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Ultrasound Imaging: Differentiating Benign and Malignant Hepatic Tumors

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Abstract **Review Article**

Hepatic tumors, whether benign or malignant, pose significant health concerns and require accurate diagnosis for appropriate treatment planning. Among the various imaging modalities available, ultrasound plays a crucial role in the initial evaluation of hepatic lesions due to its widespread availability, cost-effectiveness, and lack of ionizing radiation. Ultrasound is a tomographic imaging technique that can provide anatomical and functional images with high resolution and great flexibility at low cost [22]. In ultrasound contrast is produced by the tissues' structure at submillimeter level and is chiefly attributable to the differences in rigidity and density between fluids, watery tissue, connective tissue and fat. The tomograms are formed very rapidly, allowing real time imaging so that studies are quick and interactive. Immediate viewing of tissue motion is intrinsic to ultrasound imaging. The procedure is well tolerated, the only practical problem for the liver being abdominal tenderness that may make probe contact painful. This article aims to explore the utility of ultrasound in differentiating between benign and malignant hepatic tumors.

Keywords: Ultrasound (US), contrast-enhanced ultrasound (CEUS), focal nodular hyperplasia (FNH), Hepatocellular carcinoma (HCC).

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INTRODUCTION

Tumor detection is based on the performance of the method and should include morphometric information (three axes' dimensions, volume) and topographic information (number, location specifying liver segment and lobe/lobes). The specification of these data is important for staging liver tumors and prognosis [1].

Tumor characterization is a complex process based on a sum of criteria leading towards tumor nature definition. Often, other diagnostic procedures, especially interventional ones are no longer necessary. Tumor characterization using the ultrasound method will be based on the following elements: consistency (solid, liquid, mixed), echogenicity, structure appearance (homogeneous or heterogeneous), delineation from adjacent liver parenchyma (capsular, imprecise), elasticity, posterior acoustic enhancement effect, the relation with neighboring organs or structures (displacement, invasion), vasculature (presence and characteristics on Doppler ultrasonography and contrast-enhanced ultrasound (CEUS) [6].

Particular attention should be paid to the analysis of the circulatory bed. Microcirculation investigation allows for discrimination between benign and malignant tumors. Characteristic elements of malignant circulation are vascular density, presence of vessels with irregular paths and size, some of them intercommunicating, some others blocked in the end with "glove finger" appearance.

Diagnosis and characterization of liver tumors require a distinct approach for each group of conditions, using the available procedures discussed above for each of them. The correlation with the medical history, the patient's clinical and functional (biochemical and hematological) status are important elements that should also be considered.

Benign Liver Tumors

They generally develop on normal or fatty liver, are single or multiple, exhibit clear demarcation from the surrounding liver parenchyma on ultrasound images. This distinct boundary facilitates differentiation from adjacent liver tissue. with increased echogenity (hemangiomas, benign focal nodular hyperplasia) or absent, with posterior acoustic enhancement effect (simple cysts, hydatid cyst), lack of vascularization or show a characteristic circulatory pattern, displace normal liver structures and even neighboring organs (in case of large sizes), do not invade liver vessels. The patient has

a good general status, as tumors are often asymptomatic, being incidentally discovered.

Liver Cysts

Hepatic cysts are a common finding, being found in 1%–3% of routine liver, they are more often discovered in women and are usually asymptomatic [2].

They can be single or multiple, with variable size, generally less than 20 mm (congenital). Rarely, sizes can reach several centimeters, leading up to the substitution of a whole liver lobe (acquired, parasitic). They tend to increase in number and size with age. They may be associated with renal cysts, in this case the disease has a hereditary, autosomal dominant transmission (von Hippel Lindau disease) [1], rarely they may present as" complicated" cysts due to the presence of hemorrhage or inflammation.

The ultrasound appearance is a well-defined lesion, with very thin, almost unapparent walls, without circulatory signal at Doppler or CEUS investigation. The content is transonic suggesting fluid composition. The presence of membranes, abundant sediment or cysts inside is suggestive for parasitic, hydatid nature. Acoustic enhancement phenomenon is seen, which strengthens the suspicion of fluid mass. They typically displace normal liver vessels but no vascular or biliary invasion occurs.

Hamartoma

Also known as hepatic adenoma-like lesion, its appearance on ultrasound imaging can sometimes mimic malignant liver tumors, making accurate diagnosis crucial. Small hamartomas are usually echogenic if discretely seen. Often tiny individual hamartomas cannot be resolved and are instead interpreted as diffuse heterogeneous liver echotexture. Larger hamartomas (>10 mm) may appear hypoechoic or anechoic and comet-tail artifact may be seen [9]. The appearances may mimic metastases.

Hemangioma

It is the most common liver tumor with a prevalence of 0.4 - 7.4%. It is generally asymptomatic but also can be associated with pain complaints or cytopenia and/or anemia when it is very bulky. It can be associated with other types of benign liver tumors. Characteristic 2D ultrasound appearance is typically well-defined hyperechoic lesions with sizes of 2–3 cm or less, a small proportion (10%) are hypoechoic which may be due to a background of hepatic steatosis, where the liver parenchyma itself is of increased echogenicity, color Doppler: may show peripheral feeding vessels [3]. Usually located in contact with the diaphragm, a "mirror image" phenomenon can be seen.

CEUS investigation has real diagnosis value due to the typical behavior of progressive CA enhancement of the tumor from the periphery towards the center. The enhancement is slow, during several minutes.

Focal Nodular Hyperplasia

The echogenicity of both focal nodular hyperplasia and its scar is variable, and it may be difficult to detect on ultrasound. Some lesions are well-marginated and easily seen whereas others are isoechoic with surrounding liver [4]. Detectable lesions characteristically demonstrate a central scar with displacement of peripheral vasculature on color Doppler examination. However, these findings are seen in only 20% of cases [5].

CEUS examination allows characterization of tumor nature based on central contrast enhancement and centrifugal dispersion, typical focal nodular hyperplasia shows early arterial centrifugal filling (from the center outwards) with prominent feeding vessel may be seen at arterial phase then at late arterial phase centrifugal filling (opposite to hemangioma and adenoma) and at portal venous phase sustained enhancement (as opposed to adenoma), also unenhanced scar may be present [4].

Adenoma

It has an incidence of 0.03%. Its development is induced by intake of anabolic hormones and oral contraceptives. The tumor is asymptomatic, but may be associated with right upper quadrant pain in case of internal bleeding [6]. 2D ultrasound shows solitary, well-demarcated, heterogeneous mass. Echogenicity is variable: hypoechoic: 20-40%, hyperechoic: ≤30%, often due to fat [7]. A hypoechoic halo of focal fatty sparing is also frequently seen.

Doppler examination shows no circulatory signal [6]. Color Doppler: may show perilesional sinusoids. CEUS exploration is quite ambiguous and cannot always establish a differential diagnosis with hepatocellular carcinoma. Thus, during the arterial phase there is a centripetal and inhomogeneous enhancement. During the portal venous phase there is a moderate wash out. During late phase the appearance is isoechoic or hypoechoic, due to lack of Kupffer cells [8].

Malignant Liver Tumors

Malignant liver tumors develop on cirrhotic liver (hepatocellular carcinoma, HCC) or normal liver (metastases). They are single or multiple (especially metastases), have a variable, generally imprecise delineation, may have a very pronounced circulatory signal (hepatocellular carcinoma and some types of metastases), have a heterogeneous structure (the result of intratumoral circulatory disorders, consequence of hemorrhage or necrosis) and are firm to touch, even rigid. The patient's general status correlates with the underlying disease (vascular and parenchymal decompensation for liver cirrhosis, weight loss, lack of appetite and anemia with cancer) [8].

Hepatocellular Carcinoma (HCC)

Is the most common primary malignancy of the liver. It is strongly associated with cirrhosis, from both alcohol and viral etiologies [10]. Hepatocellular carcinoma is the fifth most common cancer in the world and is the third most common cause of cancer-related death (after lung and stomach cancer). The incidence of hepatocellular carcinoma is rising, largely attributable to a rise in hepatitis C infection [11].

HCC appearance on 2D ultrasound variable appearance depending on the individual lesion, size, and echogenicity of background liver. Typically: small focal hepatocellular carcinoma appears hypoechoic compared with normal liver, larger lesions are heterogeneous due to fibrosis, fatty change, necrosis and calcification [12], a peripheral halo of hypoechogenicity may be seen with focal fatty sparing, diffuse hepatocellular carcinoma may be difficult to identify or distinguish from background cirrhosis.

Contrast-enhanced ultrasound: arterial enhancement from neovascularity, then at portal venous phase decreased echogenicity relative to background liver ("washout") [13], variants have been described with arterial phase hypovascularity with no enhancement or arterial enhancement with no "washout" [10].

Cholangiocarcinoma

Usually it develops on non-cirrhotic liver [6]. The appearance on 2D ultrasound will vary according to the growth pattern [14].

Mass-Forming

Tumors will be a homogeneous mass of intermediate echogenicity with a peripheral hypoechoic halo of compressed liver parenchyma. They tend to be well delineated but irregular in outline and are often associated with capsular retraction [15], which, if present, helps distinguish cholangiocarcinomas from other hepatic tumors.

Periductal Infiltrating

Tumors typically are associated with altered caliber bile duct (narrowed or dilated) without a well-defined mass.

Intraductal

Tumors are characterized by alterations in duct caliber, usually duct ectasia with or without a visible mass. If a polypoid mass is seen, it is usually hyperechoic compared to surrounding liver [15]. CEUS may aid with the diagnosis of cholangiocarcinoma [16], at arterial phase peripheral irregular rim-like enhancement noted with heterogeneous central hypo enhancement then at portal venous phase /delayed phase decreased echogenicity relative to background liver ("wash out") [14].

Hepatic Metastases

18-40 times more common than primary liver tumors [17]. Ultrasound examination is required to detect liver metastases in patients with oncologic history. In addition, the method can incidentally detect metastases in asymptomatic patients. Early identification (small sizes, small number) is important to establish an optimal course of treatment. In addition, discrimination of synchronous lesions that have a different nature is also important knowing that up to 25-50% of liver lesions less than 2 cm detected in cancer patients may be benign [6].

Ultrasound sensitivity for metastases detection varies depending on the examiner's experience and the equipment used and ranges between 40-80%. Sensitivity is conditioned by the size and acoustic impedance of the nodules. For a lesion diameter below 10 mm US accuracy is greatly reduced, reaching approx. 20%. Other elements contributing to lower US performance are: excessive obesity, fatty liver disease, hypomobility of the diaphragm, and certain patterns of hyperechoic or isoechoic metastases that can be overlooked or can mimic benign conditions [6].

Ultrasound appearance: [18], hypoechoic: most common 65% (lung cancer, breast cancer, lymphoma), hyperechoic (colorectal carcinomam, renal cell carcinoma, neuroendocrine tumors).

Peripheral halo: a hypoechoic halo is a concerning feature, sometimes called the target or bull's eye lesion/sign which common in many (lung cancer). Calcified (mucinous adenocarcinoma, gastrointestinal, ovarian mucinous adenocarcinoma).

Cystic (squamous cell carcinoma, ovarian cancer, Pancreatic adenocarcinoma, colorectal carcinoma). Poorly defined (infiltrative) noted at (melanoma, breast cancer, lung cancer).

Contrast-enhanced ultrasound [18], may be useful to increase the conspicuity of lesions and/or guide biopsy, at arterial phase: variable depending on primary tumor: hypovascular (gastrointestinal, ovarian, pancreatic adenocarcinoma), hypervascular (neuroendocrine, melanoma, renal), then at portal venous and late phase "wash out" (decreased echogenicity relative to background liver due to the lack of enhancement); may be the most useful phase for detection as all of the liver metastases show this phenomenon.

Pseudotumors and Inflammatory Masses of the Liver

Besides the entities listed above inflammatory masses or even pseudo- masses can occur. Their diagnosis is quite difficult and the criteria used for differentiation are often insufficient, requiring morphologic diagnostic procedures, use of other diagnostic imaging methods or patient reevaluation from time to time. This includes lesions developed on liver

parenchyma reconstruction, as occurs in cirrhosis, steatosis accumulation or in case of acute or chronic inflammatory diseases [6].

Focal Steatosis

It consists of localized accumulation of fat-rich liver cells. In some cases, this accumulation can mimic a liver tumor. Sometimes the opposite phenomenon can be seen, that is an "island" of normal parenchyma in a “shining” liver. In both cases ultrasound examination identifies a well- defined, un-encapsulated area, with echostructure and vasculature similar to those of normal liver parenchyma. The lesion can have different forms, most cases being oval and located in the IVth segment, anterior from the hepatic hilum. It occurs in dyslipidemic or alcohol intake patients with normal physical and biological status. Benign diagnosis confirmation is made using CEUS examination which proves a normal circulatory bed similar to adjacent liver parenchyma in all three phases of investigation [6].

Liver Abscesses

Are localized collections of necrotic inflammatory tissue caused by bacterial, parasitic, or fungal agents [19]. At ultrasound typically poorly demarcated with a variable appearance, ranging from predominantly hypoechoic (with some internal echoes) to hyperechoic. Gas bubbles may also be seen [20]. Color Doppler will demonstrate the absence of central perfusion [19].

Contrast-enhanced ultrasound shows wall enhancement during arterial phase and progressive washout during portal or late phases. The liquefied necrotic area does not enhance. The use of contrast allows one to characterize the lesion, measure the size of the necrotic area, and depict internal septations for management purposes. In small abscesses (under 3 cm) and in highly septated abscesses, drainage is not recommended [19]. In patients with monomicrobial K. pneumoniae abscesses, the lesion may appear solid and mimic a hepatic tumor [21].

CONCLUSION

Ultrasound imaging plays a critical role in the differentiation of benign and malignant hepatic tumors. By carefully assessing various sonographic features and employing additional imaging techniques, clinicians can make more accurate diagnoses and facilitate appropriate treatment planning. It is important to acknowledge that challenges and limitations exist in differentiating hepatic tumors solely through ultrasound imaging. Overlapping features between benign and malignant lesions can pose diagnostic challenges, necessitating a multimodal approach and, in some cases, image- guided biopsies to achieve a definitive diagnosis.

The ability to differentiate between benign and malignant hepatic tumors has significant clinical implications. Accurate diagnosis enables clinicians to develop appropriate treatment strategies, including surveillance protocols, interventional procedures, and surgical interventions. Furthermore, regular follow-up and monitoring are crucial to detect any recurrence or progression of malignant tumors and ensure timely intervention. While ultrasound imaging serves as a valuable tool in the initial evaluation of hepatic tumors, collaboration with healthcare professionals and radiologists is essential for comprehensive assessment and treatment decisions.

In conclusion, ultrasound imaging, in conjunction with additional imaging techniques, plays a pivotal role in differentiating benign and malignant hepatic tumors. Its diagnostic significance lies in enabling accurate diagnosis, facilitating appropriate treatment planning, and guiding surveillance protocols for optimal patient care.

REFERENCE

1. https://www.intechopen.com/chapters/27578.
2. Mathieu, (1997). Van Sonnenberg, 1994.
3. https://radiopaedia.org/articles/hepatic-haemangioma-3?lang=us
4. https://radiopaedia.org/articles/focal-nodular-hyperplasia?lang=us
5. Riccardo, L., Dania, C., Carlo, B. (2004). Focal Liver Lesions, ISBN: 9783540644644 - Google Books.
6. https://radlines.org/Ultrasonography_of_liver_tumors#cite_note- BadeaIoanitescu2012-1.
7. John, P., McGahan, B. B. (2007). *Goldberg. Diagnostic Ultrasound*, ISBN: 1420069780.
8. https://www.intechopen.com/chapters/27578.
9. Zheng, R. Q., Zhang, B., Kudo, M., Onda, H., & Inoue, T. (2005). Imaging findings of biliary hamartomas. *World journal of gastroenterology: WJG*, *11*(40), 6354.
10. https://radiopaedia.org/articles/hepatocellular-carcinoma?lang=us.
11. Parkin, D. M., Bray, F., Ferlay, J., & Pisani, P. (2001). Estimating the world cancer burden: Globocan 2000. *International journal of cancer*, *94*(2), 153-156.
12. Au, W. Y. (2008). *Hepatocellular Carcinoma. World Scientific Pub Co Inc*, ISBN:9812707999. Read it at Google Books - Find it at Amazon.
13. Malhi, H., Grant, E. G., & Duddalwar, V. (2014). Contrast-enhanced ultrasound of the liver and kidney. *Radiologic Clinics*, *52*(6), 1177-1190. doi: 10.1016/j.rcl.2014.07.005.
14. https://radiopaedia.org/articles/cholangiocarcinoma?lang=us.
15. Chung, Y. E., Kim, M. J., Park, Y. N., Choi, J. Y., Pyo, J. Y., Kim, Y. C., ... & Choi, S. Y. (2009). Varying appearances of cholangiocarcinoma: radiologic-pathologic correlation. *Radiographics*, *29*(3), 683-700. doi:10.1148/rg.293085729.
16. Malhi, H., Grant, E. G., & Duddalwar, V. (2014). Contrast-enhanced ultrasound of the liver and

kidney. *Radiologic Clinics*, *52*(6), 1177-1190. doi: 10.1016/j.rcl.2014.07.005.
17. https://radiopaedia.org/articles/hepatic-metastases-1?lang=us.
18. https://radiopaedia.org/articles/ultrasound-appearances-of-hepatic- metastases?lang=us.
19. https://radiopaedia.org/articles/hepatic-abscess-1?lang=us.
20. Gebel, M. (2000). *Ultrasound in gastroenterology and hepatology*. Wiley- Blackwell, ISBN:0632055286. Read it at Google Books - Find it at Amazon.
21. Hui, J. Y., Yang, M. K., Cho, D. H., Li, A., Loke, T. K., Chan, J. C., & Woo, P. C. (2007). Pyogenic liver abscesses caused by Klebsiella pneumoniae: US appearance and aspiration findings. *Radiology*, *242*(3), 769-776. doi:10.1148/radiol.2423051344.
22. https://link.springer.com/chapter/10.1007/3-540-26354-3_1.