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Invited Commentary

Fine-needle aspiration cytology of liver diseases

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Ultrasonography, CT and magnetic resonance have been widely used in the diagnosis of liver diseases in the past 20 years, but the final definite diagnosis of liver space occupying (LSO)lesions can not be made only by imaging methods. Ultrasonograp hy has been used in combination with fine-needle aspiration biopsy in the diagn osis of liver diseases since the 1970s. The accuracy of differential diagnosis of both benign and malignant lesions could reach 88.8%. Since then, this technique h as become popular in the diagnosis of LOS lesions in large hos pitals in China. Dr. Edoute reported 279 cases of LSO lesions in 1976-1988 diagnosed by non-ultrasonically-guided aspiration biopsy, which is of great importance in the diagnosis of LSO lesions by ultraso nically-guided fine-needle aspiration biopsy.

ADVANTAGES AND DISADVANTAGES OF FINE-NEEDLE ASPIRATION CYTOLOGY(FNAC)

FNAC leads to little tissue damage and few complications. Pneumothorax occurred in only one case of the 279 cases reported by Dr. Edoute. It has been proved in our practice that one focus can be aspirated 3-5 times.

The disadvantage of FNAC is that smear cytological examination can only determine whether the cells are malignant, but can not type the tissues. Big needle aspiration biopsy should be performed in order to make the final definite classification of tumors, e.g., to differentiate the subtypes of primary hepatic cancer, but it has more complications than fine-needle asp iratio n biopsy. Furthermore, fine-needle aspiration biopsy can reduce the risk of puncture by incorporating the advantages of both fine-needle and big-needle aspir ation biopsies, but the tissue core is relatively small which sometimes can not meet the needs of multiple biopsies of tissue slices.

INDICATIONS AND CONTRAINDICATIONS OF FNAC

FNAC is mainly used at present in the diagnosis of LSO lesion s by ultrasonography and CT. Fine-needle liver aspiration biopsy is performed when the final definite diagnosis can not be made. Big-needle aspiration biopsy is usually used in the diagnosis of diffuse hepatic lesions while fine-needle aspiration biopsy is mainly used in the diagnosis of focal hepatic lesions.

Indications of FNAC

Indications of FNAC are: primary liver cancer, secondary liver cancer, deep hepatic hemangioma, hepatic abscess, circumscribed fatty liver, and cystic tumor or cancer of liver.

Contraindications of FNAC

The contraindications of FNAC are: patients with hemorrhagic tendency such as those with noticeably prolonged prothrombine time, patients with suspect ed extrahepatic obstructive jaundice, patients with suspected hepatic echinococcosis, patients with hepatic surface hemangioma, and those who fail to cooperate.

PREOPERATIVE PREPARATION, PROCEDURES AND POSTOPERATIVE MANAGEMENT

Preoperative preparation

Preoperative examination of prothrombine time, bleeding and clotting time.

Ultrasonography is used to determine the site of LSO lesions, and the site of needle insertion and its depth.

Aspiration needle

The external diameter of the fine-needle is less than 1mm, while that of the big-needle is greater than 1mm. Berlin Charife Hospital succeeded in fine-needle (its external diameter was 1mm) aspiration cytology biopsy i n 1931. Swedish physicians began to use it in the 1950s and named it fi ne-needle aspiration biopsy.

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Fine-needle. PTC needle is used for aspiration biopsy in China, which consis ts of the needle scabbard and the needle core. The needle is 15 cm-20 cm-long and its external diameter is 0.6 mm-0.8 mm. Its tip is sharp with a 30° -45° oblique angle. Fine-needle aspiration can be performed in both cytological examination and the diagnostic aspiration biopsy of vario us cysts and fluid lesions.

Big-needle. The external diameter of big-needle for transcutaneous aspiration is greater than 1 mm. Its appearance, structure and length-are identical to fine-needle, but the needle with-1.2 mm external diameter are commonly used.

Fine-needle aspiration histology. Number 21-23 Sute-cut needles, which are id entical in external diameter with fine-needle, are usually used in hepatic tum or biopsy. When the needle is being inserted into the light target, the operator lifts the piston in the needle handle, making the need le core move up, so that the tissue strips can be inlaid in the space of the needle sheath in which the pressure is negative. The aspirated tissue for biopsy is 0.4 mm in diameter and 3 mm long.

Guiding needle.The fine-needle(its external diameter is 0.7 mm) is rather soft and easy to bend in the process of transcutaneous aspiration, which often results in failure. When the guiding needle (it is 5 cm-long and its external diameter is 1.6 mm) is supplemented, success can be achieved. After the guiding needle is inserted into subcutaneous tissues, the fine-needle is used to aspirate in order to avoid its bending.

OPERATIONAL PROCEDURES OF ULTRASONICALLY-GUIDED FNAC

Preoperative measurement of blood pressure and pulse for postoperative control. For determination of the site of LSO lesions by ultrasonography, horizontal position is taken for patients with lesions in the left hepatic lobes, while left lateral position is taken for patients with lesions in the right hepatic lobes. After routine sterilization, the aspiration site is determined by aspiration probe. The guiding needle is inserted into subcutaneous tissues after local anesthesia reaches Glisson's capsule. The fine-nee-dle is inserted into the guiding needle hole. The patient is asked to hold his breath while the fine-needle is inserted into the target of the liver along the aspiration line displayed on the screen of ultrasonic detector. A solid sense can be felt when the needle has been inserted into the focal tissues. Then, the patient is asked to resume his normal respiration while the needle core is pulled out and connected to a 10-mL injector. Soon after the negativ e pressure is removed by lifting and inserting the needle point 3 or 4 times, the needle is pulled out. The aspirated tissues are placed on a glass slide and prep ared into a round-shaped smear to observe whether there are yellowish particles. The liver tissues are aspirated when yellowish particles are found. After the dried smear is fixed in 950 mL/L-alcohol for 10 min, it is taken out and stained for cytological examination. The second aspirated tissues are placed on a piece of filter paper and fixed in 100 mL/L formalin for histologica l examination. The third ones are placed on a piece of filter paper and fixed in 30 mL/L-glutaraldehyde for electron micros copy.

Postaspiration treatment. The patient is asked to rest in bed for 4 h-6 h. Two hours after aspiration, blood pressure and pulse are measured every 30 minutes, then once an hour for 4 successive times if no change is found.

COMPLICATIONS AND DEATH RATE

Fine-needle aspiration results in little liver damage and has a high safety. It was reported by Livraghi *et al*[1] in 1983 that the occurrence rate of complica tions was 0.05% in the 11 700 cases receiving fine-needle abdominal aspir at ion biopsy.Smith *et al*[2] in 1985 reported a total rate of complication of 0.16% and a death rate of 0. 006% in the 63 108 cases receiving fine-needle abdominal aspiration biopsy. Among them, noticea ble bleeding was found in 17, bile leakage in 51, infection in 16, and death in 4. In the study by Cheng MH *et al*[3], bleeding was found in 2 cases, liver cancer in 1 case, and caver nous hemangioma in 1 case a mong the 160 cases of LSO lesions receiving ultrasonically-guided fine-needle aspiration biopsy.

In theory, pulling out the fine-needle when it has been inserted into tumor may result in contamination of a small number of malignant cells on the surface of fine needles. However, TAO *et al*[4] reported that no tumor implantation was found in the 2 500 cases receiving transcut aneous aspiration biopsy, while it was found in 2 cases among the 11 700 cases reported by Livraghi *et al*.[1] No tumor implantation has been reported so far in China, although tens of thousands cases received fine-needle aspiation biopsies.

FUTURE DEVELOPMENT

It is not difficult to find out LSO lesions with wide application of imaging methods, but it is still troublesome to make an accu rate and definite diagnosis of tumors. Combined methods should be advocated for the diagnosis of LSO lesions by ultrasonically-guided fine-needle aspiration biopsy in order to improve the accuracy of its diagnosis.

Ultrasonically-guided FNAC biopsy

The positive rate of the diagnosis of liver parenchyma occupying malignant lesions is 77%-90%. FNAC biopsy is helpful for the rapid diagnosis of liver cancer and can provide the basis for cytological diagnosis and avoid unneccessary exploratory laparotomies.

However, it is difficult for FNAC to classify tumors and to make differential diagnosis of atypical proliferation of liver cells and well-differentiated hepatocellular carcinoma. FNAC can not serve as an exclusive diagnostic method for malignant tumors due to its 10%-23% false positive rate.

Ultrasonically-guided fine-needle aspiration histology (FNAH) biopsy

In our studies, the aspirated tissues are placed on a small piece of filter paper and fixed in 100 mL/L-formalin for histological examination since FNAC could not classify the tissues. Among the 4 cases of liver cancer, 2 were diagnosed by FNAC as having interdegenerative cells and the other 2 as having hepatocytes due to cirrhosis, while all of them were diagnosed by FNAH as well-differentiated hepatocellular carcinoma. Positive cancer cells were found in 8 cases of secondary liver cancer by FNAC. Of them, 1 case was diagnosed as liomyoma, 2 as squamous epithelial carcinoma, and 5 as adenocarcinoma by FNAH.

Ultrasonically-guided fine-needle aspiration ultrastructural (FNAU) biopsy

Histological classification could not be made since the tissues taken by FNAH were small. Ghadially reported that 1%-8% tumors could not be diagnosed only by histological examination (optica l microscope). We have achieved satisfactory results in the diagnosis of tumors by electron microscopy, which can further confirm the histological diagnosis of tumor and show their histogenesis, and is helpful for the localizat ion of the primary focus of hepatic metastatic carcinoma. Combination of F NAC and FNAU can increase the positive rate of tumor diagnosis, but FNAU is limited in its use due to the difficulties in specimen preparation and tissue localization.

Ultrasonically-guided fine-needle immuno histochemistry

It is advocated to label the different cell antigens by immunoohistochemistry for the differentiation of their types when it is difficult to diagnose the fine-needle aspirated cells by routine staining. For instance, neuroendocrine labelling is helpful for the diagnosis of carcinoid and positive AFP labelling supports the diagnosis of hepatocellular carcinoma. The current tendency is to prepare more specific antibodies so as to make the differential diagnosis of tumors more accurate and easier.

Ultrasonically-guided fine-needle molecular biology

The wide application of molecular biology techniques has made it possible to detect the level of nucleic acid and various kinds of oncogenes. A large number of biopsies can not be performed due to the limited specimens of fine-needle aspirated tissues or cells while oncogene biopsy is not limited by the amount of specimens because the diagnosis of tumors at gene level can be made on the basis of a few cells. Therefore, molecular biology biopsies such as in situ hybridization and PCR are the future hot points of fine- needle aspiration cytology.

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