Malignant Tumours of The Liver

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By
Sherif Adly Farid

Under Supervision of
Prof. Dr. M. Samir Abou Zeid
Prof. and Head of General
Surgery Department.
Faculty of Medicine
Ain Shams University

Dr. Alla Abdalla
Lecturer of General Surgery
Faculty of Medicine
Ain Shams University

Faculty of Medicine
Ain Shams University

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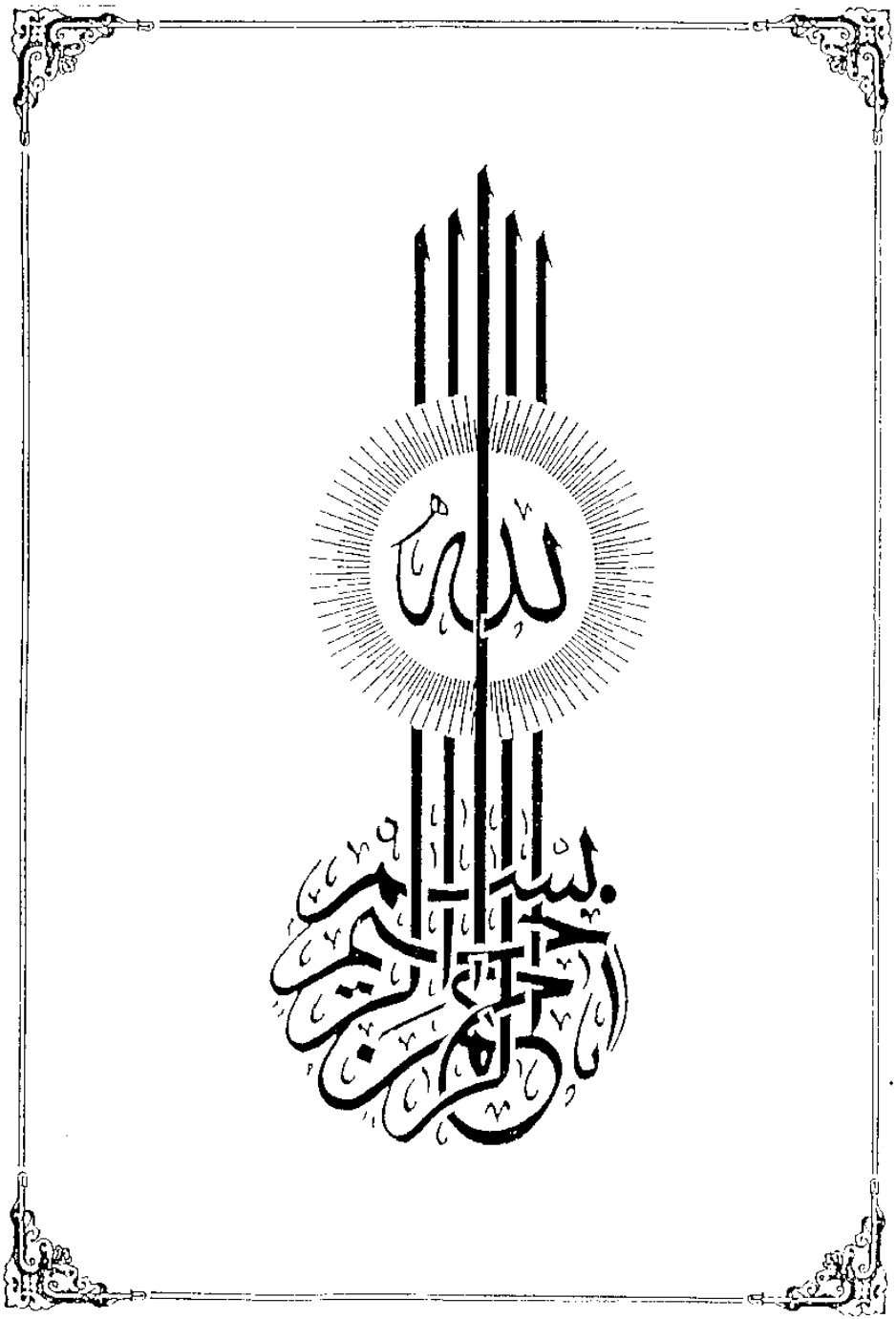

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INTRODUCTION

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The incidence of malignant tumours of the liver is increasing, possibly due to the evolution of the diagnostic tools specially the radiological ones.

In this review, the pathology, aetiology and diagnosis of the malignant tumours of the liver will be discussed.

The treatment will be discussed in details with special stress on liver resections.

PATHOLOGY

The liver is composed of hepatocytes, billiary epithelial cells, and mesenchymal tissues that form the supporting structures and vascular channels, (Goodman et al., 1985).

The two major types of malignant epithelial tumours of the liver are hepatocellular carcinoma, the predominant one, and intrahepatic bile duct carcinoma, commonly designated cholangio-carcinoma or cholangio-cellular carcinoma. Other less common malignant epithelial tumours primary to the liver include combined hepatocellular and cholangiocarcinoma, hepatoblastoma, bile duct cystadenocarcinoma, mucoepidermoid carcinoma, carcinoid and squamous cell carcinoma (Okuda et al., 1985).

Non-parenchymal malignant tumours are those whose cell of origin or pattern of differentiation is considered to be that of the various mesenchymal tissues or their precursors. Thus, the liver may be the site of primary fibrosarcoma, leiomyosarcoma, rhabdomyosarcoma, malignant fibrous histocytoma, angiosarcoma, and undifferentiated (embryonal) sarcoma. These are all quite rare (Goodman et al., 1985).

The liver virtue of its location, blood supply, anatomy and other poorly understood factors, provides a prime location for metastases from malignant tumours. Metastases are by far the most common malignant neoplasms of the liver (Pickren et al., 1982).

Table (1): Classification of Primary Tumours of the Liver

From (Vitale et al., 1986).

Benign	Malignant
Epithelial tumours	
Liver cell adenoma	Hepatocellular carcinoma
Bile duct adenoma	Cholangiocarcinoma
Billiary Cystadenoma	Billiary cystadenocarcinoma
Carcinoid tumour	---
-----	Squamous carcinoma
-----	Mucoepidermoid carcinoma
Mesenchymal tumours	
Cavernous haemangioma	----
Infantile haemangioendothelioma	----
-----	Haemangiosarcoma
-----	Undifferentiated (embryonal) sarcoma
Fibroma	Fibrosarcoma
Lipoma	-----
Leiomyoma	Leiomyosarcoma
-----	Epithelioid Leiomyoma
Benign mesenchymoma	Malignant mesenchymoma
Mixed tumours	
----	Hepatoblastoma
----	Mixed hepatic tumour
----	Carcinosarcoma
Teratoma	
Tumour like lesions	
Focal nodular hyperplasia	
Mesenchymal hamartoma	
Microhamartoma (Von Meyenburg complex)	

HEPATOCELLULAR CARCINOMA

Our knowledge of the worldwide distribution of cancer remained anectodal until the introduction of systematic population-based registration (Waterhouse et al., 1977).

Hepatocellular carcinoma (HCC) is one of the few cancers that show a distinct geographic distribution. Its prevalence varies from country to country and even within the same country (Okuda et al., 1985).

Hepatocellular carcinoma (HCC) is one of the most common malignant tumour in sub-Saharan Africa and South Asia and uncommon variety in Northern Europe. In Mozambique, where primary liver cancer is the most frequent malignancy, it has the highest frequency of HCC in the world. HCC is the third commenest solid malignancy in men in Japan and the tenth in the United States (Okuda et al., 1985).

The geographical variation in the frequency of HCC are closely related to socioeconomic and cultural factors than geographical ones (Arthur et al., 1984). For examples, Africans and Asians who migrate to countries of lower incidence tend to aquire their adapted environment. This is true for negros long established in the United States, for chinese moved to Singapore a generation ago (Hutt., 1971).

Aetiology:

In all countries, including the UK, most cases of HCC (approximately 80%) arise in cirrhotic, classically macronodular liver (Millward- Sadler et al., 1986).

In the presence of cirrhosis, the risk of malignancy increases due to the fact that an increased rate of cell replication in the liver (due to first hit) enhances the effect of many carcinogens (second hit) (Anthony, 1979).

Evidences from many studies published since 1970 suggest that HBV infection is a major cause of liver disease in areas where liver cell carcinoma is common. These studies have generally been of the case/control type, comparing results of testing for the various antigenic components of HBV and the antibody responses to them in patients with cirrhosis and/or liver cell carcinoma versus normal subject, blood donors and patients suffering from other diseases (Anthony, 1979).

There are many supportive evidences for the aetiological role of this virus, these evidences are, the parallelism between the prevalence of HCC and the frequency of HBsAg carriers, the high rate of positive HbsAg (90%) or high titres of antibody against virus core antigen in patients with HCC, production of HBsAg by several cell lines derived from human HCC and the

integration of HBV genome into the cancer cell DNA (Okuda et al., 1985).

Aflatoxins are toxic metabolites produced by the moulds Aspergillus flavus and, less commonly Aspergillus parasiticus, these aflatoxins include a number of closely related substances which occur in two series: aflatoxin B_1 and derivatives with their blue fluorescence and aflatoxin G_1 and derivatives with their yellow fluorescence, unfortunately, B_1 is the most potent toxin and carcinogen of the group (Anthony et al., 1979).

Aflatoxin have been found in many foodstuffs including peanuts, soya bean, corn, rice, wheat, barley and cotton-seed, the risk is greatest in developing tropical countries where storage conditions encourage the growth of fungi (Anthony et al., 1979).

Aflatoxins produce a severe acute liver injury in man when ingested in large dose, yet none of the survivors has developed liver cancer, so perhaps chronic exposure is necessary for liver cancer to occur (Okuda et al., 1985).

The role of aflatoxin in the aetiology of human HCC is unclear, in the hepatocyte, aflatoxin B_1 is metabolized by microsomal mixed function oxidase system to produce AFB_1- 2,3 epioxide, which is

believed to be the carcinogen. Alternatively, aflatoxins may suppress cell mediated immunity and facilitate persistent hepatitis B infection and eventually HCC (Lohiya et al., 1987).

In temprate climates, alcohol has been associated with HCC, particularly in older patients, there is a four fold risk of primary hepatocellular carcinoma in alcoholics in northern Europe and North America (Nonomura et al., 1986).

The development of HCC seems to be hastened by habitual intake of more than 25.2 ml of ehanol per day in HBsAg positive patients and by excessive habitual drinking in HBsAg negative patients (Ohnishi et al., 1982).

Although alcoholism results in micronodular cirrhosis, HCC in HBV-negative alcoholics is mostly associated with mixed or macronodular cirrhosis, this is because, micronodular cirrhosis in alcoholics, by time will be converted to macronodular (Anthony, 1979).

Alcohol can cause alterations in serum immunoglobulin levels, in circulating (T) and (B) cell and in in-vitro lymphocyte responsiveness (Anthony, 1979).

Contraceptive pills had been increminated as an aetiological factor for HCC as, there is well accepted

relationship between synthetic estrogenic oral contraceptives and benign adenoma of the liver (Arias et al., 1988).

Henderson and colleagues from Los Angeles (1983) showed that women with HCC diagnosed between 1975 and 1980 had a greater use of the pill than matched controls.

The role of oral contraceptives may be an enzyme-inducer that may potentiate the carcinogens of certain compounds by increasing their rate of conversion to carcinogenic metabolites (Sherlock, 1985).

Estrogen in pills may induce vascular changes or cell hypertophy and that results in the early presentation of an early developing tumour (Neuberger et al., 1986).

Many drugs contain amino groups that can, at least theoretically, undergo nitrosation in the body to nitrosamines which have been shown to be powerful liver carcinogens in many animal species (Anthony et al., 1979).

A common example of these drugs are androgenic-anabolic steroids which produce some histologic precursor lesions as hyperplasia of the hepatocytes and sinusoidal cells and peliosis, the term which refers to the occurrence of multiple blood filled cavities in the liver parenchyma and which are infrequently lined by endothelium (Anthony, 1979).

In 1981, Westaby reported 33 patients with androgen-associated hepatic tumours, 14 of these patients had recieved androgens as therapy for fanconi´s anaemia, and 19 patients for various other potential androgen-responsive illness. In 1984, Wylie et al. reported a case of a young man who developed a primary hepatic malignancy after taking androgens to increase his skeletal muscle mass.

Another common example of drug which may predispose to liver malignancy is thorotrast which is colloidal preparation of thoruim dioxide, it emits alpha, beta and gamma rays, with a biological half life of 50 years. Thorotrast was used as an intra-arterial or intravenous contrast agent, actively taken by macrophages in the liver, spleen and bone marrow with 7.0% going to the liver (Ebie et al., 1986).

The use of radioactive phosphorus in polycythaemia vera has been associated with HCC in man (Moore et al., 1976).

Another aetiological factor of HCC is alpha -1--antitrypsin defficiency which is a genetically determined condition associated with pulmonary emphysema and liver cirrhosis (Anthony, 1979).

Patients with alpha 1 antitrypsin defficiency have a much higher risk of cirrhosis than has been