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Imaging and Pathologic Features of the Common Hepatic Focal Lesions

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Authors' contributions

This work was carried out in collaboration between all authors. Author LM did the study design, provision of the study patients and data collection. Author MMN did data analysis and interpretation. Authors WEA and ZZ did the literature searches. Author ZZ wrote the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Background and Study Aims: Focal liver lesions are considerably detected in every day practice. Radiological imaging has a significant role in the detection and follow up of hepatic focal lesions. At times, the pathological study is absolutely necessary to confirm a definite diagnosis. The aim of this study was to estimate the probability that radiological scans to diagnose different types of focal liver lesions as primary imaging modalities are inconclusive.
Methods: This study was carried out at National Hepatology and Tropical Medicine Research Institute, Egypt. Abdominal ultrasonography, triphasic computed tomography +/- magnetic resonant imaging and ultrasound guided percutaneos core biopsy of 42 patients with suspected hepatic focal lesions were carried out.
Results: Out of 42 patients with liver focal lesions detected by transabdominal ultrasound and with inconclusive criteria by triphasic computed tomography +/- magnetic resonant imaging then

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confirmed by pathological examination, 8 were regeneration nodules, 18 hepatocellular carcinoma (HCC), 6 adenomas, 5 haemangiomas, 1 undifferentiated carcinoma,1 sarcoma., 2 abscesses and 1 dysplastic nodule.

Conclusions: Ultrasound is a safe and rapid method of detecting hepatic focal lesions, also allowed ultrasound guided interventions. High proportions of inconclusive criteria by additional scans were observed in this study. In this case histopathology is recommended to confirm the diagnosis.

Keywords: Liver focal lesions; ultrasound; computed tomography; magnetic resonant imaging; histopathology.

ABBREVIATIONS

FNH : Focal Nodular Hyperplasia
HCC : Hepatocellular Carcinoma
CT : Computed Tomography
MRI : Magnetic Resonance Imaging
AFP : Alpha Fetoprotein
US : Ultrasound
AURC : Area under ROC Curve

1. INTRODUCTION

Hepatic focal lesions whether solid or cystic masses range from benign lesions with an indolent clinical course to aggressive malignant tumors. They are common findings as a result of increasing use of imaging modalities in patients with nonspecific abdominal complaints. The definite diagnosis is settled using both imaging techniques and histopathology [1].

Conventional ultrasonography has an important diagnostic role regarding the liver and focal liver masses. Confidently identify and diagnose liver cystic lesions. Can suggest the diagnosis of solid lesions based on their variable appearance; consequently in many cases when a mass seen on ultrasonography is referred for contrast-enhanced CT or MR imaging for an accurate diagnosis [2].

Despite the safety and low cost of unenhanced ultrasound, it lacks the characterization of liver lesions which is essential for the final diagnosis and then treatment strategy decision. Contrast-enhanced ultrasound is an emerging modality that has some utility but is not widely available yet [3].

Triple-phase CT scan for a late arterial phase, a portal venous phase, and a delayed venous phase which is the most important aspect and distinct from a standard abdominal CT that includes only a portal venous phase and a delayed phase. A technically appropriate CT or MRI will provide information to the clinician about the characteristics of liver lesion, its location and relationship to anatomical structures (such as hepatic vasculature and the gallbladder) and in case of malignancy, allow tumor staging [3].

In addition, US surveillance is recommended in patients with liver cirrhosis, since CT +/- MRI may provide confident diagnosis of HCC and liver biopsy may be not necessary in many cases.

Pathological study is highly accurate in the evaluation of focal liver lesions when the diagnosis cannot be reliably confirmed radiologically. Which is useful in showing the characteristics and origin of metastatic lesions, and to distinguish dysplastic lesions from hepatocellular carcinoma, to differentiate liver adenoma from FNH, or to confirm the nature of atypical lesions [1]. Core biopsies have greater diagnostic accuracy compared to fine needle aspiration and allows assessment of both architectural and cytological features [4].

In this study, our aim was to estimate the probability that radiological scans to diagnose different types of focal liver lesions as primary imaging modalities are inconclusive.

2. PATIENTS AND METHODS

The study was approved by the institutional ethical committee, and all patients provided an informed consent.

This was a prospective study of 42 cases with suspected hepatic focal lesions at National Hepatology and Tropical Medicine Research Institute, Egypt that was conducted from February 2015 to October 2015.

2.1 Inclusion Criteria

Cases of focal hepatic lesions detected by transabdominal ultrasound during the study period.

2.2 Exclusion Criteria

Diffuse fatty infiltration, Storage disorders, and diffuse infiltrative malignancies, lymphoma and leukemia.

2.2.1 Patients

There were 32 men and 10 women, their age range 28-72 years, mean age 55.74±9.44 years.

All patients were subjected to detailed history, thorough clinical examination, and laboratory tests including: Complete blood count (CBC), transaminases; aspartate aminotransferase (AST), and alanine aminotransferase (ALT), alkaline phosphatase (ALP), serum albumin, total bilirubin, INR**,** alpha fetoprotein (AFP), hepatitis seromarkers for HCV (anti HCV) and for hepatitis B virus (HBV); (HBsAg, anti HBc and anti HBs) using ELISA technique.

2.2.2 Imaging technique

All patients were referred for ultrasound diagnosis where conventional ultrasonographic examination was performed on all lesions and an ideal plane was selected to allow clear and accurate showing of the lesion and the surrounding liver parenchyma including identification of the lesion and determination of its size and morphologic characteristics.

Scanning process included: scanning of the liver was concerned with its size in both midline and mid-clavicular line, the surface of the liver and special emphasis on the presence of focal lesions and its description as regards the site, number, size, echopattern (hypoechoic, hyperechoic, isoechoic or heterogeneous). The rest of the liver parenchyma was also scanned for diffuse liver pathology e.g. cirrhosis. The portal vein diameter and patency (to exclude the presence of thrombus inside). Scanning of the spleen included the size, textural changes and the presence of focal lesions. Scanning for ascites or any masses was also done.

Then all patients were referred to triphasic CT +/- MRI for characterising hepatic focal lesions that were seen by convensional abdominal ultrasonography.

2.2.3 Histopathological examination

All patients were then subjected to ultrasonographically guided percutaneous core biopsy for pathological confirmation as previous liver imaging has been inconclusive.

2.3 Statistical Analysis

Continuous data were presented as mean ± standard deviation while categorical data were presented as number (percent). A p value less than 0.05 was considered statistically significant. Receiver operating characteristic curve was constructed to identify the AFP cutoff value that predicts focal liver lesions. All statistical calculations were done using computer programs SPSS.

3. RESULTS

The present study was conducted on forty two patients with suspected focal liver lesions detected by trans-abdominal ultrasonography and confirmed by histopathological examination at National Hepatology and Tropical Medicine Research Institute, Egypt.

After pathological confirmation of all lesions, they were 8 regeneration nodules, 18 HCC, 6 adenomas, 5 haemangiomas, 1 undifferentiated carcinoma, 1 sarcoma., 2 abscesses and 1 dysplastic nodule Table 1.

Table 1. Distribution of 42 cases diagnosed by histopathological examination

Lesion type	Number	%
- Regeneration nodule	8	19.0
- HCC	18	42.9
- Adenocarcinoma	6	14.3
- Haemangioma	5	11.9
- Undifferentiated carcinoma	1	2.4
- Sarcoma	1	2.4
- Abscess	2	4.8
- Dysplastic nodule	1	2.4

There were 32 men and 10 women, their age range 28-72 years with mean age 55.74±9.44 years. Total bilirubin was statistically significant in patients with malignant masses compared to benign cases (p= 0.01), while AFP did not show a statistical significant difference between malignant and benign masses Table 2.

AFP at cut off 20.7 ng/ml can predict presence of hepatocellular carcinoma with a sensitivity and specificity 92.9% and 74% respectively with AURC 0.88 Fig. 1.

Table 2. Clinical data of 42 studied patients

	Benign cases (n= 16)	Malignant cases (n= 26)	P value
Sex male/female	12/4	20/6	0.89
HbsAg +ve/-ve	0/16	1/25	0.43
HCV Ab +/-	10/6	15/10	0.87
	Mean±SD	**Mean±SD**	
Age (years)	54.57±10.90	56.40±8.70	0.56
HB	12.29±1.50	11.98±2.33	0.67
WBC	6.06±1.82	6.57±3.06	0.54
Plt	166.46±80.39	182.82±124.55	0.67
T.Bil	1.05±0.39	1.63±0.87	**0.01**
ALT	65.98±57.57	49.38±36.62	0.31
AST	83.00±74.66	67.43±51.48	0.47
Albumin	3.67±0.65	3.44±0.63	0.33
INR	1.23±0.27	1.18±0.13	0.47
AFP	34.77±97.69	641.79±2650.53	0.38

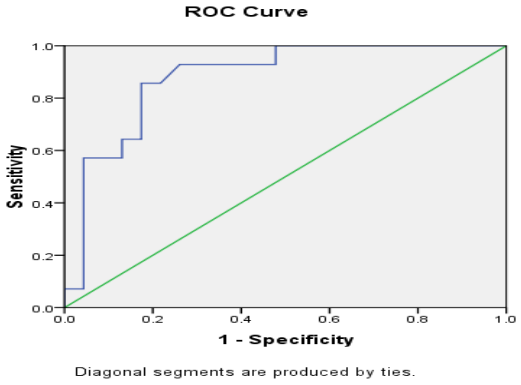

Fig. 1. ROC curve for AFP

Table 3. Distribution of 42 cases after CT +/- MRI scans

CT +/- MRI	Number of cases	Pathology
- Regeneration nodule	3	8
- HCC	2	18
- Adenocarcinoma	0	6
- Haemangioma	4	5
- Undifferentiated carcinoma	4	1
- Sarcoma	0	1
- Abscess	0	2
- Dysplastic nodule	1	1
Total	14	42

The ultrasound findings of the studied patients showed that 52.4% of the studied hepatic focal lesions were detected in the right lobe followed by33.3% in both lobes. Lesions were single in (50%) of patients and multiple in (26.2%). The size of focal lesions was less than 3 cm in (76.2%), 3-5 cm in (4.8%) and more than 5 cm in (19.0%).

Subsequent CT +/- MRI revealed suggestive diagnosis only in 14 cases with inconclusive criteria Table 3.

4. DISCUSSION

Transabdominal ultrasound is highly sensitive in the detection of hepatic focal lesions such as primary malignant liver tumors, metastasis, Liver abscess and hydatid lesions which are common focal liver lesions. Hepatic cysts and haemangiomas with a classic appearance can be safely diagnosed with ultrasonography alone [5].

Hapani et al. [5] assessed the specificity of ultrasound in diagnosing liver focal lesions and reported a specificity of 75%, 85.7%%, 94.4%%, 100%% for primary malignant liver tumors, metastasis, Liver abscess and hydatid lesions respectively and found a significant association between ultrasonography findings and fine needle aspiration cytology diagnosis.

The National Institute for Health and Care Excellence (NICE) defined the inconclusive scan as "an unenhanced ultrasound scan in which a FLL is detected, but not characterized". It was estimated that 43% of ultrasound scans were inconclusive, so require further diagnostic investigation [6].

The main aim of liver imaging is to distinguish between malignant and benign lesions that are not likely need further treatment. If focal liver lesion detected by unenhanced ultrasound scan, patient is usually referred to CT and/or MRI to

exclude metastasis of various gastrointestinal organs, and when the imaging criteria is not conclusive, liver biopsy is mandatory for definite diagnosis.

In this study we aimed to estimate the probability that radiological scans to diagnose different types of focal liver lesions as primary imaging modalities are inconclusive.

High Alpha fetoprotein serum levels have been found in 60–70% of patients with Hepatocellular carcinoma in the absence of other causes that increase this protein. Alpha fetoprotein levels ≥200 and 400 ng/mL in patients with an identified liver mass by imaging techniques are diagnostic of hepatocellular carcinoma with high specificity [7]. In this study, AFP at cut off 20.7 ng/ml can predict presence of hepatocellular carcinoma with a sensitivity and specificity 92.9% and 74% respectively with AURC 0.88.

Although CT and MRI with their improved diagnostic capability are considered the modalities of choice for an accurate diagnosis without the need for a liver biopsy [8]. However, in our study, around 33% of cases (14/42) with identified focal liver lesions were described as inconclusive by the operator, and in the remaining cases, the imaging scans not leading to a firm conclusion. Actually, HCC can be diagnosed with ≥ 90% accuracy with imaging alone when a lesion is 2cm, thus avoiding the requirement for liver biopsy in almost all cases [8].

The various liver focal lesions included in this study were regeneration nodules, HCC, adenomas, haemangiomas, undifferentiated carcinoma, sarcoma, abscesses and dysplastic nodule.

Regarding liver abscesses, pyogenic Liver Abscess; ultrasound usually present spherical, oval or mildly irregular hypoechoic lesions with distal enhancement in 75% of cases. A considerable number of abscesses show higher reflectivity than the adjacent normal hepatic tissue. They are usually centerally and rarely reaching the hepatic capsule [5]. However, in this study the imaging criteria was not conclusive and the diagnosis of liver abscesses was done by histopathological examination.

Regarding hemangioma, which is the most common primary liver tumor; ultrasound appearance is a well circumscribed, uniformly hyperechoic lesion. This classic appearance occurs in up to 70%. A minority of hemangiomas may present a hypoechoic or an isoechoic mass relative to the liver parenchyma. Hemangiomas more than 2.5 cm are usually show posterior enhancement. Some hemangiomas, especially if they are large (greater than 5-6 cm in diameter) present a heterogeneous ultrasound echo pattern. This atypical appearance makes difficult differentiation from other focal lesions [5]. Similarily in this study, imaging modalities diagnosed hemangiomas in 4 cases out of 5 cases obtained by pathological study.

CT, MRI, and US techniques are reliable to confirm the diagnosis of hepatic hemangioma as this lesion presents with unique features upon imaging with peripheral nodular enhancement and progressive centripetal fill-in. MRI is preferred in cases where the lesion is < 3 cm or found close to the heart or intrahepatic vessels. Contrast-enhanced US, if available, can increase both the sensitivity and specificity of US and is effective in the diagnosis of hepatic hemangioma [9,10].

As regard hepatocellular Carcinoma, HCC is the most common primary liver cancer occurring in 80% of primary liver malignant tumor. Ultrasound appearance of HCC is variable in echogenicity, Mostly the small HCC (< 5 cm) are hypoechoic with thin peripheral hypoechoic halo corresponding to a fibrous capsule, with increasing in size, the masses tend to become more heterogeneous secondary to necrosis and fibrosis. Calcification is uncommon. Also small tumors may appear diffusely hyperechoic, as a result of fatty metamorphosis or sinusoidal dilatation, making them unrecognized from hemangiomas. In addition ultrasound can provide information on shape, growth pattern and vascularity of the tumor. Also ultrasound can provide guided biopsy or FNAC with sensitivity of 91% and 95%, with a specificity of 92%-100% [11].

A CT or MRI should be performed in cirrhotic patients with identified focal lesion > 1 cm by ultrasound, an elevated α-fetoprotein in absence of liver lesion by ultrasound, or when HCC is clinically suspected. 85% of HCC have arterial enhancement with washout according to the suspected guidelines for HCC diagnosis [12-14]. In our study, CT+/- MRI were suggestive in only 2 cases out of 18 HCC cases by pathology.

The liver is one of the commonest sites for metastasis and the most common primary tumors are those of the gut, breast, lung and melanoma [5]. Accordingly, liver biopsy is useful in showing the characteristics and origin of metastatic lesions.

5. CONCLUSIONS

Ultrasound is a safe and rapid method of detecting hepatic focal lesions, also allowed ultrasound guided interventions. High proportions of inconclusive criteria by additional scans were observed in this study. In this case histopathology is recommended to confirm the diagnosis.

SUMMARY BOX

- Radiological imaging has a significant role in the detection and follow up of hepatic focal lesions.
- The aim of this study was to estimate the probability that radiological scans to diagnose different types of focal liver lesions as primary imaging modalities are inconclusive.
- High proportions of inconclusive criteria by CT and MRI scans were observed in this study.
- Sometimes, the pathological study is absolutely necessary to confirm a definite diagnosis as found in the present study.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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