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Focal hepatic lesion ultrasound-guided biopsies

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Abstract

Purpose: To compare the results of pathologic and cytologic reports of specimens acquired from focal liver lesions using ultrasound-guided biopsy and to evaluate the necessity of performing both techniques in the same patient. **Materials and methods:** 21 patients were eligible for enrollment in the study. Specimens for both pathologic and cytologic examination were obtained from 16 lesions using a 17G needle guide in a single puncture attempt. In 2 cases the diagnosis was based on cytologic smears. In 3 cases only histologic sections were acquired. The needle was introduced under continuous ultrasonographic control using a freehand technique. A cytologist was present at all times. **Results:** The diagnostic sensitivity of cytologic examination was 83.33% and that of histologic examination was 94.74%. Histology diagnosed all cases of benign lesions and was proved inconclusive in 1 patient. The diagnostic sensitivity and accuracy of both methods combined reached 100%. In 94.4% malignancy was immediately diagnosed by cytology. **Conclusions:** Combination of both methods should increase the sensitivity and accuracy in diagnosing focal liver lesions performing a safe minimally invasive technique.

Keywords: focal liver lesions, ultrasound-guided biopsy, pathologic and cytologic examination

Rezumat

Scopul lucrării: de a compara rezultatele examenelor anatomopatologic şi citologic ale probelor obţinute prin puncţie hepatică ghidată ecografic din leziuni hepatice focale şi de a evalua necesitatea efectuării ambelor tehnici la acelaşi pacient. **Material şi metodă:** în studiu au fost incluşi 21 de pacienţi. Din 16 leziuni s-au obţinut probe atât pentru examenul anatomopatologic, cât şi pentru cel citologic, folosind un ac de ghidaj de 17G prin efectuarea unei singure puncţii. În 2 cazuri diagnosticul a fost bazat pe probele citologice. În 3 cazuri s-au obţinut doar secţiuni histologice. Acul a fost introdus sub control ultrasonografic continuu folosind tehnica freehand. Medicul citolog a fost prezent în toate cazurile. **Rezultate:** Diagnosticul citologic are o sensibilitate de 83,33%, iar cel histologic de 94,74%. Examenul histopatologic a diagnosticat toate cazurile de leziuni benigne, într-un caz diagnosticul s-a dovedit neconclusiv. Sensibilitatea şi acurateţea ambelor metode combinate ajunge la 100%. În 94,4% malignitatea a fost imediat diagnosticată citologic. **Concluzii:** Asocierea celor două metode creşte sensibilitatea şi acurateţea diagnosticului leziunilor hepatice focale utilizându-se o metodă sigură şi puţin invazivă.

Cuvinte cheie: leziuni hepatice focale, biopsie ghidată ultrasonografic, examen histologic şi citologic

Introduction

Investigation of focal liver lesions is not always feasible by the means of imaging techniques despite the fact that imaging modalities are constantly evolving. Thus percutaneous hepatic biopsy is inevitable in a number of cases. Ultrasound (US) guidance is preferred to Computer Tomography (CT) guidance as it is a cheaper, easier and often more available method, allowing real-time surveillance of the procedure.

US guided, percutaneous hepatic biopsies are frequently performed in the Radiology Department of Athens' General Hospital in order to obtain samples for pathologic and cytologic examination, to compare the reports of these specimens and to evaluate the necessity of performing both techniques in the same patient, at the same time.

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Materials and methods

During a two-year period of time a total of twenty-seven patients aged between 35 and 86 years old underwent US-guided percutaneous hepatic biopsies in our hospital. All patients and control subjects gave consent to participate in the study, which was approved by the local Ethics Committee. The histopathology and cytology departments' databases were searched for all patients having undergone the particular diagnostic procedure. In four out of hospital patients, reports could not be retrieved. Two cases of focal lesions turned out to be abscesses. The rest twenty one (12 male and 9 female) patients were adequate as well as qualified to join this study, after written consent was obtained. Most lesions were located in the right liver lobe and measured 3-11 cm. One lesion that proved to be hepatocellular carcinoma inhabited the caudate lobe. One patient had peritoneal implants and ascites by the time of the diagnosis.

Coagulation screening was performed and all patients met the standardized coagulation criteria (platelet count greater than $60x10^9$/L and international normalized ratio less than 1.5). Specimens for both pathological and cytological examination were obtained from sixteen lesions using a 17 G needle guide in a single puncture attempt. In two cases only Fine Needle Aspiration (FNA) was performed and the final diagnosis was based on cytological, imaging and clinical findings. Three patients underwent Core Needle Biopsy (CNB). All biopsies were undertaken by experienced interventional radiologists. Before the procedure a fast ultrasound scan enabled the radiologist to decide on the safest and shortest needle trajectory so as to adjust the patient's position. The needle truck was carefully chosen in order not to penetrate the pleura. A free hand technique was used at all times.

The initial attempt to approach the lesion was made by placing an adjustable coaxial automated CNB system. The selected entry site was prepared in a sterile fashion. The system consists of a 17 G outer cannula with an introducing stylet, serving the accurate positioning of the needle. As soon as the correct position of the needle is confirmed by ultrasound in two different imaging planes, the stylet is then removed and an aspiration syringe is suitably adjusted. The needle is moved back and forth within the nodule, vertically in order to separate cell clusters and facilitate aspiration. The pathologist immediately coats a smear on a slide. In patients exclusively undergoing FNA a fine needle (21 G) was used, without a guide needle, under free hand technique.

The acquisition of tumor fragments was made possible by carefully inserting a coaxial automated or semi-automated biopsy gun (18 G) through the needle guide. Safe repositioning of the needle and sampling from a different tumor site was feasible under continuous US control, in order to obtain two specimens from two different sides of the tumor. The cylindrical clusters were fixed in a formalin solution after being visually examined to determine their adequacy. After preparing the smears the

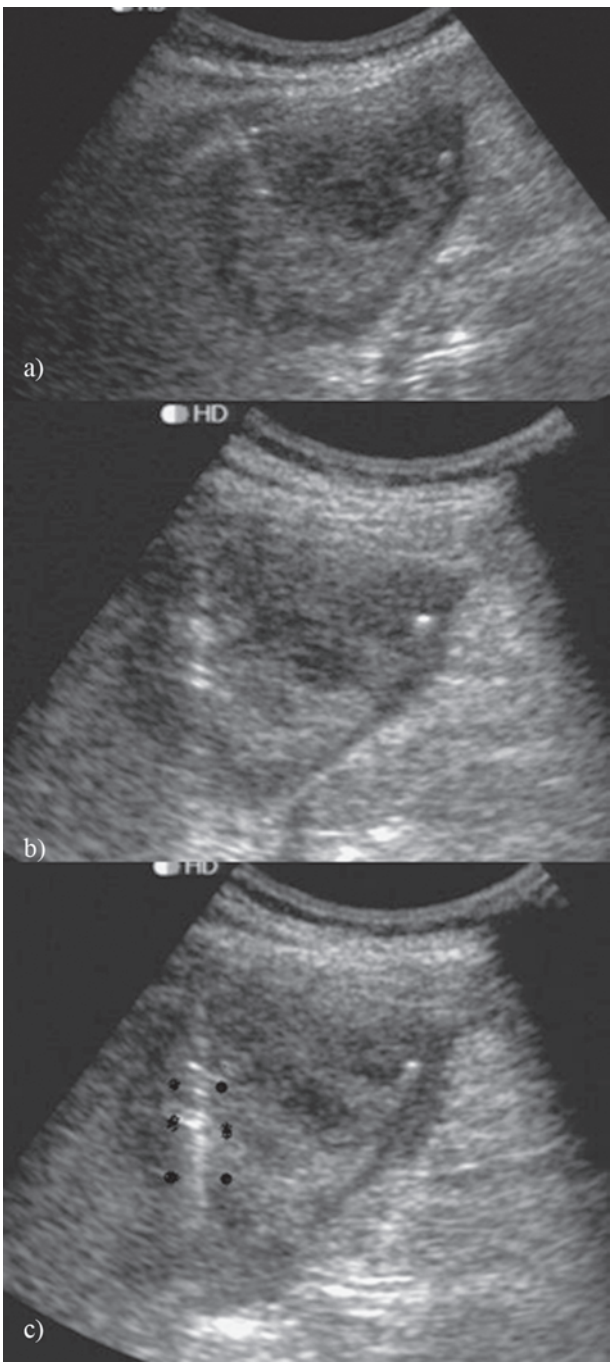


Fig 1. The insertion as well as the destination of the biopsy needle under ultrasonographic guidance is seen, in a case of a large liver lesion, which was proved to be a metastases

needles were rinsed in normal saline so as to wash up the tissue remnants. The formalin box was then sent to the histopathology laboratory.

The needle was again smoothly moved back and forth within the nodule in order to separate cell clusters and facilitate aspiration of an adequate amount of cells for the second cytology specimen. The 17 G needle was then withdrawn under constant aspiration. Afterwards the needle was rinsed by the cytologist using a Thin Prep solution so as to sweep along the remaining tissues.

A final US sweep completed the procedure to discover possible early complications such as hematoma, arteriovenous communication or pseudoaneurysm. Patients having been punctured through the right anterior or middle axillary line were placed in the right lateral position tamponading the site of the puncture in order to avoid bleeding. The vast majority of the patients were already hospitalized. The outpatients remained for vital signs (pulse, blood pressure) monitoring for twenty-four hours. If no complications were noticed the patients were allowed to leave the hospital.

Results

Each patient was already diagnosed with one or more focal liver lesions by various imaging modalities. Clinicians raised suspicion of cancer in the vast majority of cases. Out of a total of twenty-one patients twelve were male and nine were female, with an age range of 35 to 86 years.

In one patient the initial insertion of the 17 G outer cannula caused bleeding within a tumor which was proved to be extremely hypervascular at CT. The patient was scheduled for CNB in a later session where the needle tract was plugged by injecting gel foam during slow withdrawal of the needle. There were no other major complications. In a case of a patient with ascites a catheter was inserted and secured to the skin for continuous external drainage and was left in place before biopsy took place.

Cytological and pathological reports were compatible in twelve cases. Six patients were diagnosed having metastatic cancer, five patients with hepatocellular carcinoma (HCC) and one patient with Non-Hodgkin Lymphoma.

In three cases the results differed between the two methods. In the first case the cytological examination distinguished shells more compatible with hepatic adenoma, whereas the pathologic examination suggested focal nodular hyperplasia. The final diagnosis was based on patient's health history, age and sex, in combination with the later. In the second case the cytological smear was proven to be inadequate. In the third case the cytological examination ruled out malignancy although the accurate diagnosis of chronic active hepatitis B (HBV) was made by histology.

The histological cores were found inadequate in one case due to minimal material quantity. Cytological smears were inadequate in one case bearing multiple spaces of necrosis, inflammation and fibrosis. Overall eighteen cytological smears and nineteen histological cores were extracted.

Sensitivity was calculated as the sum of true positive punctures divided by the sum of true positive punctures plus the sum of positive cases that biopsy had mistakenly showed to be normal. Sensitivity of cytology was estimated 83.3% (15/18), whereas sensitivity of histology 94.74% (18/19). Diagnostic sensitivity of cytology in the evaluation of HCC was 100% (5/5) and 90% (10/11) in the evaluation of metastatic disease. Sensitivity of histology in detection of HCC was 100% (5/5) and 90.9% (10/11) for metastases. CNB led to accurate diagnosis in all cases of benign conditions. Total sensitivity of histology was greater than that of cytology. Both methods showed the same sensitivity in scanning for malignancy. Combination of both methods led to the correct diagnosis at all times.

Cytology results were obtained within a time interval of forty-eight hours to four days. Histopathology reports were available with a delay of seven to thirty days.

Diagnostic accuracy is determined by the ability of a method to diagnose malignancy and is calculated by the sum of true positive malignant cases plus true negative cases divided by the total number of patients undergoing the examination. Cytology managed to rapidly inform the existence of malignancy in seventeen out of eighteen cases. Diagnostic accuracy reached 94.4%. Similarly the histology's diagnostic accuracy achieved 94.7%, counting the single case of the non-diagnostic specimen. Diagnostic accuracy of both methods was found to be 100%.

Fifteen out of eighteen lesions undergoing cytological examination were immediately diagnosed as malignant, setting the correct diagnosis at once. Cytology report was indefinite in one case, though ruling out malignancy. Chronic active hepatitis (HBV) was the case in that particular patient. The two methods diverged in one case, where the histological report diagnosed focal nodular hyperplasia and cytological report confirmed a hepatic adenoma. Still both methods excluded the potential of malignancy.

Discussion

With the advent of imaging modalities a greater sensitivity and higher resolution has been achieved. This way isolation and identification of small focal liver le-

sions was made easy. In cases where imaging, laboratory and clinical data proved to be insufficient the patient is directed to biopsy.

FNA is safer, cost effective and more tolerable by the patient. Cytological report is available within a short period of time. However, FNA's low negative diagnostic value in characterizing malignant lesions limits its utility [1]. FNA provides with cell clusters proven insufficient in most cases to diagnose benign conditions, where cellular architecture must be intact, for it to be differentiated by normal hepatic parenchyma. CNB can provide that possibility by acquisition of cylindrical tissue blocks.

Many investigators have managed to substantiate that biopsy performed using an automated 18 G gun is a safe and effective method [2-6]. Yu S et al investigated 129 patients which underwent a total of 137 US guided biopsies of focal liver lesions, measuring less than three centimeters in diameter. According to the investigators' conclusions the 18 G needle bares a sensitivity of 96.4%, the specificity and the positive predictive value was found to be 100%, the negative predictive value up to 94.6% and total accuracy up to 97.8% [5].

In a Greek study of Thanos L et al (2005) 767 patients with focal liver lesions were investigated within a five-year period of time. The purpose of the study was to evaluate the efficacy and safety of the 18 G needle in biopsies guided under CT control. All extracted cores were considered adequate. No major complications as death, hemorrhage or infection were described. Minor complications were seen in three patients [2].

Coaxial technique is the method of choice in many institutes. The significant advantage of this procedure is that needle placement is performed once [7]. In that manner, complications such as hemorrhage, pneumothorax and tumor seeding along the needle track are minimized. Specimens of more than one lesion areas can be taken by changing the needle's trajectory without completely extracting the needle.

Many authors support the combined use of cytological and histological examination in the identification of liver lesions through their investigations. Stewart CJR et al (2002) studied 141 patients carrying abdominal lesions having gone through both FNA and CNB and compared the results [2]. These investigators came to the conclusion that the two methods must be considered as complementary and that their combination raises the diagnostic accuracy and sensitivity of biopsy.

Franca AVC et al (2003) showed that the use of FNA can improve CNB's diagnostic accuracy in focal liver lesions. A total of 62 patients underwent 68 FNA's and 49 CNB's. The investigators came to the conclusion that if one technique is not able to prove malignancy in a tumor carrying high clinical suspicion, then the other technique must also be used as complementary [8].

FNA and CNB used separately in 49 patients bared a diagnostic accuracy of 78% each:combining both methods raised the diagnostic accuracy to 88%. Having excluded non diagnostic specimens, diagnostic accuracy reached 93%. Sensitivity, specificity, positive and negative predictive value agreed for both methods. The great advantage of using the two methods simultaneously was reducing false negative results. Negative predictive value of each method separately was 64% and that percentage reached 78% by combining both methods.

Appelbaum et al (2009) retrospectively studied 1910 ultrasound guided biopsies, 208 of which concerned focal liver lesions [9]. In all cases an 18 G needle was used extracting specimens for both histological and cytological examination. Specimens were sufficient in 205 cases (98.6%), while in 3 cases were proven inadequate due to necrosis. In 25 cases histological and cytological reports were incompatible. Amongst them 15 cytological and 7 histological specimens were inadequate. There were no major complications reported.

The study showed no statistically significant relation between size and location of the lesion and the number of passes. Investigators believe that smaller tumors are more compact and therefore contain no necrotic or mucinous areas which can prove to be non diagnostic. Tumor type was found to correlate with the number of passes. Malignant tumor cells' morphology is quite different from that of healthy liver parenchyma and benign tumor cells. Metastatic nodules required a mean amount of 1.9 passes in order to reach diagnosis, whereas benign nodules required 2.8 needle punctures. In conclusion, investigators believe that 3 passes are sufficient in 90% of cases, without a pathologist present. The percentage is even higher in the presence of a pathologist. Diagnostic accuracy of 18 G biopsy gun is more than 98.6%.

Advances in imaging technology have lead to a drastic reduction of biopsies performed. According to the protocol set by EASL (European Association for the Study of the Liver), the use of FNA under ultrasound guidance are limited to nodules measuring 10-20 mm in diameter in the cirrhotic liver [10]. Nodules less than 10 mm require frequent follow up with ultrasound and a-fetoprotein levels measuring. CT and MRI (Magnetic Resonance) are used accurately for nodules measuring less than 20 mm [11, 12].

Caturelli E et al (2004) performed a prospective multicentric study that in a nine year period of time concluded that FNA must be performed in very small nodules less than 10 mm. The study enrolled 4375 patients diagnosed as cirrhotic. Amongst them 294 newly detected nodules

measuring less than 20 mm were punctured using a fine needle, under ultrasound control and 258 of them were proved to be HCC. 33 of those nodules were less than 10 mm. The overall diagnostic accuracy of the method was 89.4% and that of lesions less than 10 mm was 88.6%. The study concludes that over half of very small lesions appearing in the cirrhotic liver are proved to be HCC and about 90% of those are recognized by FNA [13].

Ultrasound guided FNA can be proved as the method of choice for the detection of HCC. A Japanese study referred in Caturelli's work combined DSA (Digital Substraction Angiography), MR and US guided biopsy in the detection of 180 nodules measuring less than 20 mm in diameter, proved that only 68% of lesions measuring between 11 to 20 mm were diagnosed by imaging techniques. The remaining lesions required biopsy. The contribution of biopsy was more important in lesions less than 10 mm, in which only 45% could be diagnosed by imaging techniques [1].

Reported percentages of seeding along the needle track vary between 0.6 to 5.1%, using various biopsy techniques, in a study period of 2 months to 6 years until its appearance [6,8,9]. Maturen et al (2006) reported that coaxial technique bares no danger of seeding cancerous cells along the needle track. The investigator performed a total of 1012 biopsies under imaging guidance, using a 17 G insertion needle and a biopsy gun with an incorporated 18 G cutting needle. The first needle stayed in place while the second one performed multiple passes.

Conclusions

The constraint of our study was the inadequate specimens which could not be analyzed, mainly in cases of cytological examination by FNA. The result greatly depends on the lesions' composition. Cytology has the great advantage of providing quickly with results in patients with cancer, immediately planning the therapeutic approach or excludes malignancy, especially in young patients.

Histology is able to accurately diagnose benign conditions of the liver and differentiate hepatocellular nodules from regenerating nodules in cirrhotic patients. Its' large drawback is the delay on the final results. The combination of both methods diagnostically covered all cases, in a small period of time, for the vast majority of patients, in one session, and a minimally invasive manner, without major complications. According to our experience we suggest simultaneous performance of both methods in order to identify focal liver lesions.

Conflict of interest

None of the authors had any conflict of interest.

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