FINE NEEDLE ASPIRATION CYTOLOGY OF FOCAL HEPATIC LESIONS USING RAPID AND ROUTINE CYTOLOGICAL STAINS VERSUS ROUTINE HISTOPATHOLOGY

Thesis Submitted In Fulfillment for

the Master Degree in Tropical Medicine

By

Rasha Mohamed Tawfik El Etreby
M.B., B.Ch.
Faculty of Medicine – Cairo University

Supervised by:

Prof. Eman Ismael Ramzy
Professor of Tropical Medicine
Faculty of Medicine – Cairo University

Prof. Hany Mahmoud Khatab
Professor of pathology
Faculty of Medicine – Cairo University

Dr. Dalia Abd Alhameed Omran
Lecturer of Tropical medicine
Faculty of Medicine – Cairo University

Faculty of Medicine
Cairo University
2009

ABSTRACT

BACKGROUND:

Hepatocellular carcinoma is currently considered the leading cause of death amongst cirrhotic patients. Needle core biopsy (NCB) has been the standard procedure for histopathological diagnosis of focal hepatic lesions. In recent years, fine needle aspiration cytology (FNAC) has emerged as a minimally invasive and relatively inexpensive method of pathological evaluation of primary or metastatic hepatic masses. It can also provide rapid on-site diagnosis.

OBJECTIVE:

The aim of this study was to compare the accuracy of FNAC of focal hepatic lesions using rapid and routine cytological stains versus routine histopathology.

METHODS:

The study included 30 patients, who had focal hepatic lesions detected by Ultrasound and/or triphasic CT, in non cirrhotic or in child A or B cirrhotic patients. Biopsy together with FNAC were taken from each case. Some FNAC smears were used for bed site cytological examination with rapid stain equivalent to Rapi-Diff II stain. Others were used for routine cytology with papanicolaou stain, while core biopsies were preserved in 10% formaldehyde and sent for histopathological examination.

RESULTS:

The specificity, sensitivity, positive and negative predictive value of FNAC with routine stains when compared to histopathological examination were 100%, 85.7%, 100%, and 33.3% respectively , while the specificity, sensitivity, positive and negative predictive value of rapid cytology when compared to histopathological examination were 100%, 82.1 %, 100%, and 28.6% respectively, and specificity, sensitivity, positive and negative predictive value of rapid cytology when compared to routine cytological examination were 100%, 95.8%, 100%, and 85.7% respectively

Key words: HCC, Core biopsy, FNAC, rapid cytology.

ACKNOWLEDGEMENT

I feel always indebted to "GOD" the kindest and the most merciful.

It was an honor to work under the supervision of eminent professors:

PROF. DR. NABIL EL-KADY
PROF. DR. IMAN RAMZY
PROF.DR.HANY KHATTAB
DR. DALIA OMRAN

Who lent me their whole hearted support and immense facilities as is their usual with their candidates. To them, I owe more than I can record.

I pray to" God" to surround them with his blessing, protection, and to give them by his mercy the best .

I am greatly honored to express my deep gratitude and faithfulness to PROF. DR. NABIL EL-KADY, Professor of Endemic Medicine, Cairo University; he gave me the idea of the study, and carried out the whole practical work of cases with devoted comprehensive technical help through out the work, meticulous invaluable advice and support that cannot be expressed in words .

I am extremely grateful to the eminent PROF. DR. IMAN RAMZY, Professor of Endemic Medicine , Cairo University , for her choice of me for this work, for her sincere guidance and support. She gave me much of her experience, meticulous invaluable advice and support that can't be expressed in words. To her therefore, I express my deep sense of gratitude.

I wish to express my gratitude and appreciation to PROF.DR.HANY KHATTAB, Prof. of pathology department, Cairo University, for his great help, faithful advices, kind support from the start and all through the work until its completion, and immense facilities he offered.

I wish to thank DR. DALIA OMRAN for her generous help and goodness, meticulous revisions all through the work. She gave me much of her time, experience and support. Her valuable comments, efforts and collaboration were the causes to complete this work properly.

I would like to thank DR.DALIA IBRAHIM, Assistant Professor of community medicine; Cairo university, who did the statistical analysis of this study with much patience, faithfulness and devotion.

I would like to express my sincere thanks and deepest appreciation to the head of the department, PROF.DR.MAHASEN ABD ALRAHMAN, all eminent professors, staff members, and my colleagues and friends in Endemic Medicine Department.

And for those who filled this work with life, the patients, many thanks for the co-operation they have shown. I hope that with this and with other studies we can alleviate their sufferings.

Last but not least, allow me to send my deepest gratitude, my great appreciation & sincere thanks to my great family, my father, mother, husband, sister and brother, for their sacrifice in order to make me stand where I am today.

Table of contents

- **List of tables……I**
- **List of figures ……..…IV**
- **List of abbreviations……VI**
- **Introduction……..1**
- **Aim of work……..4**
- **Review chapters:**

- Chapter I: FOCAL HEPATIC LESIONS

- **Introduction…….. ..5**
- **Classification of focal hepatic lesions……...5**
- **Some important benign focal lesions:……8**

-Cavernous Hemangioma……8

- Hepatic Adenomas…… … 11

-Focal Nodular Hyperplasia…… 13

-Simple Liver Cysts…… 16

-Hydatid disease of the liver…… 17

-Focal Fat or Fat Sparing…… 18

-Pyogenic abscess …… 20

-Amoebic abscess…… 21

- ***Malignant focal hepatic lesions:***

-Liver Metastases…… 23

-Cholangiocarcinoma (CCA)…… 25

-Hepatic lymphoma…… 28

-Other rare tumours…… .29

Chapter II: HEPATOCELLULAR CARCINOMA

- *Epidemiology*…….. 30
- *Risk factors*…… 30
- *Clinical features*…… .31
- *Surveillance of HCC*…….. 32
- *Diagnosis:*…… … 35

-Serum markers…… 36

- Imaging studies…… 44

- Percutaneous biopsy…… 49

- *Histopathology*…… 53
- Genetic and biological research of HCC…….. 57

Chapter III: FNAC AND CORE NEEDLE BIOPSY

- *Diagnostic value*…… 60
- *Diagnostic approach to FNAC of focal hepatic lesions*… 64
- *Diagnostic approach to needle biopsies of hepatic focal lesions*…… … 66
- *STAINS:*…… … 74

- Hematoxylin and eosin (H&E) stains…… … 74

-Papanicolaou staining…… … 75

-Quick stains …… …… 76

- ***Patients an methods*…… ……79**
- ***Results*…….……...…... 88**
- ***Discussion*…….. .114**

- ***Summary*……..……124**
- ***Conclusions*……..……128**
- ***Recommendations*……..…..129**
- ***References*……*130***
- ***Arabic summary.***

List of Tables

Table	Subject	Page
Table (1a)	Age and sex of the studied patients	**88**
Table (1b)	Sex distribution of the studied patients.	**88**
Table (2)	Clinical manifestations of the studied patients	**89**
Table (3)	Laboratory data of the studied patients	**90**
Table (4)	Patient's classification according to modified Child scoring	**91**
Table (5)	Ultrasonographic Findings of the Studied Patients.	**92**
Table (6 A)	Ultrasonographic Findings of the studied focal lesions	**93**
Table (6 B)	Focal hepatic lesion size.	**93**
Table (7)	The histopathological findings of the studied group.	**94**
Table (8)	Comparison between (PAP), rapid cytology, and Histopathological examination, considering histopathology the standard examination.	**99**

Table (9)	Specificity, sensitivity, positive and negative predictive value of rapid cytology as compared to routine cytology.	**100**
Table (10)	Specificity, sensitivity, positive, negative predictive value and diagnostic accuracy of combined rapid and routine cytology as compared to histopathology.	**101**
Table (11)	Comparison between histopathology, PAP, and rapid cytology in subtyping of malignant focal hepatic lesions	**102**
Table (12)	Sex distribution in relation to the results of histopathology	**105**
Table (13)	Shows the clinical presentations in relation to histopathological results.	**106**
Table (14)	Comparison between patient's groups as regarding state of cirrhosis and Child scoring.	**108**
Table (15)	AFP level in different types of malignant focal hepatic lesions.	**109**
Table (16)	US characteristics of different focal hepatic lesion	**110**
Table (17)	Comparison between US and Triphasic CT findings of focal hepatic lesions.	**111**

Table (18)	characters of lesions not diagnosed by cytology	**112**
Table (19)	Imaging characteristics of lesion not diagnosed by rapid cytology.	**113**

List of Figures

Figure		Page
Figure (I)	Ultrasonographic appearance of hepatic haemangioma.	**9**
Figure (II)	MRI shows typical hepatic haemangioma.	**10**
Figure(III)	A suggested algorithm for investigation of a nodule found on ultrasound during screening or surveillance	**52**
Figure (1)	Histopathological diagnosis of FHLs	**95**
Figure (2)	HCC grades.	**95**
Figure (3)	Paraffin section of a case of HCC grade II, trabecular pattern (H & E, X 400).	**96**
Figure (4)	Paraffin section of a case of HCC grade I, trabecular pattern (H & E, X 400).	**96**
Figure (5)	Paraffin section of a case of sclerosing adenocarcinoma grade II, (H & E, X 400).	**97**
Figure (6)	Paraffin section of a case of hepatic lymphoma (H& E, X 400).	**97**
Figure (7)	Specificity, sensitivity, positive and negative predictive values of routine cytology (PAP), and rapid cytology as compared to histopathology.	**99**

Figure (8)	Specificity, Sensitivity, Positive predictive value (PPV), Negative predictive value (NPV) of rapid cytology as compared to routine cytology.	**100**
Figure (9)	A case of HCC grade II showing clusters of malignant cells (PAP, X 200).	**105**
Figure (10)	A case of HCC with focal glandular formation, showing clusters of malignant cells.	**105**
Figure (11)	A case of HCC grade II showing few malignant cells (Quick stain, X 400).	**106**
Figure (12)	A case of HCC grade II showing few malignant cells (Quick stain, X 400).	**106**

List of Abbreviations

AASLD	American association of the study of liver disease
AE	Alveolar ecchinococcosis.
AFP	Alpha feto protein.
AFU	Alpha 1- fucosidase.
AML	angiomyolipoma.
CC	Cholagiocarcinoma
CCA	Cholangiocarcinoma.
CE	Cystic echinococcosis.
CLD	Chronic liver disease
CT	Computed tomography.
DCP	Des- gamma carboxy prothrombin
DN	Dysplastic nodule
EH	Epithelioid haemangioendothelioma
ERCP	Endoscopic retrograde cholangiopancreatography.
FHL	Focal hepatic lesion.
FNAC	Fine needle aspiration cytology
FNH	Focal nodular hyperplasia.
GP73	Golgi protein 73.
GPC3	Glypican- 3.
(H&E)	Hematoxylin and eosin stains
HA	Hepatic adenoma.
HBV	Hepatitis B virus.
HCC	Hepatocellular carcinoma.
HCV	Hepatitis C virus.
HGDN	High grade dysplastic nodule.
HGF	Hepatocyte growth factor.
LCA	Lens culinaris agglutinin.
LGDN	Low grade dysplastic nodule
MRI	Magnetic resonance imaging.

MRN	Macro-regenerative nodule
NCB	Needle core biopsy
No.	Number.
NPV	Negative predictive value.
NS	Not significant.
OLT	Orhotopic liver transplantation
PAP	PAPANICOLAOU staining
PET	Positron emission tomography.
PHL	Primary hepatic lymphoma.
PIVKA- II	Protein induced by vitamine k absence or antagonist – II.
PPV	Positive predictive value.
PTC	Percutaneous transhepatic cholangiography
SCCA	squamous cell carcinoma antigen
SD	standard deviation
TGF- B 1	Transforming endothelial growth factor.
US	Ultrasound.
VEGF	Vascular endothelial growth factor
WHO	World health organization.