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Diagnostic Interventions of Small < 2.5mm Focal Liver Lesions: US and CT-guided Biopsy

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***Abstract*— Purpose : The present study assess factors affecting the success of US and CT-guided liver biopsy of focal lesions on the basis of experience when cytopathologic examination results were available.Methods and Materials: 175 liver biopsies and punctures in 175 patients(120 male and 55 female) were performed under US or CT control. Lesions ranged in diameter from 9mm to 25 mm. We utilized US guidence in 103(66.02%) cases and CT guidence in 53(33.97%) cases. Ultrasound equipment supplied with 3.5 and 7 MHz linear and convex transducers, MDCT machine and biopsy needles were used. The on-site cytologic evaluation guided the radiologist to continue to another biopsy pass and avoid a nondiagnostic biopsy result.**

Results: During a 4-year period we performed FN liver biopsies or punctures in 175 patients (120 males and 55 females) with small (9-25mm) liver lesions. The CT guidance was utilized for biopsy of deep, small liver masses of ultrasonographically non visible and subdiaphragmatically located lesions. Interventional procedures under imaging control of small focal liver lesions had a sensitivity of 97.76 %, specificity of 80.48 % and accuracy of 93.71 %. The PPV (positive predictive value) is 94.24 % and the NPV (negative predictive value) –91.66%. Conclusion: Interventional procedures under imaging (US and CT) control of the small focal liver lesions is a highly reliable, safe, inexpensive invasive procedure with great diagnostic value in suspected HCC less than 2 cm in diameter, liver metastases, as well as all benign tumors without typical findings on either dynamic multi-detector CT or CEUS.

***Index Terms*— Focal Liver lesions, Imaging control, Fine-needle aspiration Biopsy, Fine-needle puncture.**

I. Introduction

Focal liver lesions are increasingly being discovered with the widespread use of diagnostic imaging modalities, and differentiation is considered to be critical for determining treatment options. Tremendous advancements in imaging techniques, including ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI) have resulted in these modalities being accepted as effective and thus widely used to characterize focal liver lesions [1-4]. With the advantages of non-invasiveness, no radiation, contrast-enhanced (CEUS) has become increasingly important in the detection and characterization of focal liver tumors over the past years [6-9].

Nevertheless the US and CT guided interventional procedures of solid and liquid liver lesions is a widely accepted method when characterization of lesion nature is needed. It is an accepted standard of practice that image guidance is used in order to guide and direct the liver biopsy(LB) and punctures(LP) [10,11].

II. Purpose

The present study assess factors affecting the success of US and CT-guided liver biopsy of focal lesions on the basis of experience when cytologic and pathologic examination results were available.

III. Material and Methods

A. Patients

One hundred and seventy five liver biopsies in 175 patients /120 males and 55 females/ were performed under US or CT guidance between December 2010 and October 2014 years. HCCs exceeding 2.5 cm in diameter without typical radiological findings and those less than 2.5 cm in diameter, the liver metastases, as well as all benign tumors without typical findings on either dynamic multi-detector CT or CEUS were confirmed using cyto-pathological results from percutaneous biopsy or surgery. The database included clinical data, as well as technical parameters related to the procedure performed, such as needle size, needle type, the number of passes performed, and whether a cytologist was present during the biopsy. Lesions size ranged from 9 mm to 25 mm in diameter. The indications for invasive manipulation and imaging control were clinically discussed and the patients were generally prepared for the invasive manipulations. All patients considered for liver biopsy met preestablished laboratory criteria: a platelet count of greater than 60×109/L and an international normalized ratio of less than 1.5 at the time of the procedure. Patients with coagulopathy were treated prior to the biopsy. The invasive manipulations were performed with the informed consent of patients.

B. Image guided biopsy technique:

Biopsies were performed by one of three interventional radiologists each of whom had more than 5 years experience. The number of biopsy passes is usually determined by the radiologist performing the biopsy by consulting results of an on-site cytologic evaluation (performed by a cytologist), on the basis of findings from a rapid touch preparation smear. This on-site cytologic evaluation guides the radiologist to continue to another biopsy pass and avoid a nondiagnostic biopsy result on one hand and potentially reduces the rate of repeat biopsies on the other hand. However, the service of an

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on-site cytologist is not always available. The liver was scanned with a Ultrasonic equipment - with 3.5 and 7 MHz linear and biopsical transducers and MDCT machine. The "Chiba "needles 16,18,20 G, catheters pig-tail 7-8F, 18 G multiple-side hole needle were used/Fig.1/.

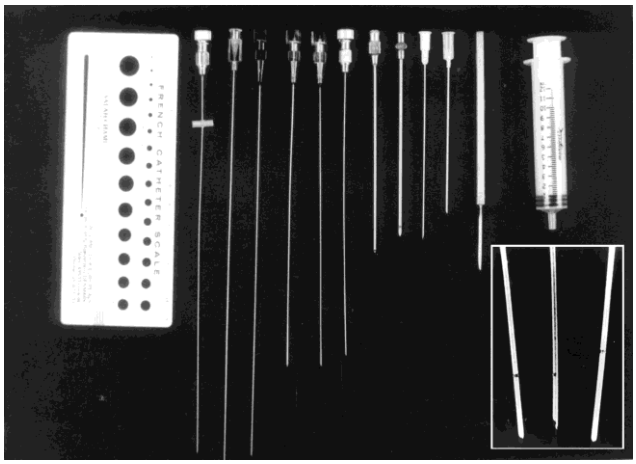

Figure1: Set for interventional procedures and modified "Chiba" needles.

The patient was positioned to facilitate access to the lesion with the shortest and safest needle trajectory. A large amount of ascites was considered a relative contraindication to the procedure, and paracentesis was performed prior to biopsy in six patients. After proper skin disinfection and administration of a local anesthetic, an biopsy needle was advanced into the lesion under real-time US or CT guidance and a sample was taken (Fig.2).

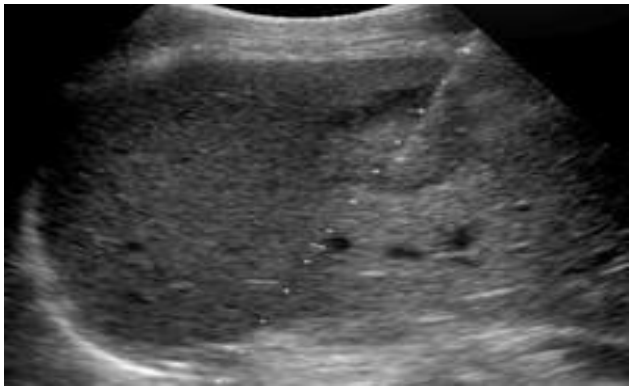

Figure 2: Percutaneous US-guided biopsy in 53-year-old man. Heterogeneous focal liver lesion, with the needle traversing the lesion.

In heterogeneous lesions, the needle was advanced to the periphery to avoid central necrosis. The cytopathologist was with more than 10 years of experience. Tissue cores were rolled on a glass slide (touch prep), and two smear preparations were made. One slide was air dried and stained with a modified Giemsa stain for rapid on-site interpretation. The other slide was fixed in alcohol and stained with the Papanicolaou method. The biopsy procedure was terminated when at least one solid core was obtained from the lesion and the cytologist immediately outside the biopsy suite considered the touch prep results to be satisfactory, with a sufficient amount of tissue for analysis. Tissue cores were then preserved in formalin and sent to the Department of Pathology for histologic examination by a histopathologist.

IV. Results

During a 4-year period we performed FN liver biopsies or punctures in 175 patients (120 males and 55 females) with small (9-25mm) liver lesions. In all cases, after a precise localization and volume measurement of the lesion under US or CT control, access to the region of interest were determined. The obtained diagnostic results are presented on Table 1.

Table 1: Distribution of the patients according to the final diagnosis of the liver lesions and type of the invasive procedures performed under imaging control.

Invasive procedures / Diagnosis	FNAB under US control	FNAB under CT control	FNP under US control	FNP under CT control	All
Hemangioma	4 (2.28%)	1 (0.57%)	-	-	5 (2.85%)
FNH	18 (10.28%)	13 (6.85%)	-	-	31 (17.71%)
Adenoma	4 (2.28%)	6 (3.42%)	-	-	10 (5.71%)
Metastases	48 (27.42%)	20 (11.42%)	-	-	68 (38.85%)
HCC	29 (16.57%)	13 (7.42%)	-	-	42 (24.00%)
Abscesses	-	-	8 (4.57%)	2 (1.14%)	10 (5.71%)
Necrotic Neoplastic zones	-	-	8 (4.57%)	1 (0.57%)	9 (5.14%)
All	103 (58.85%)	53 (30.28%)	16 (9.14%)	3 (1.71%)	175 (100%)

A total of 123 lesions (70.28%) were located in the right lobe of the liver, and 52 lesions (29.71%) were located in the left lobe. There was no relationship between the lesions anatomic position in the liver and the diagnostic accuracy of the specimen or the number of passes needed. In all of these invasive manipulations of focal liver lesions the US or CT control was sufficient for the exact penetration to the region of interest, proper location of the top of the needle and obtaining material for cytological and pathologic examination(Fig.3).One hundred and twenty three lesions (70.28%) were located in the right lobe of the liver, and 52 lesions (29.71%) were located in the left lobe. Among right lobe lesions, 49 (39.83%) were located in the superior portions of segments VII and VIII (subdiaphragmatic), 74(60.16%) in the V and VI segments. 25 (48.07%) of the left lobe lesions were located in the upper subdiaphragmatic

area of segment IVa or II. There was no relationship between the lesion's anatomic position in the liver and the diagnostic accuracy of the specimen or the number of passes needed.

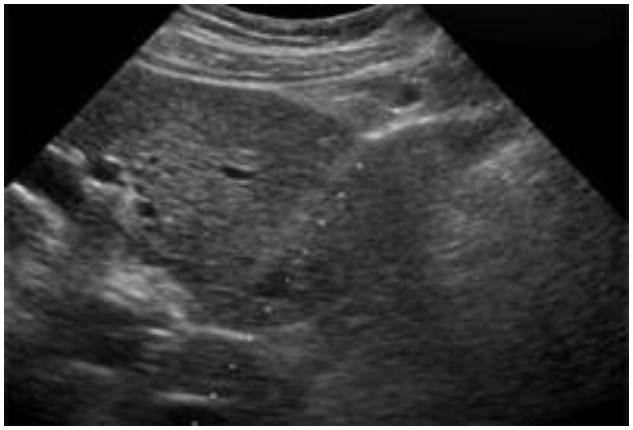

Figure 3: Transverse US images show 1.4cm hypoechoic left lobe liver lesion. The biopsy needle is seen in an eccentric location in the lesion.

All results were verified by cytologic and pathologic examination. One hundred and fifty-six/89.14%/ FNAB of the included patients with liver solid regions were performed under imaging control. In 103(66.02%) of these we used US control for guiding the invasive manipulation. Using original "Chiba" needle and modified one with a hole 8 mm distant from the tip, we took sufficient and of good quality material for cytological and in some cases pathologic examination. In all of these invasive manipulations of solid liver lesions the US control was sufficient for the exact penetration to the region of interest, proper location of the top of the needle and obtaining material for cytologic and pathologic examinationz/Fig.3/.

In 53 (33.97%) of all 156 cases with solid liver lesions FNAB were performed under CT guidance because of deep (subphrenical) location of the lesion and insufficient evaluation under US control (when the lesion is isoechogenic)Fig.4. In 16 (84.21%) of all 19 liver fluid containing lesions FNA were performed under US control. 10 abscesses, 9 necrotic neoplastic zones were proven. Ten FNA were continued with evacuation of the liquid collection and application of wide spectrum antibiotic (in cases with abscesses) or cytostatics in 9 cases with necrotic neoplastic zones.

No major complications were observed, and most patients tolerated the procedure well. Nine patients (5.14%) experienced moderate pain, which required the use of analgesics, but symptoms subsided within a couple of hours in all cases, and no bleeding was noted at postprocedural US performed in these patients. None of the patients was hospitalized as a result of the biopsy.

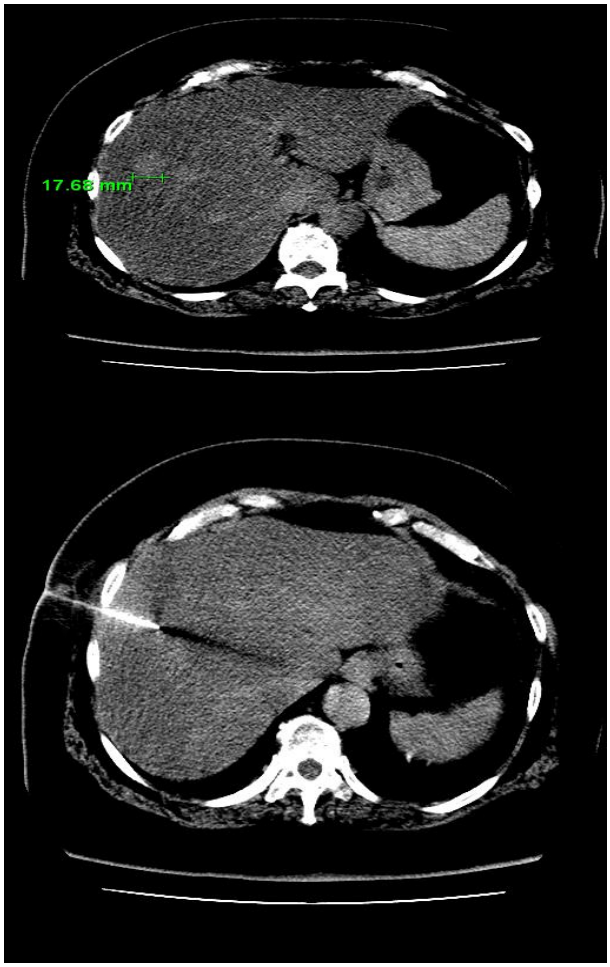

Figure.4/ b/ Percutaneous CT- guided FNAB biopsy of isodense solid liver lesion. **a.** Lesion during the biopsy- the needle is better visualized in the focal lesion.

Using invasive LB(FNAB) under US or CT control of the examined 175 patients with focal liver lesions we obtained the following results: there were 131 true positive cases, 33 true negative, 8 false positive and three false negative results. Overall this demonstrated that interventional procedures under imaging control of small focal liver lesions had a sensitivity of 97.76 %, specificity of 80.48 % and accuracy of 93.71 %. The PPV(positive predictive value) is 94.24 % and the NPV(negative predictive value) – 91.66 %.

We preferred a real-time US control for better visualization of all steps of the invasive manipulations of small solid and liquid liver regions – detection and proper localization, planning the path of penetration to the lesion, following the position of the needle to avoid complications. On-site cytologic examination (touch prep) can be helpful for limiting the number of passes required to achieve the diagnosis and, in a limited number of cases, may be the only diagnostic test.

V. Discusions

The role of image-guided percutaneous liver biopsy as a safe and accurate diagnostic procedure for the evaluation of focal liver disease has been well established, especially with the advent of biopsy needles and improvements in image quality [12]. US and CT guidance are the techniques of choice for liver biopsy. In comparison with CT, US is often

more readily available. US-guided biopsies may be easier to perform, faster, and less expensive and do not expose the patient to radiation [12].

Automatic biopsy guns simplify the technique. This is an advantage in biopsy of small hepatic lesions, such as all in our study that were less than 3 cm in maximal diameter. The larger caliber 18-gauge needle can also be guided more easily than fine, highly flexible needles, and its greater visibility on the US image permits more precise targeting of small lesions [13]. In our experience, the automated 18-gauge biopsy gun is very accurate and reliable.

We found no statistical relationship between the number of needle passes and lesion size in our study. Small hepatic lesions are more challenging to target, and one might expect higher miss rates in small versus large lesions. But on the other hand, small tumors may have a more uniform distribution of cancerous tissue, without the hemorrhage, necrosis, or sclerotic changes that are common and often make diagnosis challenging in large lesions[13].

Lesion type, however, did affect the number of passes. Metastatic lesions usually demonstrate characteristic cells, which are different from both liver cells and benign or nonspecific tissue. In metastatic lesions, a fine-needle aspiration biopsy is often sufficient for diagnosis[14]. In our study, the anatomic location of the lesion within the liver was not a factor in the success of the biopsy. Of all biopsies in "difficult-to-access" lesions, only two resulted in a sample that was insufficient for diagnosis, and the reason was necrotic tissue.

However, the service of an on-site cytologist is not always available. This brings up a question: Can we predict in which biopsies the cytology service would be essential and which could be managed without it? We assumed that on-site cytologic evaluation would be more important in small lesions, which are more challenging to sample. We also assumed that a metastasis would be easier to differentiate from a lesion such as a hepatocellular carcinoma originating from hepatocytes.

There were several limitations to our study. No long-term follow-up for complications was performed, and we did not check for subclinical bleeding. The use of larger or smaller needles could have affected the success rates because of the different amounts of tissue obtained, but we believe that the use of a single needle size makes our results more homogeneous. Another limitation may be related to sampling error in the lesion sampled for biopsy. In 16 cases, biopsy disclosed either inflammatory changes or normal liver. These diagnoses may not represent the real underlying process in the targeted lesions.

In conclusion, successful biopsy of metastatic liver lesions requires fewer passes than required for benign lesions or primary liver tumors. Our findings suggest that lesion size and location do not influence the number of passes needed and three passes would be diagnostic in almost 90% of all US-guided focal liver biopsies.

VI. Conclusion

Interventional procedures under imaging (US and CT) control of the small focal liver lesions is a highly reliable, safe, inexpensive invasive procedure with great diagnostic value in suspected HCC less than 2,5 cm in diameter, liver metastases, as well as all benign tumors without typical findings on either dynamic multi-detector CT or CEUS. Therefore, we recommend US or CT-guided liver biopsy as a routine method for the diagnosis of difficult to differentiate focal liver lesions.

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