

Fine Needle Aspiration Cytology of Hepatocellular Carcinoma

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Abstract

A prospective study of (13) patients, from both sex, with hepatocellular carcinoma was done in Salahuldeen government in Tikrit teaching hospital in period extent from Feb. 2006 to Aug. 2010. Patients divided into: 1-Those underwent FNAC for liver mass (5 patients) (38.5%), for diagnosis in addition to clinical and radiological evaluation with measurement of alfa-fetoprotein (AFP) level in the serum of them. 2-Those didn't undergo FNA and diagnosis made by clinical and radiological evaluation, and measurement of serum AFP level, in addition to excisional biopsy for liver mass. Follow up of patients for both groups made by 6-12and18 months by clinical and radiological evaluation for tumor seeding along needle tract, distant spread and median survival. It has been showed that tumor seeding along needle tract didn't encountered in this study. Distant spread included brain, bone, lung and abdominal wall no statistically differ in both group, and seen in three patients of those underwent FNA (60%),and five patients of those didn't undergo FNAC (62.5%) (P=0.7).

Median overall survival rate was 13 months(8-18 months) in FNA group and 12 months in non-FNA group (8-16). The cumulative 6, 12- and 18 months overall survival were 80%, 60% and 40% respectively for FNAC group and 75%, 50 and 37.5% respectively for non FNAC group. There was no statistically differences between two groups (P= 0.77).

Introduction

The liver is the largest organ of the body weighing approximately 1.5kg, the nutrients absorbed in the digestive tract are processed for use by other parts of the body. Most of its blood (70-80%) comes from the portal circulation, the smaller percentage is supplied by the hepatic artery.(1)

Liver tumors:- classified into

I. Benign tumors:-

1. Hepatic adenoma:- these affect premenapausal women and are predisposed by estrogen containing oral contraceptive.(2, 3)
2. Bile duct adenoma:- may mistaken for metastatic tumor at laparotomy,

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because their appearance as small white nodules. (2, 3)

3. Hemangioma.

II. Malignant tumors:-

A. Primary tumors:- include

1. hepatocellular carcinoma (HCC):- typically arise in the setting of chronic hepatitis and cirrhosis. World wide, viral hepatitis B and C are the most common cause. Other causes include chronic alcohol abuse, aflatoxin exposure (produced by fungus *Aspergillus's flavus* which frequently contaminated stored nuts and grains), hemochromatosis and antitrypsin deficiency and tyrosinemia. Hepatocellular carcinoma is the commonest primary liver tumors (∞80%). (2, 3)

2. cholangiocarcinoma:- this is an adenocarcinoma arising from the intrahepatic bile duct epithelium, it account for 5-10% of all cases of primary liver tumors.

Viral hepatitis B and C infection are more frequently associated with HCC. Chronic alcoholism has been reported as a risk in both. Other predisposing factors include chronic inflammatory disease of intrahepatic biliary tree (particularly sclerosing cholangitis) and trematodes infection (liver flukes) e.g clonorchic sinensis. (2, 3, 4)

Most cholangiocarcinomas are diagnosed at an advanced stage and have a poor prognosis (no more than 6 months).

3. angiocarcinoma:- highly malignant tumors, derived from vascular endothelium. They are rare tumors, unless there has been exposure to:-

a) Thorotrast (a radiological contrast agents used until the 1950s).

b) Vinyl chloride monomer used in plastic industry.

c) Arsenic (administrated in the past in certain tonics).

d) Anabolic steroids.

B. Secondary tumors:- the majority of malignant liver tumors are metastatic. The most common primary carcinoma which metastasize to the liver are of breast, colon, lung and stomach.

Mode of spread via blood stream, through the portal circulation (GIT tumors) and systemic circulation(other tumors)

Fine Needle Aspiration Cytology (FNAC)

FNAC:-can be defined as aspiration of tumor cells by a thin needle with a core diameter of less than 1mm (18-21 gauge) percutaneously or endoscopically.(4, 5, 6, 7)

Aspiration of the liver usually guided by imaging techniques (Ultra- sounography, CT-scan, or MRI)(6, 7, 12)

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Before aspiration, the lesion in the liver must be localized by one of the imaging technique. Guided FNA biopsy is increasing being recognized as an excellent diagnostic method for detecting hepatic malignant.(4, 5, 6, 7)

In experienced hands, FNA is safe, minimally invasive, accurate and cost effective, and it can be used to detect malignancy anywhere in the liver e.g. left lobe or in the area of the porta hepatis where the use of large bore needle may be too risky, in addition to obtaining multiple samples using the FNA technique on the basis of finding visualized by imaging technique. The chance of obtaining a representative samples are greatly increased.

Three punctures or more with slight modification in the angle of approach would yield a representative samples and diagnostic accuracy to 94%.(5, 6, 7)

The sensitivity for diagnosis of hepatic malignancy range from 92% to 96%. False positive results are more often a reflection of the lack of experience of the examiner and can be eliminated with increasing experience.

The occurrence of complications after FNA is rare, include:- (6, 7)

1. Hemorrhage:- is often related to vascularity and location of the lesion, as well as the needle size.(6, 7)

2. Another concern is subcutaneous seeding of tumor along the needle tract during percutaneous liver FNA. The incidence varies with the diameter of the needle, the number of passes and the amount of normal parenchyma around the lesion to be traversed by the needle. It is still an extremely rare complication.(6, 7, 8)

Absolute contra- indications for FNA of liver include:-

uncorrectable bleeding diathesis, a lack of safe access route e.g. vascular structure in the biopsy path, and un cooperative patient. (9,10, 11)

The aims of the this study are to determine the role of guided fine needle aspiration biopsy as diagnostic procedure of liver tumors and the possible risk of tumor seeding a long needle tract and its effects on median overall survival of patients with hepatocellular carcinoma.

Patients and methods

Over a period lasting from Feb. 2006 to Dec. 2010, a thirteen patients from both sex with hepatocellular carcinoma were studied prospectively at Salahuldeen government. The age of the patients

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ranging 44-62 years (median age 53 years).

The diagnosis of HCC was done by:-

History taking:- familial liver disease, viral hepatitis, work, drugs, chemical exposure, alcohol intake...etc.

Physical examination:- hepatomegaly, jaundice, bleeding tendency, and ascitis,

Biochemical assay for Alkaline phosphates and total serum bilirubin (TSB).

Serological examination for:- HBsAg, HCV.

Measurement of serum alfa-feto protein (AFP): >1000 ng/ml.

Radiological evaluation of liver tumor include:-

Ultrasonography, CT-scan, MRI.

With or without guided FNAC.

Radiological localization of liver tumor is essential for FNAC. Three punctures with slight medication in the angle of approach, with a thin needle (18-21 gauge) percutaneously, yield a representative samples.

It is crucial to handle the aspirate quickly and optimally in order to

minimize artifacts. Smears are made by spreading of aspirated material on prelabeled slides fixed in 95% ethanol and then processed and stained with hematoxylin and eosin. Finally, light microscopical examination of the cytology.

Excisional biopsy for those didn't undergo FNAC; need hospitalization & time consuming; but take definite diagnosis

The radiological findings of single large mass with or without

smaller satellite lesion is more typical of HCC, while metastatic lesions often present with multiple lesions of similar size.

A marked elevation of serum AFP level > 1000ng/ml is highly suggestive of HCC.

The patients grouped into:-

Those underwent FNAC , five patients (38.5%)

Those didn't undergoing FNAC, eight patients (61.5%) .

All patients were followed up at Tikrit Teaching Hospital by clinical and radiological examination for peritoneal, distant spread and tumor implantation along the fine needle tract.

Follow up of the patients made at 6 ,12and18 months, for tumor seeding along needle tract and median overall survival.

Results

Thirteen patients from both sex, with hepatocellular carcinoma participated in this study. The patient's age ranging 44-62 years (median age 53 years).Eight of them were males (61.5%) .

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The majority of the patients (10 patients) had showed liver cirrhosis (77%).

HBsAg infection has the highest percentage as a major cause of liver cirrhosis in this group of patients (60%), followed by infection with HCV (20%). Other causes of liver cirrhosis include chronic drug abuse (especially antipsychotic drugs), and alcoholism (20%), as showed in table (1).

It has been showed that 23% of the patients (3 of total number), HCC arise without liver cirrhosis and their serum were negative for HBsAg or HCV, with no history of alcohol for drug abuse.

All patients showed markedly elevated serum AFP (> 1000 ng/ml). Follow up of the patients done for 6, 12 and 18 months showed that there is no tumor implantation along fine needle tract, or intrahepatic tumor spread in those underwent FNAC.

Distant spread included lung, bone, brain, and abdominal wall seen in (60%) (three of those underwent FNAC), which was not statistically different from those didn't undergo FNAC (62.5%) (five patients of them) (P=0.68).

Median overall survival was 13 months (8-18 months) in FNAC group and 12 months in non-FNAC group (8-16 months). The cumulative 6, 12 and 18 months overall survival rates were

80%, 60% and 40% respectively for the FNAC group and 75%, 50% and 37.5% respectively for the non FNAC group. There was no statistically significant differences between the two group (P=0.77).

Discussion

Although clinical and /or radiological findings can't reliably distinguish hepatocellular carcinoma from met static disease. They can help to narrow the differential diagnosis. The age of the patient may suggest certain process e.g. secondary and primary liver malignant tumors more frequently affect older patient, while benign lesions e.g. hepatic adenoma tend to occur in younger patient often with history of long term steroid use. Hepatoblastoma occur primarily in infants. (6, 7, 8, 9)

Another informative clue, is the presence or absence of liver cirrhosis. For patients with cirrhosis, HCC is a more likely finding, as estimated in this study (77%) of all cases.(6, 7, 8, 9)

A markedly elevated serum AFP level (> 1000ng/ml), is highly suggestive of HCC. A moderate increase in serum AFP, however, is non specific and can be seen in a wide variety of benign and malignant conditions. (6, 7)

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The finding of a single, large mass with or without smaller satellite lesions on imaging is more typical of a HCC, whereas metastatic lesions often present with multiple lesions of similar size, (6, 7, 12).

Vergara *v. et al* 1993, revealed the incidence of needle tract seeding is quite low, (9).

Yomada N. *et al.* 1993, explained that guided FNAC was performed on patient with HCC. Thirteen months after the FNAC, the patient palpated a hard subcutaneous nodule 1.5cm in diameter of tumor implantation in the right lower anterior chest wall at the insertion site of fine needle (10).

Ka mm. *et al.* 1995 showed tumor seeding of the abdominal wall during FNAC of the liver is a very rare complication.(11)

David C. Chhieng *et al* 2005 showed that the occurrence of complications after hepatic FNAC is rare, they are limited largely to hemorrhage, subcutaneous seeding of tumor along the needle tract which is still on extremely rare complications.(6)

It has been revealed in this study no tumor implantation encountered & distant spread of HCC included lung, bone, brain and abdominal wall seen in (52%) of those underwent FNAC, which not statistically

different from those didn't undergo FNAC (50%) (P=0.8).

The same observation was made by Kelvin Kwok-chai Ng *et al*, at 2004.(7)

It has been reported that median overall survival was 13 months in FNAC group and 12 months in the non FNAC group. The cumulative 6, 12 and 18 months overall survival rate were 80%, 60% and 40% respectively for the FNAC group, and 75%, 50%, 37.5% respectively for the non FNAC group. There was no statistically significant difference between the two groups (P=0.7).

Kelvin Kwok-Chaing *et al* at 2004, found there was no statistically significant difference between the two groups in median overall survival.(7)

FNA is a useful & relatively safe diagnostic test for evaluating patients with discrete hepatic masses. However, liver FNAC poses a number of diagnostic challenges. Correlation with clinical, radiological and cytological findings is helpful in arriving at the correct diagnosis and therefore increase overall accuracy and cost-effectiveness of the procedure.

Conclusion

It has been showed that guided FNAC of liver mass is a cheap, time consuming, accurate, and relatively safe diagnostic

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procedure and showed no effects on median overall survival of the patients.

Recommendation

guided FNAC of liver mass with three punctures or more with slight modification in the angle of approach would yield a representative samples and diagnostic accuracy to 94% .

References

- 1-Carol L. Junquiera. Basic Histology. 5th ed. 1989. 16: 316-320.
- 2-Bethon Goodman Jones. Pathlogy. Mosby, 1998, 156-162.
- 3-Robbins and Cotran. Atlas of Pathology, 2nd ed. 2010, 8: 220.
- 4-Marluce Bibbo. Comprehensive Cytopathology. 2nd ed., 2nd volume, 1997; 32: 838- 846.
- 5-Barbara F. Atkinson. Atlas of Diagnostic Cytopathology. 1992, 8: 317.
- 6-David C Chhieng . fine needle aspiration biopsy of liver- an update. 2004. 2:5.

7-Kelvin Kwok- Chai Ng ;Ronnie Tung-PingPoon. Impact of preoperative fine needle aspiration Cytologic examination on Clinical outcome in patient with hepatocellular carcinoma in a tertiary referral center. 2004; 139: 193-200.

8-Roussel F. the risk of tumoral seeding in needle biopsies, 1989; 33: 936-939.

9-Vergara V,Garripooli A. Colon cancer seeding after percutaneous fine needle aspiration of liver metastasis, 1993; 18: 276-278.

10-Yamada N;Shinzawa H. subcutaneous seeding of small hepatocellular carcinoma after fine needle aspiration biopsy. J. Gastroenterol. Hepatol. 1993; 8: 195-198.

11-Ka MM, Dangou JM. tumor Seeding of abdominal wall after fine needle cytologic puncture of the liver. Ann. Gastroenterol. Hepatol. 1995; 31: 221-225.

12-Kanematsu M;HoshiH. Abdominal wall tumor seeding at sonographically guided needle-core aspiration biopsy at hepatocellular carcinoma. AJR. Am J. Roentgenol. 1997; 169: 1198-1199.

Table (1): causes of liver cirrhosis.

Causative	No.	%
- HBsAg	6	60%
- HCV	2	20%
- Other causes	2	20%
Total	10	

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Table (2): causes of HCC.

Cause	No.	%
Liver cirrhosis	10	77%
Denovo	3	23
Total	13	