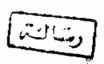
RECENT ADVANCES IN MANAGEMENT OF PRIMARY MALIGNANT NEOPLASMS OF THE LIVER

ANESSAY

Submitted for Partial Fulfillment of the Master Degree in General Surgery

616.99476 A.F

84



Ali Fouad Ali El Sawi M.B., B. Ch., Ain Shams University

Under The Supervision of

Dr. SAYED MOHAMED RASHAD

Assisstant Prof. of General Surgery Faculty of Medicine, Ain Shams University

Dr. AWAD EL KAYAL

Lecturer of General Surgery
Faculty of Medicine, Ain Shams University

Faculty of Medicine Ain Shams University 1993



47873

ACKNOWLEDGEMENT

I would like to express my deepest gratitude to Prof. Dr. SAYED MOHAMED RASHAD, Assisstant Professor of General Surgery, Faculty of Medicine Ain Shams University for his eminent supervision, generous help, continuous guidance and encouragement. It was only because of his tireless energy that this work was completed.

I, also, wish to acknowledge the help, advice and encouragement offered by $\mathcal{D}r$. \mathcal{AWADEL} \mathcal{KAYAL} , Lecturer in General Surgery Ain Shams University.

Ali Fouad Ali El-Sawi



Contents

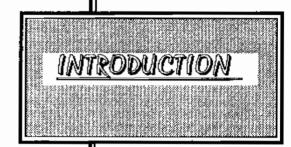
• Introduction

Chapter 1: Anatomy	
- Embryology	1
- Anatomy	10
* Surgical anatomy of the liver	10
* Surface anatomy	11
* Peritoneal relations of the liver	12
* Topographic relations of the liver	13
* Stability	18
* Lobes and segments of the liver	19
* Orientation of hepatic lobes in sectional imaging	25
* Blood vessels of the liver	27
* Intrahepatic biliary tree	38
* Lymphatics of the liver	38
* Nerve supply to the liver	40
- Histology	42
Chapter II: Pathology	
- Classification of hepatic primary malignant neoplasms	51
- Hepatocellular carcinoma	53
- Cholangio carcinoma	72
- Neuro endocine tumours	73

- Biliary cystadenocarcinoma of the liver	73
- Vascular tumours:	
* Angiosarcoma	75
* Malignant Haemangiopericytoma of the liver	75
* Epithelioid haemangioendothelioma of the liver	77
- Other primary hepatic tumours:	
* Undifferentiated Embryonic sarcoma	77
* Primary squamous cell carcinoma of the liver	77
* Non Hodgkin's lymphoma presenting as a primary	77
tumour of the liver	
* Primary hepatic carcinoid tumour	79
* Primary leiomyosarcoma of the liver	79
- Liver Tumours in Infancy	
* Hepatoblastoma	79
* Hepatocellular carcinoma	80
- Clinical picture	84
Chapter III: Investigations	
- Laboratory investigations	88
* Haematological tests	90
* Hepatitis virus markers	91
* Hepatic tumour markers	91
- Radiolocial studies	
* Plain X-ray	93
* Ultra sonography	94

• Colour Doppler flow imaging	98
• Ultrasound angiography with intra-arterial CO2	
microbubbles	98
* Isotopic studies	101
• Emission tomography	102
• The use of Radiolablled monoclonal antibodies	104
* C.T. of the liver	107
* M.R.I.	114
Magnetization transfer	116
• Multi section FLASH method	116
* Angiography	119
- Liver biopsy	128
* Aspiration biopsy	130
- Laparoscopy	137
- Percutaneous aspiration cytology	141
- Assessment of diagnostic techiques for liver masses	143
- Laparotomy and minilaparotomy	148
 Chapter IV: Treatment of Primary Hepatic Malignancy 	
- Medical Treatment	152
* Embolization of liver tumours	152
* Arterial embolization and dearterialization	155
* Therapeutic basis of hepatic arterial infusion	
chemotherapy	159
• Immunotherapy	162

* Primary hepatic tumours in childern	164
* Ethanol injection	165
- Surgical treatment	167
* Liver resection	167
• Right hepatectomy	172
Right hepatic lobectomy	174
• Left hepatectomy	181
• Extended left hepatectomy	181
• Left hepatic lobectomy	181
Hepatic resection for hilar cholangiocarcinoma	187
* Ultrasonically guided segmentectomy and	
subsegmentectomy, application in the cirrhotic	
liver	192
 Techniques of subsegmentectomy 	195
* Liver transplantation	
• Immunological aspect	200
Anaesthesia and pre operative care	204
• Orthotopic liver transplantation	212
• Liver transplantation in children	219
Heterotopic liver transplantation	224
Summary	227
	.527
References	229



Introduction

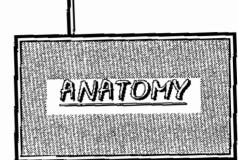
In Recent years, an increased understanding of the segmental anatomy of the liver, the surgical anatomy of the hepatic viens and portal radicles, the pathological picture of the different types of 1ry. liver tumours and of refined laboratory and imaging techniques including tumour markers.

Colour Doppler flow imaging, enhanced dynamic C.T., Multi Section FLASH MRI imaging and Fine needle biopsy techniques has been associated with an increase in the use of surgical methods in treatment of liver cancer.

The recent different lines of management of primary malignant hepatic neoplasms are discussed including medical treatment as palleative therapy or as preoperative chemotherapy for cytoreduction and sequential resection.

Surgical treatment in the form of hepatectomy, lobectomy, segmentectomy or subsegmentectomy and liver transplantation as the last resort.

Our aim in this essay is to throw light on the most recent and accurate methods of management.



and the right and left hepatic ducts. That part of the original pars hepatica adjacent to the pars cystica becomes the comon hepatic duct. (Fig : 2)

Pars hepatica sends solid hepatic cords into the adjacent mesenchyme of the septum transversum. Some of the mesenchymal cells form blood islands or isolated vesicles and others differentiate into haemocytoblasts.

- The endothelial lining cells of the blood islands retain the potentiality to develop into machrophages (Kupffer cells).
- As the hepatic cords continue to grow and anastomose, the isolated vesicles containing blood cells become confluent to form continuous channels which become small blood vessels.
- As the anastomosing hepatic cords grow out laterally with the interdigitating vessels, the vitelline and umbilical veins become incorporated into or confluent with, the small vessels, thus the liver sinusoids develop in situ (Lipp, 1952).

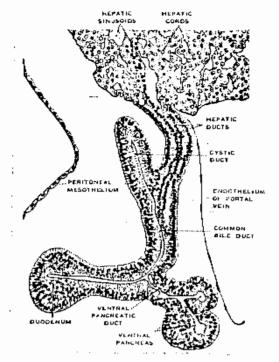
Major vessels within the liver can be identified by the 32nd day (5mm C.R. Length embryo). The vessels are right and left umbilical veins, the transverse portal sinus and the hepatic portion of the inferior vena cava.

In the 6mm C.R. length embryo, a large venous trunk develops in the sinusoid system and shunts the blood directly from the umbilical vein to the inferior vena cava. This is the ductus venosus which atrophies soon after birth, remaining as the ligamentum venosum. The right umbilical vein atrophies at about the 34th day (7mm C.R. length embryo). So that during the prenatal period oxygenated and nutritive blood passes to the liver via the left umbilical vein.

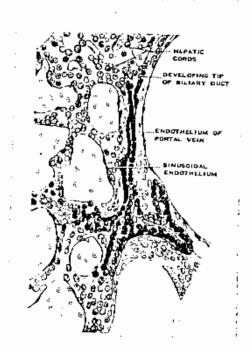
- The hepatic cords, soon aquire a lumen which progresses from the lumen of the original hepatic diverticulum distally, providing the hepatic parenchyma with an anastomosing tubular pattern, and thus the pars hepatica establishes the architectural pattern characteristic of the adult liver. (Elias, 1949 a and b). (Fig : 3)
- The mesoderm of the septum transversum is the principal site of haematopoiesis during the embryonic and fetal periods of development. Haematopoiesis attains its maximal activity in the liver towards the 6th to 7th month.
- Hepatic haematopoiesis then regresses apidly and the liver possesses only a few disseminated island of haematopoiesis at birth. (Du Bois, 1963)

At about the 46th day (18mm C.R. length), the meoderm round extra-hepatic ducts begin to migrate into the liver along the major branche of the portal vein. As the mesoderm accumulates round the portal vessels, the adjacent parenchymal cells, develop into duct epithelium. The mesoderm round the portal vein and it branches differentiates into connective tissue.

- The hepatic artery and a branch of the vagus nerve migrate into the liver, with the mesoderm adjacent to the portal vein.
- The hepatic triad i.e., the bile ducts, hepatic artery and portal vein constitutes embryomically and morphologically the most central and proximal units of the liver and thus are considered as being intra-lobular structures in a portal lobule.
- The central veins are interlobular. The cells which exhibit the most active DNA metabolism are those closest to the structures



A scheme to show the development of the pancreas, cystic duct and hepatic ducts in an 8mm human embryo (Fig : 2)



A scheme to show the differentiation of the biliary ducts in the cords of hepatic cells. There is an abrupt transition from the epithelium of the biliary ducts to the hepatic cells.

(Fig:3)

constituting the hepatic triad while those least active are found closest to the central veins.

- The rapid proliferation of the liver cells causes the organ to increase in size and to occupy most of the space in the upper part of the developing abdominal cavity. Its dorsal extension takes a part in the obliteration of the pleuroperitoneal canals.

At 35mm stage the liver is approximately 10% of the body weight and becomes red in colour owing to accumulation of erythroblasts.

- Erythrocytes which come from erthyrobasts, pass through the walls of the venous sinusoids and enter the fetal circulation.
- At a later stage the hepatic growth rate gradually diminishes so that the liver at birth is only 5% of the body weight.
- The mesoderm of the septum transversum caudal to the developing diaphragm surrounds the developing liver and is continuous from the lesser curvature of the stomach and duodenum to the ventral body wall. It can be divided into 3 portions:
- 1- The portion which persists as the coronary and triangular lig. and the falciform ligament. The umbilical vein which is enclosed in the falciform ligament becomes obliterated shortly after birth and is then called the ligamentum teres.
- 2- The portion which becomes the hepatic capsules (Glissons capsule).
- 3- The portion extending from the liver to the stomach and the foregut part of the duodenum. This persists as the lesser omentum which can be divided into gastrohepatic and hepatoduodenal ligament which has

the bile duct in its free edge.

Electrone Microscopy:-

- In the late embryonic and fetal stages of development the hepatocytes contain both rough and smooth endoplasmic reticulum. Also possesses mitochondria with well developed cristae and an abundance of particulate glycogen.
- Bile canaliculi are present as expansions of the intercellular space between 2 or more hepatocytes. Short microvilli project into the lumen of the bile canaliculus from the portions of the cell membrane bordering the bile canaliculus.
- The surface of adjacent hepatocytes bounding a canaliculus are linked by desmosomes in the immediate vicinity of the canaliculus. Several membrane limited bodies with dense heterogenous content are found in the cytoplasm near each bile canaliculus which have been identified as lysosomes.

The endothelium of the simosoids rests on the tips of a large number of irregularly oriented microvilli on the surface of the hepatocytes.

Between the hepatocytes and the endothelium a perivascular space is found which has been called the space of Disse. The sinusoids communicate with the space of Disse through fenestrations in the endothelial cells. Plasma gains access to the space of Disse through the fenestrations and thus bathes the hepatocytes directly, facilitating the exchange of metabolities.