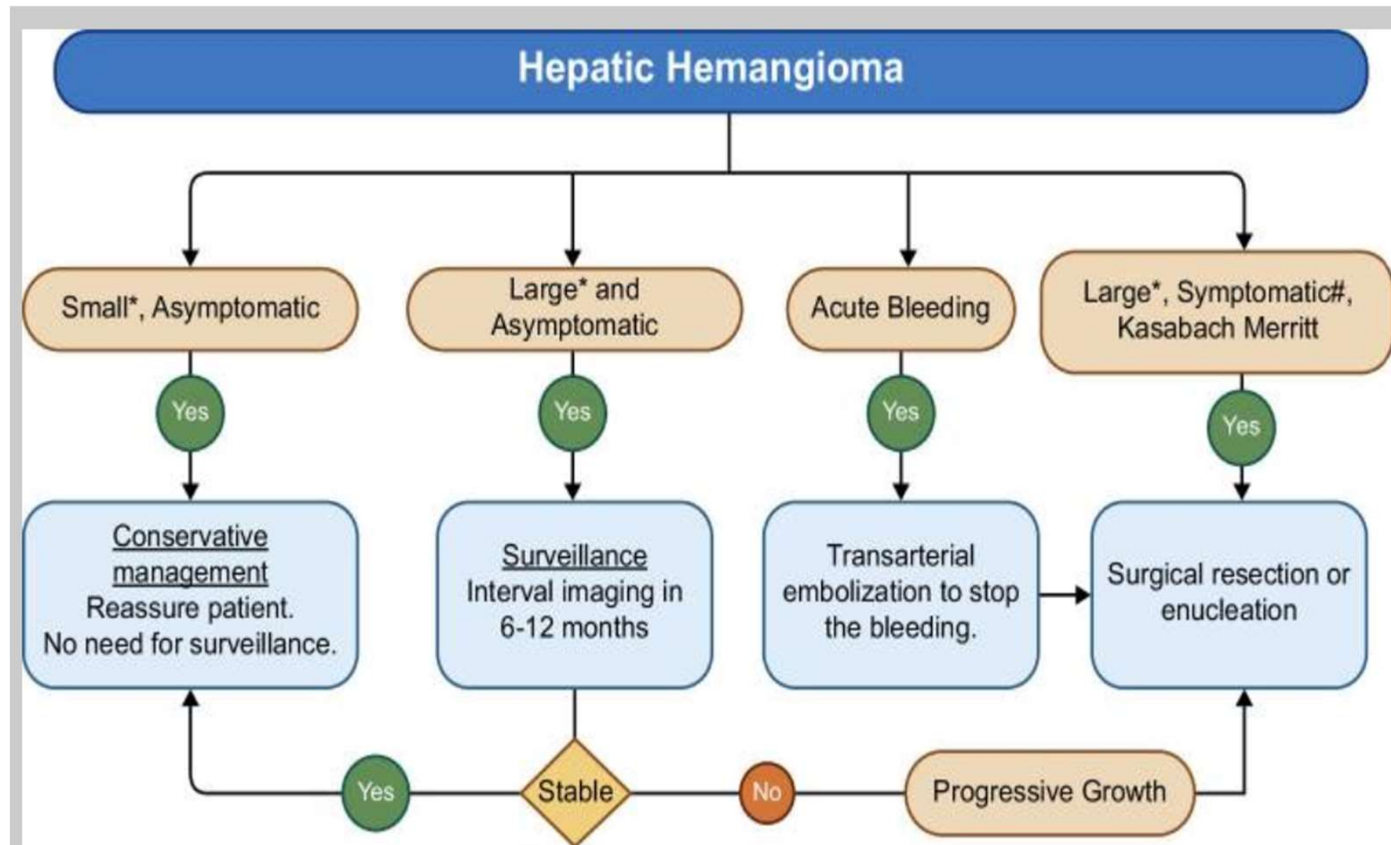
- Diagnostic approach for suspected hemangiomas starts with ultrasound, followed by CT or MRI for definitive characterization.
- Ultrasound- Hemangiomas appear homogeneous hyperechoic lesions with posterior acoustic enhancement.
- Ultrasound has 94% sensitivity and 80% specificity
- CT -Sensitivity (76%) and specificity (90%).
- MRI- sensitivity (98%) and specificity (99%).

Sandulescu LD, Urhut CM, Sandulescu SM, Ciurea A-M, Cazacu SM, Iordache S. One stop shop approach for the diagnosis of liver hemangioma. World J Hepatol. 2021

Diagnosis- MRI



Management



Reguram R, Ghonge A, Tse J, Dhanasekaran R. Practical approach to diagnose and manage benign liver masses. Hepatol Commun. 2024 Oct 30;8(11)

Case 2

- 30 yrs old female seen at primary care office for intermittent abdominal pain for past one year , associated with mild nausea

- PMH- None
- PSH- None
- Medications – None

AST- 23

US Abdomen: Hyperechoic lesion in right lobe 4.4X3.8cm

ALT- 20

Diagnosis ?

AP- 70

TB- 0.8

Focal Nodular Hyperplasia -FNH

- FNH is the second most frequent benign solid liver lesion and accounts for 8% of liver lesions in clinical practice.
- Overall prevalence is estimated to be 0.3%–3% in the general population.
- Highest prevalence in 30–50-year-old women, with a female-to-male ratio of 8:1.
- There is no clear link between the development, size, or prognosis of FNH and hormonal exposure from taking oral contraceptive pills (OCPs) or pregnancy.
- FNH are well-demarcated, nonencapsulated solid lesions composed of nodules of hyperplastic hepatocytes and expand as kupffer cells in the background of normal liver histology.

Marrero JA, Ahn J, Rajender Reddy K, American College of Gastroenterology . ACG clinical guideline: The diagnosis and management of focal liver lesions. Am J Gastroenterol. 2014;109:1328–1347.

Corallo C, Bell J, Laverty A, Mohsin M, Prasad R, Albazaz R. Suspected focal nodular hyperplasia in male adults: 10-year experience from a large liver centre. Abdom Radiol (NY). 2023;48:2292–2301.

Bioulac-Sage P, Cubel G, Balabaud C, Zucman-Rossi J. Revisiting the pathology of resected benign hepatocellular nodules using new immunohistochemical markers. Semin Liver Dis. 2011;31:91–103

Clinical Presentation

- FNH is usually asymptomatic and tends to be detected incidentally on imaging.
- FNH ranges in size from 2-20 cm , however upto 85% cases are < 5cm in size.
- Only one-third or fewer patients present with abdominal pain or discomfort.
- Most FNHs remain stable in size however 10% can show growth, and another 10% can regress over time.
- FNH is not at risk of undergoing malignant transformation, necrosis, rupture, or hemorrhage, and usually does not need treatment unless it causes symptoms.

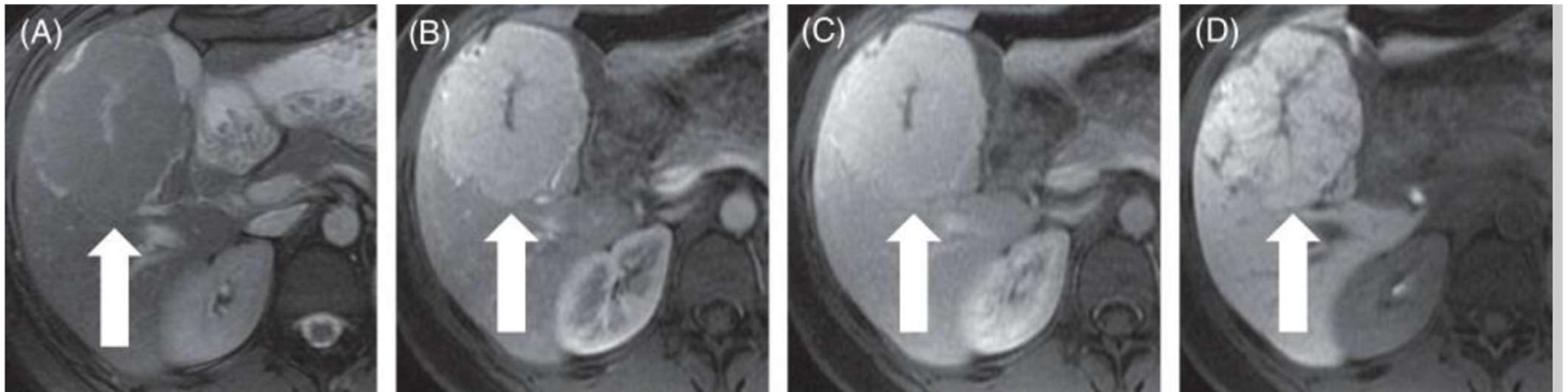
LeGout JD, Bolan CW, Bowman AW, Caserta MP, Chen FK, Cox KL, et al. Focal nodular hyperplasia and focal nodular hyperplasia-like lesions. Radiographics. 2022;42:1043–1061.

Diagnosis

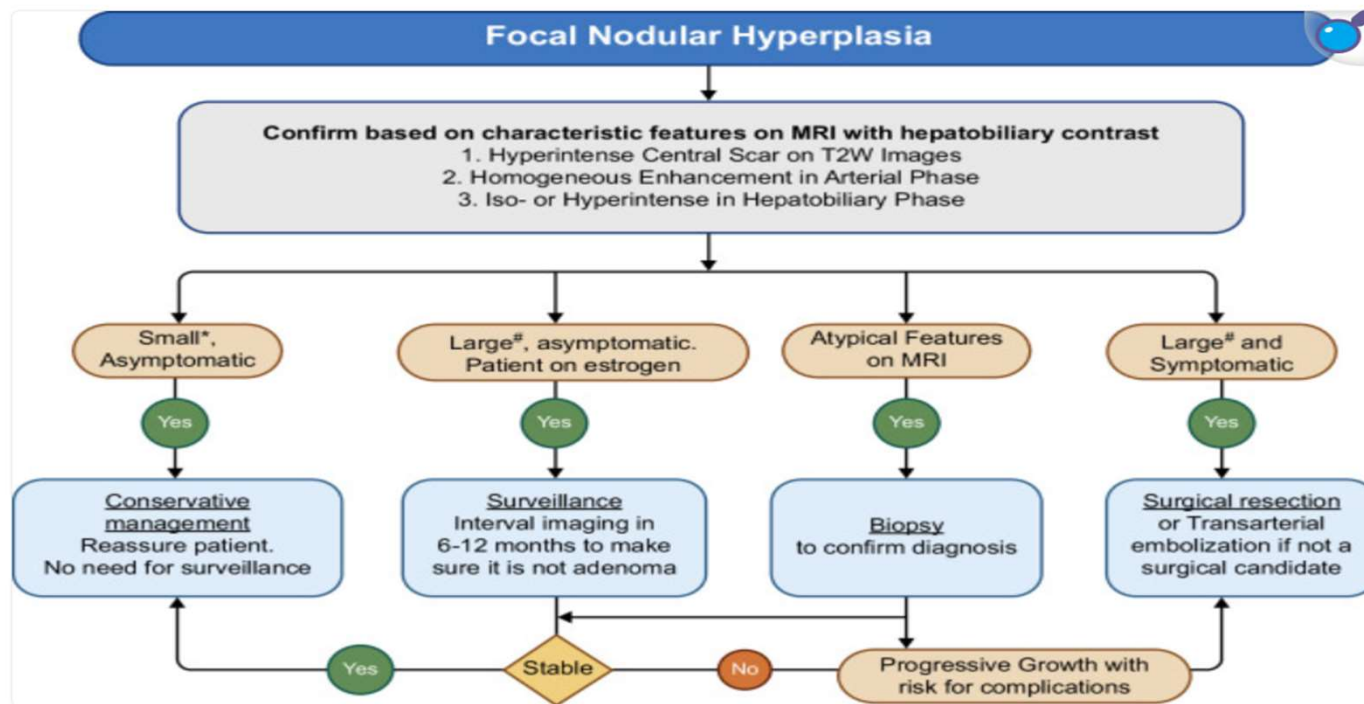
- A central stellate scar is considered the hallmark imaging feature of FNH- However it is only present in 20% of cases and is usually seen in lesions >3 cm in size.
- Other features of FNH are vascular features like characteristic central spoke-wheel pattern, with branching arteries radiating peripherally from the feeding artery at the center of the lesion.
- US- sensitivity 95% and specificity 86%.
- CT – sensitivity 60% and specificity 60%.
- MRI with contrast – Sensitivity 97% and specificity 100%.

LeGout JD, Bolan CW, Bowman AW, Caserta MP, Chen FK, Cox KL, et al. Focal nodular hyperplasia and focal nodular hyperplasia-like lesions. Radiographics. 2022;42:1043–1061

Diagnosis- MRI



Management



Reguram R, Ghonge A, Tse J, Dhanasekaran R. Practical approach to diagnose and manage benign liver masses. Hepatol Commun. 2024 Oct 30;8(11)

Case 3

- 20 yrs old female presents to primary care office with abdominal pain and nausea
- PMH- PCOS, obesity
- Medications- oral contraceptive pills
- PSH- None

AST 25

ALT 29

AP 111

TB 0.5

US Abdomen – 4 cm hyperechoic mass in right lobe

Diagnosis ?

Hepatic adenoma- HA

- Hepatic adenomas are relatively rare benign liver tumors that predominantly affect women, with a female-to-male ratio of 9:1.
- Risk factors include oral contraceptive pills (OCP), obesity, metabolic syndrome, anabolic steroids and glycogen storage diseases
- Annual incidence of adenomas in users of OCPs is ~30–40 cases per million, compared to 1 case per million among nonusers.
- *Rich NE. Changing epidemiology of hepatocellular carcinoma within the United States and worldwide. Surg Oncol Clin N Am. 2024;*
- *Clinical features and natural history of hepatocellular adenomas: The impact of obesity. Aliment Pharmacol Ther. 2011*

Hepatic adenomas – Subtypes

Inflammatory adenoma

30%–35% of hepatocellular adenomas.

Associated with OCP, obesity, steatotic liver disease, and glycogen storage disorders

HNF1A-inactivated adenomas

35–40% of all hepatocellular adenomas

Associated with maturity onset diabetes of young (MODY)

Histopathologic analysis reveals macrovesicular fat and lack of liver fatty acid-binding protein expression.

β -catenin–mutated adenoma

10–15% of all adenomas

carries a mutation in cadherin-associated protein β 1 gene (*CTNNB1*) at exon 3 or exon 7/8.

β -catenin–mutated adenomas at exon 3 have the highest risk for malignant transformation and are more common in men.

They occur more frequently in men and are associated with male hormone administration, glycogen storage disease and familial adenomatous polyposis (FAP)

Sonic hedgehog adenoma

10% of all adenomas

characterized by mutations in sonic hedgehog pathway

- Associated with OCP use and obesity
- These adenomas are highly vascular and prone to bleeding.

7% of adenomas do not fall into the above categories and remain unclassified.

Nault JC, Couchy G et al, Molecular Classification of Hepatocellular Adenoma Associates With Risk Factors, Bleeding, and Malignant Transformation. Gastroenterology. 2017 Mar;152(4):880-894

Clinical Presentation

- HA are often asymptomatic
- Symptoms are variable ranging from mild abdominal pain, bloating to severe RUQ pain associated with nausea, dizziness in setting of ruptured adenoma.
- Risk for bleeding increases with tumor size and reaches a significant level of >20% risk when adenomas are larger than 5cm.
- Rupture occurs in up to 27% of HCAs, resulting in a 5% to 10% mortality rate
- β -catenin–mutated adenomas, sonic hedgehog adenomas, and inflammatory adenomas have the highest risk of bleeding, HNF1A adenomas have the least.

van Aalten SM, de Man RA, IJzermans JNM, Terkivatan T. Systematic review of haemorrhage and rupture of hepatocellular adenomas. Br J Surg. 2012

- Malignant transformation of hepatic adenomas into hepatocellular carcinoma (HCC) is rare with reported frequency of 4.2%
- Risk factors for HCC include β -catenin–mutated exon 3 subtype, tumor larger than 5 cm, male sex, and glycogen storage disorders.
- Most HCC that arises from hepatic adenomas appear to be well-differentiated with low risk for recurrence.

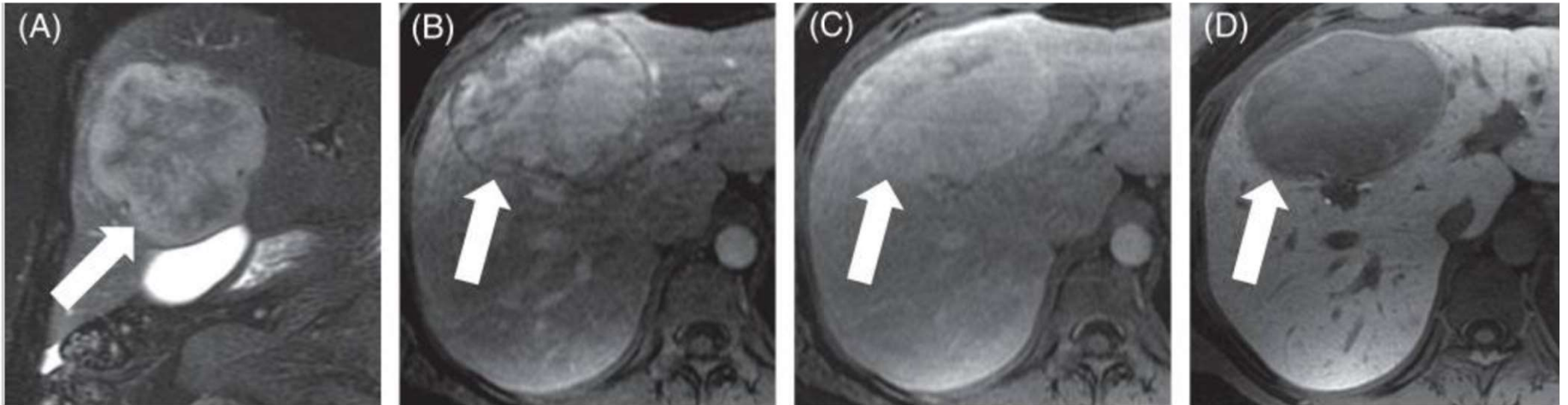
Stoot JH, Coelen RJ, De Jong MC, Dejong CH. Malignant transformation of hepatocellular adenomas into hepatocellular carcinomas: a systematic review including more than 1600 adenoma cases. HPB (Oxford). 2010 Oct;12(8):509-22

Diagnosis

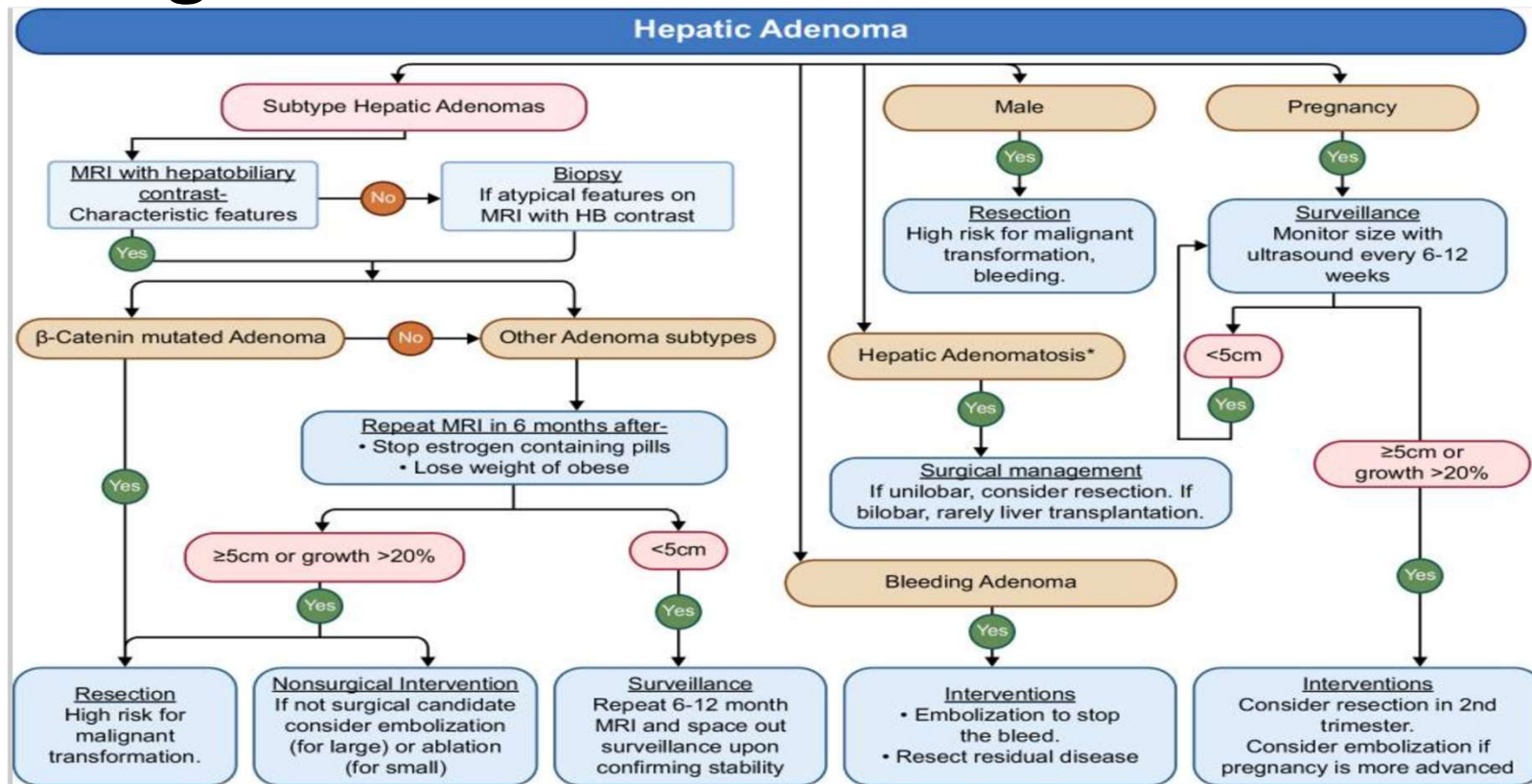
- The sonographic features of HAs lack specificity and could mimic other benign or malignant liver lesions
- US - Sensitivity ranges from 50% to 70% for HA detection
- CT- Sensitivity (80-90%) and specificity (70-80%)
- MRI –sensitivity 88% and specificity 100%

Sarah Poetter-Lang et al, Hepatocellular adenoma update: diagnosis, molecular classification, and clinical course, British Journal of Radiology, Volume 97, Issue 1163, November 2024, Pages 1740–1754

Diagnosis- MRI



Management



Reguram R, Ghonge A, Tse J, Dhanasekaran R. Practical approach to diagnose and manage benign liver masses. *Hepatol Commun.* 2024 Oct 30;8(11):

Adenomas and OCP

- Influence of endogenous and exogenous estrogen on growth of HA has been well established
- Retrospective cohort study have shown that upto 98% of adenomas remained stable or regressed after OCP cessation (follow up period of 2 yrs)
- Progesterone only pills have been linked with decrease in adenoma size in small studies
- Discussion with patient regarding risk versus benefits of OCP

Haring MPD, Gouw ASH, de Haas RJ, Cuperus FJC, de Jong KP, de Meijer VE. The effect of oral contraceptive pill cessation on hepatocellular adenoma diameter: A retrospective cohort study. Liver Int. 2019 May;39(5):905-913

Sinclair M, Schelleman A, Sandhu D, Angus PW. Regression of hepatocellular adenomas and systemic inflammatory syndrome after cessation of estrogen therapy. Hepatology. 2017 Sep;66(3):989-991

Case 4

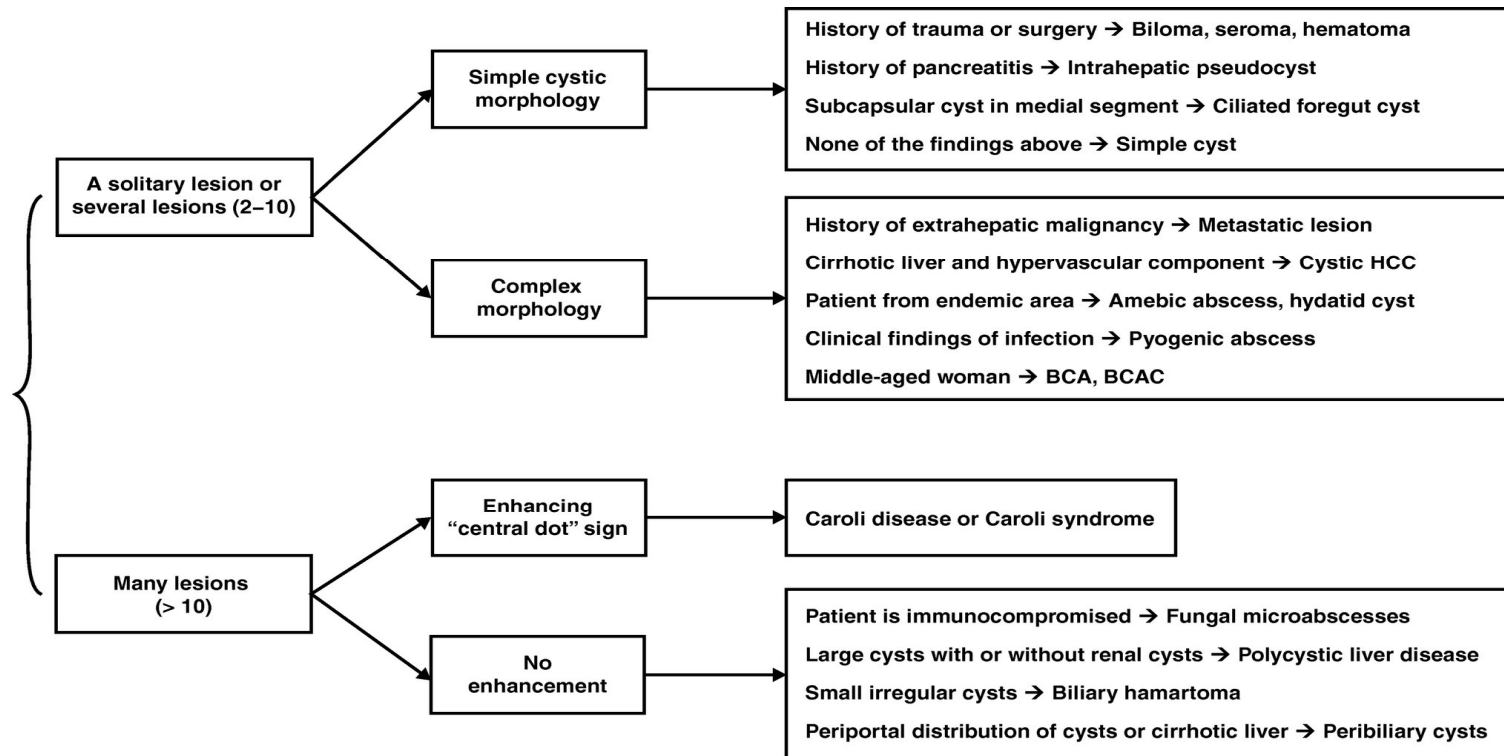
- 55 yrs old female presented to her primary care office for a regular physical exam –
- PMH- HTN
- PSH- None
- Medications- Losartan

US Abdomen -3 cm well circumscribed, right lobe anechoic lesion

AST 15
ALT 30
AP 100
TB 0.7

Diagnosis?

Hepatic cysts



Borhani AA, Wiant A, Heller MT. Cystic hepatic lesions: a review and an algorithmic approach. *AJR Am J Roentgenol*. 2014 Dec;203(6):1192-204.

Simple cyst

- Simple hepatic cysts are thin-walled masses with fluid-filled, epithelium-lined cavities.
- The prevalence of simple hepatic cyst ranges from 3% to 5% on US to as high as 18% on CT.
- Large hepatic cysts are more frequent in women older than 50 years, and the female to male ratio is 4:1
- Simple hepatic cysts measure from <1 cm to 30 cm and are more frequent in the right hepatic lobe.
- The presence of more than 20 hepatic cysts is defined as polycystic liver disease (PLD).

Lantinga MA, Gevers TJ, Drenth JP. Evaluation of hepatic cystic lesions. World J Gastroenterol. 2013;19:3543—54

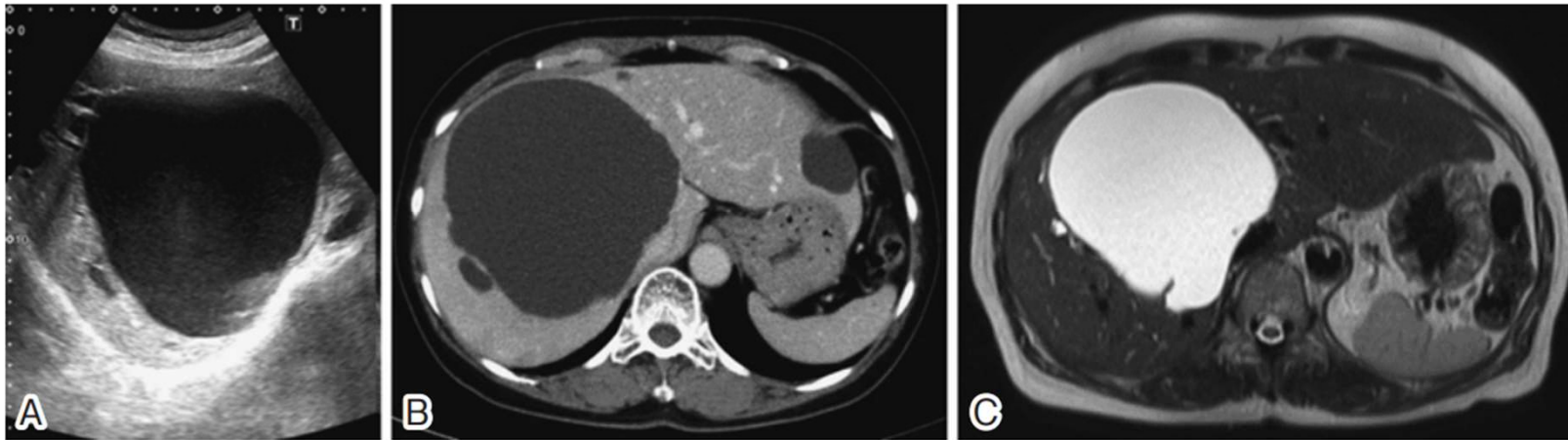
Clinical presentation

- Simple cysts are usually asymptomatic. Clinical symptoms occur in 5% of patients.
- Symptomatic hepatic cysts are more frequent in women female to male ratio, 9:1.
- Symptoms include early satiety, abdominal pain, nausea, bloating
- Complications of simple cysts include infection, spontaneous hemorrhage, rupture into the peritoneal cavity and external compression of biliary tree or major vessels

Salemis NS, Georgoulis E, Gourgiotis S, Tsohataridis E. Spontaneous rupture of a giant non parasitic hepatic cyst presenting as an acute surgical abdomen. Ann Hepatol. 2007;6:190—3.

Lantinga MA, Gevers TJ, Drenth JP. Evaluation of hepatic cystic lesions. World J Gastroenterol. 2013;19:3543—54

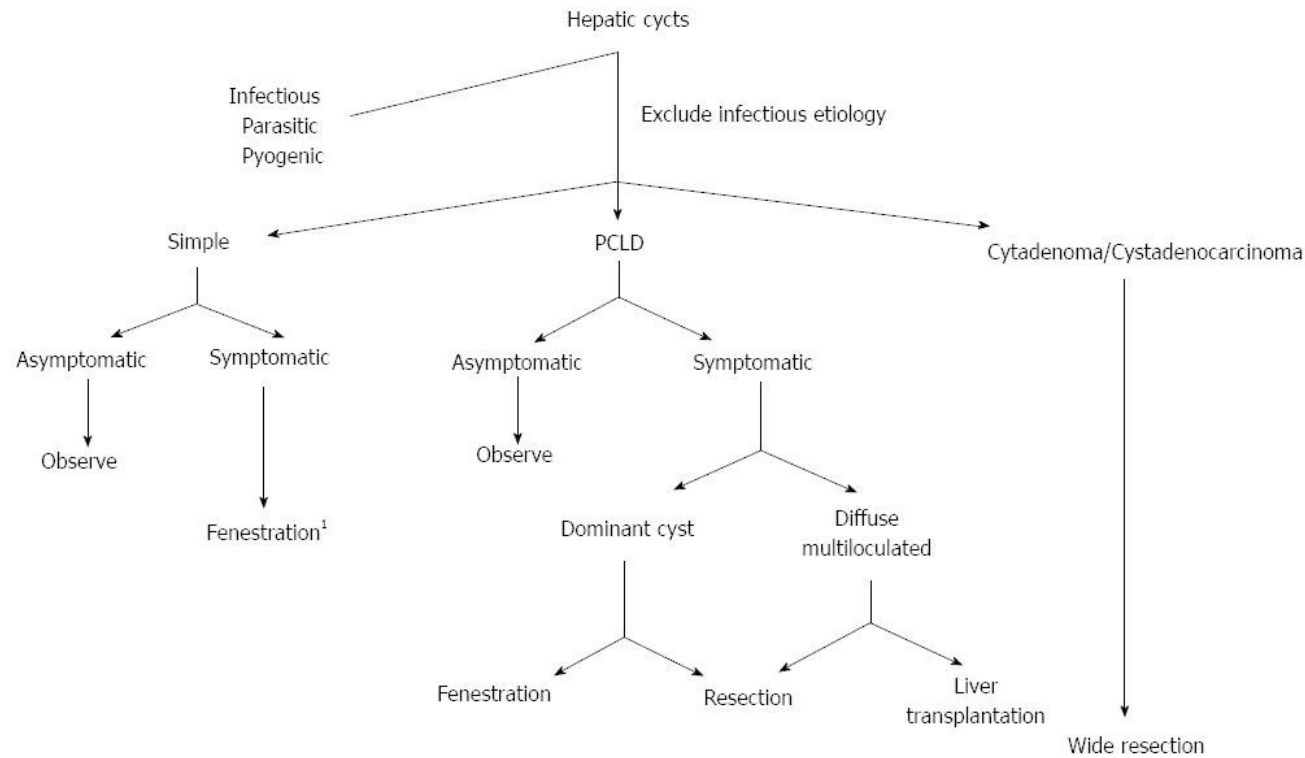
Diagnosis



A: US reveals an anechoic, fluid-filled saccular lesion with thin-walled smooth margins and posterior acoustic enhancement. B: CT shows a round, smooth, well-demarcated, and fluid-filled lesion without internal structure. C: MRI shows a homogeneous, well-defined, and spherical lesion with high signal intensity on T2-weighted images.

Shimizu T, Yoshioka M, Kaneya Y, Kanda T, Aoki Y, Kondo R, Takata H, Ueda J, Kawano Y, Hirakata A, Matsushita A, Tani N, Mamada Y, Yoshida H. Management of Simple Hepatic Cyst. *J Nippon Med Sch.* 2022 Mar 11;89(1):2-8.

Management



Macedo, Francisco Igor. "Current management of noninfectious hepatic cystic lesions: A review of the literature." World journal of hepatology 5.9 (2013): 462.

Thankyou

Questions?