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Liver Masses: Body and nucs diagnosis and IR treatments:

Hepatocellular carcinoma (HCC) develops along a spectrum. Describe the spectrum of HCC development including some imaging manifestations.

HCC starts with regenerative nodules that progress to dysplastic nodules and then to HCC. Key imaging manifestations include that dysplastic nodules tend to be dark on T2 weighted images and HCC tends to be bright on T2 weighted images. Regenerative nodules may be bright or dark on T2 weighted images but typically do not enhance or washout differently than normal liver. Dysplastic nodules may have arterial enhancement but no washout. HCC demonstrates early arterial enhancement and delayed washout. Key imaging manifestations for HCC is a T2 bright mass vs masses with arterial enhancement and delayed washout, with co-existing findings of cirrhosis and portal hypertension.

What are some of the common risk factors for development of hepatocellular carcinoma?

Cirrhosis of any cause, acute hepatitis B with or without cirrhosis and chronic hepatitis B with cirrhosis, hepatitis C, hemochromatosis (HCC accounts for about 1/3 of deaths in hemochromatosis patients), glycogen storage disease, alpha-1 antitrypsin deficiency, other entities to include Budd Chiari syndrome.

True or false: most patients with HCC will have an elevated alpha fetal protein (AFP) level?

True, up to 95% of HCC patients will have elevated AFP levels.

What are imaging manifestations for the fibrolamellar HCC variant to look for on board exams?

Buzzword on board exams for fibrolamellar HCC is a central nonenhancing T2 dark scar on MRI. The central scar may be calcified on CT. Additionally, fibrolamellar HCC tends to develop in patients younger than 35 years without cirrhosis and with normal AFP levels. Fibrolamellar HCCs are aggressive so you may also be shown local nodal and distant metastatic disease.

If you see a hepatic mass with a central scar demonstrating delayed enhancement on MRI what is this typical for?

Focal nodular hyperplasia classically has a central scar that demonstrates delayed enhancement.

What are other imaging manifestations of focal nodular hyperplasia (FNH) on MRI?

FNH presents with a spoke wheel or cut grapefruit appearance on post-contrast imaging that is commonly isointense to liver (hence a "stealth lesion") on pre-contrast T1 and T2 weighted images. With gadolinium on arterial enhanced images you often see a cut grapefruit appearance due to enhancement in the mass surrounding a non-enhancing central scar with radiating bands. On delayed post-contrast images, the central scar will classically show delayed enhancement. Most common clinical history would be a mass in a middle-aged woman. FNH's may regress with age. Note that FNH's do not demonstrate washout of contrast as in HCC.

What nuclear medicine scan should you remember for FNH diagnosis on board exams?

On board exams I would remember that FNH can show uptake on a sulfur colloid liver scan. An FNH has normal hepatocytes around abnormally arranged ducts and Kupffer cells. As the lesion contains

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reticuloendothelial system cells you would expect that the RES will show sulfur colloid uptake. Other hepatic masses such as a hepatic adenoma, HCC, or metastasis would not be expected to show sulfur colloid uptake because these do not contain functioning Kupffer cells.

If a board exam question shows you a liver lesion and gives you a clinical history of a woman on oral contraceptives, what lesion should you think of first?

A question showing a liver lesion and providing a clinical history of oral contraceptive use should make you consider a hepatic adenoma as the most likely diagnosis. An alternative history also supporting a hepatic adenoma would be a male on anabolic steroids with a liver mass. Key is that hepatic adenomas are classically hormonally induced, thus may also be seen in obese individuals.

What is the imaging appearance of a hepatic adenoma?

Most commonly hepatic adenomas will present as a potentially large solitary mass in the right hepatic lobe (most common). If you see multiple hepatic adenomas you can consider entities like glycogen storage disease (von Gierke's disease). Hepatic adenomas classically contain internal fat (although male hepatic adenomas may not have fat) and/or hemorrhage. For board exams, if you see a lesion with sulfur colloid uptake think FNH instead of hepatic adenoma. On MRI, hepatic adenomas would classically show internal fat manifested by signal dropout on out of phase compared to in phase images, with early arterial enhancement and return to normal liver enhancement levels on delayed post-contrast images. Note that hepatic adenomas do not have washout like HCC. Washout=mass enhances less than normal liver on delayed post-contrast images—hepatic adenomas typically enhance similar to liver on delayed post-contrast images.

What is common clinical management of hepatic adenomas? What is a risk of hepatic adenoma that you should be aware of?

First step is to stop OCP/steroid use and then reimaging. If a hepatic adenoma is < 5 cm in size on follow-up imaging, for board exams select that you recommend imaging surveillance as it may continue to regress. If a hepatic adenoma is >5 cm in size on follow-up this has a bleeding risk and a rare cancer HCC risk so for board exam purposes you resect hepatic adenomas > 5 cm in size. Hepatic adenomas are thought to have poor internal connective tissue support, therefore larger lesions are prone to internal trauma and hemorrhage which may lead to acute pain and in some cases internal abdominal bleeding that can be serious.

What are similarities and differences of HCC and hepatic adenomas on imaging?

Similarities include hepatic lesions that may contain fat and both can be well circumscribed. Differences include a typical homogenous post-contrast appearance of an adenoma and heterogeneous appearance of HCC. Both lesions demonstrate arterial enhancement but only HCCs classically show washout. If you have chronic liver disease it is HCC and not an adenoma on board exams.

What is the classic nuclear medicine appearance of hepatic adenoma versus focal nodular hyperplasia on a technetium sulfur colloid scan?

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FNH will show uptake on Tc sulfur colloid as it has functioning Kupffer cells. Hepatic adenomas have poorly functioning or dysfunctional Kupffer cells so these would classically not show uptake and may even appear photopenic compared to liver on a Tc SC scan.

What is the imaging appearance of hepatic hemangiomas on CT or MRI?

On MRI hemangiomas are T2 bright masses. On CT hemangiomas are hypodense lesions. On both CT and MRI hemangiomas show peripheral nodular enhancement with progressive fill in of central enhancement on delayed enhancement images. Of note, because blood flow is slow and blood pools within these lesions, hepatic hemangiomas may enhance for about 30 minutes following contrast administration. Classic for hepatic hemangiomas is peripheral nodular interrupted enhancement with progressive filling in of contrast on more delayed post-contrast sequences. Really large hemangiomas can have venous pooling in venous lakes and central blood clots and can look really heterogeneous, especially on T2 weighted images.

What is the ultrasound appearance of a hepatic hemangioma?

On ultrasound hemangiomas are well defined uniformly hyperechoic lesions. Surprisingly there is typically no visible doppler blood flow identified as the blood flow is often too slow to be identified.

Uptake with what nuclear medicine study is most typical for hepatic hemangiomas on board exams?

If you see a liver mass showing uptake on a tagged red blood cell nuclear medicine study think hepatic hemangioma. I remember this as hemangioma has “hemangio” in the name which makes me think of blood as in a tagged RBC study. If you remember that hepatic hemangiomas have slow blood flow and blood pools in the lesion it makes perfect sense that tagged RBCs would also pool in the lesion and would therefore show uptake on nuclear medicine scintigraphy. The “hemangio” in the name is your clue that this would show up on a tagged RBC scan because the name is telling you about vascularity.

What is the “starry sky” appearance of the liver on ultrasound and what disease state does this suggest?

The starry sky appearance is a sign of hepatitis on ultrasound and shows echogenic fat around portal triads that stands out due to background liver edema.

Are benign liver masses more common or less common in a cirrhotic liver?

Benign liver masses tend to go away or not develop and are much less common in a cirrhotic liver. Therefore, treat any liver lesion in a cirrhotic patient with some suspicion.

Carcinoid and HCC are both arterial enhancing masses—how do you tell the difference between these on board exams?

If you see chronic liver disease it is HCC on board exams. In general, chronic liver disease is highly inhospitable to both benign masses and metastatic disease so it is less likely to get liver metastases in the setting of chronic liver disease. So, if you see a Hypervascular mass in chronic liver disease it is HCC versus a Hypervascular metastasis such as carcinoid. Other tips include seeing the carcinoid tumor to suggest that the liver lesion is a metastasis.

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How do you tell a carcinoid metastasis from a hemangioma on CT or MRI?

Carcinoid will have a continuous rind of enhancement. Hemangioma will show interrupted/discontinuous peripheral enhancement. Also, on board exams with they would almost certainly show you the primary carcinoid tumor in the abdomen/pelvis along with the hepatic metastases.

How to you tell a hemangioma from a hepatic metastasis on board exams?

Look for the T2 bright signal to confirm a hemangioma (CSF bright). Metastases would not be expected to be as bright on T2 weighted images. Both can show interrupted peripheral nodular enhancement. Metastases also may demonstrate a thick rind of enhancement unlike hemangiomas.

What are common imaging manifestations of cholangiocarcinoma?

Cholangiocarcinoma presents as infiltrative hepatic lesion(s) with delayed enhancing soft tissue that grows around and constricts the biliary tree with co-existing peripheral biliary dilatation and contraction of the hepatic capsule. You may also see portal/hepatic vein encasement without visible tumor thrombus unlike HCC which has luminal thrombus and vascular invasion. HCC grows into the portal vein whereas cholangiocarcinoma narrows the portal vein from the outside. If cholangiocarcinoma causes biliary obstruction you can get bilomas that may have secondary inflammation due to hepatic irritation.

What are some of the common risk factors for development of cholangiocarcinoma?

Elderly males, history of primary sclerosing cholangitis (top risk factor in US), recurrent pyogenic cholangitis, clonorchis sinensis parasitic disease (aka liver fluke), hepatitis B/C, HIV, alcohol abuse, thorotrast exposure.

What is a Klatskin tumor?

A Klatskin tumor is a cholangiocarcinoma located at the bifurcation of the right and left hepatic ducts, sometimes termed a hilar cholangiocarcinoma. These are aggressive and often obstruct the biliary duct so stricture/narrowing at the bifurcation on MRCP would raise concern for a possible Klatskin tumor.

Are primary sclerosing cholangitis patients at higher risk for developing cholangiocarcinoma or hepatocellular carcinoma?

With PSC risk of cholangiocarcinoma exceeds that of HCC.

What hepatic tumor is most associated with thorotrast exposure?

Hepatic angiosarcoma which is a very rare tumor but the most common primary sarcoma of the liver. Neurofibromatosis and hemochromatosis patients are also at risk for hepatic angiosarcoma.

What MRI contrast agent is predominantly biliary secreted?

Eovist—therefore some centers use this preferentially for liver evaluation, transplant and biliary leak evaluation.

What are the 2 most common primary hepatic malignancies?

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HCC is #1. Cholangiocarcinoma is #2.

Besides hepatic cysts, what are the 2 most common hepatic masses overall?

Metastases are #1. Hemangiomas are #2.

What are the most common primary cancers that metastasize to the liver?

First, I would think of colon cancer. If you see multiple calcified hepatic metastases think mucinous tumors of the colon, ovary or pancreas. If you see hypervascular metastases consider melanoma, renal cell carcinoma, carcinoid tumor, islet cell tumor, thyroid and choriocarcinoma.

How does Kaposi sarcoma manifest in the liver and what clinical history do you expect with Kaposi sarcoma?

Always look for an AIDS history with low CD4 count in the question stem whenever considering Kaposi sarcoma. In the liver, Kaposi Sarcoma presents with infiltration of the periportal tissues and may look like biliary dilatation on non-contrast imaging. On post-contrast imaging biliary/periportal nodular enhancement is seen. *If you are presented with what looks like biliary ductal dilatation on a non-contrast CT in a patient with AIDS you always must consider Kaposi Sarcoma for board exam purposes and get a post-contrast scan to see the abnormal enhancement. An alternative history that can raise concern for Kaposi sarcoma is history of organ transplantation with immunosuppression.

How does Kaposi sarcoma present elsewhere in the body?

Kaposi sarcoma can commonly present with purple cutaneous plaques on the legs, and in addition to the liver findings of biliary infiltration with periportal enhancing nodules you can also see pulmonary nodules with mediastinal/hilar nodal enlargement. Remember that lymphoma is on the differential of Kaposi sarcoma and classically gallium 67 would classically show uptake in lymphoma but not in Kaposi sarcoma, whereas thallium 201 would show uptake in both (due to functioning Na/K ATPases in both—thallium is a potassium analogue).

How do you tell a perfusion anomaly from a liver mass or regenerative nodule?

Perfusion anomalies have arterial enhancement without washout and are often wedge shaped and non-mass like in appearance.

What options do IR doctors have to treat liver masses?

Y90: Use trans-arterial instillation of Y90 particles to embolize and radiate an HCC.

Trans-arterial chemoembolization (TACE): for palliative HCC therapy, has iodized oil that appears dense on CT

Radiofrequency ablation (RFA): Use RF coils to heat tissue to cause cellular damage of tumor cells. This can be performed percutaneously unlike TACE or Y90.

Cryoablation is another possible option.

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What factors should you consider when deciding between Y90, TACE, or RFA for treatment of malignancy in the liver?

If there is 1 tumor under 5 cm or 3 or fewer tumors under 5 cm in size you can consider percutaneous RFA. If HCC is larger than 5 cm and/or you have more than 3 tumors you can do Y90 or TACE.

Also, large lesions (about 3 cm or greater in size) may need a combination of therapy such as RFA and TACE.

What preparation is required to plan for a Y90 treatment?

First is a planning angiogram to assess anatomy and perform Tc99 MAA lung shunt fraction needs to be determined prior to Y90 treatment. Also, prior to treatment the gastroduodenal artery (GDA) and/or the right gastric artery (a branch of the left hepatic artery) may be embolized to prevent formation of non-healing gastric ulcers.

The Milan criteria is used for what? What are the Milan criteria rules?

Milan criteria is used for evaluation of liver transplantation candidacy in the setting of HCC. According to the Milan criteria you can be considered for liver transplantation if you have 1 HCC under 5 cm in size or up to 3 HCCs under 3 cm in size. You are not allowed to have any extrahepatic disease to be considered for liver transplantation.

What material is best for shielding Y90 particles?

For Y90 plastic or glass shielding is necessary as shielding with lead or tungsten will cause bremsstrahlung from interaction with high energy beta particles and formation of x-rays.

True or false: the beta radiation from Y90 can penetrate outside of the patient's body.

False: The beta radiation cannot pass through the patient's body. However, the bremsstrahlung x-rays from Y90 (that are used to create nuclear medicine images) can penetrate the patient body and cause exposure to others. But the beta particles themselves travel only a short distance in the body (about 5 mm which equals a few hundred cell distance) before they deposit their energy—thereby killing cells adjacent to where they are located.

What is the classic indication for Y90 therapy in the liver?

Y90 is classically indicated for locoregional palliative treatment of unresectable malignancy in the liver. The goal of therapy can be to obtain local control of disease, to bridge to transplant or make the patient an improved candidate for other interventions. Y90 is classically not used for curative intent historically but this is now questionable.

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Fill in the blanks: Normal hepatic parenchyma derives the majority of its blood supply from _____ and hepatic malignancies typically derive the majority of their blood supply from _____.

Normal liver parenchyma derives most blood supply from the portal vein whereas hepatic malignancies most commonly derive blood supply from the hepatic artery. Hence trans-arterial treatments of liver tumors as this preferentially deposits more therapeutic/radioactive agents in areas of malignancy versus normal hepatic parenchyma. Y90 agents are injected intra-arterially selectively to the hepatic artery and then embolize in tissue capillaries where they get stuck and radiate the surrounding tissue (preferentially areas of metastatic disease given the hepatic arterial supply that is greater to metastases in the liver compared to normal liver parenchyma).

Tips: if portal vein thrombosis is present you need to be cautious in your approach so you don't cause significant liver infarction.

Name some common contraindications to Y90 therapy.

Marked liver failure (look for very abnormal LFTs, abdominal ascites, clinical signs of liver failure in a question stem), lung shunt fraction that exceeds 20%, diffuse hepatic malignancy, contrast contraindication precluding angiography.

True or false: a pre-treatment planning Tc99-MAA planning study is required for Y90 therapy.

True.

What is the purpose of the pre-treatment MAA study prior to Y90 therapy?

To evaluate, after intra-hepatic arterial MAA injection, for significant shunt fraction to the lungs, verify that there is desired uptake in the liver lesions (therefore Y90 would be delivered successfully) and no abnormal/unexpected uptake elsewhere (such as other solid organs, the stomach, etc.). Pre-treatment MAA study can be used to identify need for pre-Y90 coil embolization procedures to try to lower shunting from hepatic artery to areas like lung, gut, stomach and then the MAA study procedure may be performed after the coiling procedure to document and ensure that shunting is now minimized and within acceptable ranges to proceed with Y90 therapy.

What are some basic differences between TheraSpheres™ and SIR-Spheres™?

Materials: TheraSpheres™ use glass beads whereas SIR-Spheres™ use resin beads. TheraSpheres™ are FDA approved for unresectable HCC and SIR-Spheres™ are FDA approved for colon cancer metastases to the liver. TheraSpheres™ have much higher activity per bead than SIR-Spheres™ so you can inject fewer particles with TheraSpheres™ to deliver the same dose of radioactivity.

Which artery is commonly coiled prior to Y90 therapy to prevent delivery of particles to the stomach?

Gastroduodenal artery (GDA)

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What is the upper limit for lung shunt fraction on a pre-Y90 therapy MAA study above which Y90 therapy typically may not be considered?

A lung shunt fraction over 20% is typically a contraindication to Y90 therapy. The goal is to prevent severe radiation pneumonitis. Shunt fractions approaching 20% may indicate dose reduction or performing pre-therapy embolization to minimize collaterals to the lungs.

True or false: For board exams lesions in the left and right lobes of the liver may be treated at the same timepoint with Y90?

Generally false. To prevent liver failure, you only treat one lobe at a time, separated by about 4 weeks to allow liver recovery/assessment of response prior to treating the other lobe of the liver.

Does the common hepatic artery most commonly arise from the celiac axis or the superior mesenteric artery?

The common hepatic artery is most commonly a branch of the celiac axis. Know what conventional celiac axis anatomy looks like and be able to identify the major branch vessels for the core exam.

On a Y90 pre-therapy planning angiogram why might you evaluate the superior mesenteric artery anatomy?

Prior to Y90 therapy you should evaluate the superior mesenteric artery anatomy to evaluate for and exclude a replaced or accessory hepatic artery that arises from the SMA. This is important to identify prior to Y90 therapy to prevent non-target embolization and to deliver the Y90 to hepatic lesions through the most appropriate feeding arterial vessels.

MAA particle size is approximately how big?

I've covered this before but MAA particles are approximately 10-100 micrometers in size. This is large enough for particles to get wedged in small capillaries but not large enough to cause significant arterial embolization of larger arteries/branches.

What variables are considered for Y90 dose calculation?

Dose calculation formulas for Y90 are something that I didn't memorize for the ABR core exam but I think it is important to know what factors influence the dose calculation. These are the desired dose to the target, the mass of the liver which can be calculated from 3D volume rendering, the lung shunt fraction, and the anticipated residual waste.

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