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"Fibrolamellar Hepatocellular Carcinoma In Mexican Patients"

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Fibrolamellar hepatocellular carcinoma in mexican patients.

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The aim of this report is to describe the frequency, clinical, and morphologic characteristics of fibrolamellar hepatocellular carcinoma in Mexican patients. Fibrolamellar hepatocellular carcinoma (FLHCC) is a rare variant of hepatocellular carcinoma. Although this tumor appears to be predominant among the Caucasian population of the U.S, FLHCC has been described in many other countries. The frequency and characteristics of FLHCC in Latin American population is almost unknown. The clinico-pathologic characteristics of seven (5.8%) Mexican patients with FLHCC, obtained among 121 hepato-cellular carcinomas are described. The frequency of these tumors was compared with the frequency reported in other geographic areas in the international literature between 1980 and 1999. There were four women and three men. Two patients had taken oral contraceptives for six months and a year prior to diagnosis; another patient had positive serology for the hepatitis B virus. Common symptoms included a palpable mass, abdominal pain and weight loss; two patients presented jaundice. In two patients the tumor had been removed eight and three years previously, and they were readmitted when FLHCC recurred. In three patients the diagnosis was suspected in radiological studies (computed tomography and/or magnetic resonance). Laboratory tests were non-specific. In four patients, resection of the tumor was performed, and in the remaining three the neoplasm was diagnosed by percutaneous hepatic biopsy. Two patients had died of disease at the time of the study, and another was alive with recurrent disease. Conclusions: fibrolamellar hepatocarcinoma is an uncommon, but not an exceptional neoplasm in our population and represents 5.8% of all hepatocarcinomas reviewed.

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Fibrolamellar Hepatocellular Carcinoma in Mexican Patients

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Abstract

Goals. To describe the frequency, clinical, and morphologic characteristics of Fibrolamellar hepatocellular carcinoma in Mexican patients.

Background. Fibrolamellar hepatocellular carcinoma (FLHCC) is a rare variant of hepatocellular carcinoma. Although this tumor appears to be predominant among the Caucasian population of the U.S, FLHCC has been described in many other countries. The frequency and characteristics of FLHCC in Latin American population is almost unknown.

Study. The clinicopathologic characteristics of seven (5.8%) Mexican patients with FLHCC, obtained among 121 hepatocellular carcinomas are here described. The frequency of this tumor were compared with the frequency reported in other geographic areas in the international literature between 1980 and 1999.

Results. There were four women and three men. Two patients had taken oral contraceptives for six months and a year prior to diagnosis; another patient had a positive serology for the hepatitis B virus. Common symptoms included palpable mass, abdominal pain and weight loss; two patients presented jaundice. In two patients the tumor had been removed eight and three years previously, respectively, and were readmitted when FLHCC recurred. In three patients the diagnosis was suspected in radiological studies (computed tomography and/or magnetic resonance). Laboratory tests were non specific. In four patients, resection of the tumor was performed, and in the remaining three the neoplasm was diagnosed in percutaneous hepatic biopsy. Two patients had died of the disease at the time of the study, and another was alive with recurrent disease.

Conclusions. Fibrolamellar hepatocarcinoma is an uncommon, but not an exceptional neoplasm in our population and represents 5.8% of all hepatocarcinomas reviewed.

Key words: Fibrolamellar, hepatocellular carcinoma, liver, neoplasm, Mexico.

Introduction

Hepatocellular carcinoma (HCC) is a tumor characterized by low resectability rates, poor response to non-surgical treatment, and infrequent long-term survival. In contrast, patients with the fibrolamellar variant of hepatocellular carcinoma have much higher resectability rates and overall longer survival (1,2). The original description of this histological variant of HCC has been referred to as either hepatocellular carcinoma with laminar fibrosis, hepatocellular carcinoma with polygonal cell type and fibrous stroma, or eosinophilic HCC with lamellar fibrosis (1). The term currently agreed upon is fibrolamellar hepatocellular carcinoma (FLHCC).

Although this tumor appears to be more frequent among the Caucasian population of the United States (U.S.) (2), FLHCC has been described in diverse countries (1-44). In our knowledge there are only two reports of FLHCC in Latin American population (3,32) The aim of this study is to report the frequency, clinical and morphologic features of seven Mexican patients and compare them with previous series of FLHCC reported in the international literature during the last two decades.

Patients and Methods.

All cases of hepatocellular carcinoma between January 1987 and April 2001 from the Department of Pathology at INCMNSZ, were retrospectively reviewed, by two pathologists (JAN, LBQ). Patients with indisputable diagnosis of FLHCC were included. Clinical data including age, sex, symptoms, laboratory tests, radiologic studies, treatment, and follow-up were obtained form hospital records. Detailed gross and microscopic features were assessed.

To compare our results, 165 FLHCC published in the international literature between 1980 and 1999 (1-45) were reviewed. For analytical purposes, a geographic distribution was performed as follows: United States of America (U.S.), Europe; Asia; Latin America; Australia, Middle East (Arab countries and Israel), and Africa. In some series for which the number of HCC and FLHCC was

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assessed, the percentage of FLHCC was obtained and compared with the frequency found in this study.

Results

Of 121 HCC, seven were FLHCC; overall frequency of FLHCC among all HCC was 5.8%. Clinico-pathologic characteristics are summarized in table 1. Case two was previously reported (3). Two patients received oral contraceptives for six months and one year respectively (patients 2 and 5). One patient showed serologic evidence of hepatitis B virus infection (patient 7). The most common symptoms included palpable mass and abdominal pain, weight loss, weakness, nausea and vomiting; two patients presented jaundice. In two patients, FLHCC was diagnosed and surgically removed eight and three years before admission to our hospital for recurrence.

Radiologic studies (computed tomography (CT) scan or magnetic resonance (MR)) demonstrated the tumor in all cases; in three patients diagnosis of FLHCC was suspected. The tumor measured more than 20 cm in one patient, between 10 and 20 cm in two patients and less than 10 cm in the remaining two. Laboratory findings revealed in most cases increase of serum alkaline phosphatase, mild elevation of serum transaminases, and anemia. In four cases the tumors were surgically removed. On gross examination, the neoplasia consisted of a yellow-brown, well-demarcated lesion; and two of them showed an irregular central scar. (Figure 1). Diagnosis in the remaining three patients was performed in liver percutaneous biopsy. Histologic features in all cases consisted of well-differentiated polygonal neoplastic cells growing in nests or cords and separated by dense fibrous bundles. Neoplastic cells showed abundant granular, eosinophylic cytoplasm with round nuclei and prominent nucleoli (Figure 2). In four patients, adjacent liver parenchyma showed non-specific alterations such as chronic pericholangitis and focal steatosis.

According to the literature review, this tumor seems to be more frequent in caucasian population of the U.S. (Table 2). Nevertheless, the frequency of FLHCC shows a wide variation from one study to other and even within series of a single country (Table 3).

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Discussion

The epidemiology of FLHCC has been the subject of some debate in the literature (22, 24, 45). Although it was once believed that this neoplasia was found only in the U.S. (2), several reports have confirmed that it can be found in other countries (table 2). The frequency and clinico-pathological characteristics of FLHCC in Latin American countries are almost unknown and we only found one series of this neoplasm between 1980-1999 period (32), and a case report in our country (3).

Although FLHCC has a better prognosis than conventional hepatocellular carcinoma (1), two patients in this series had died at the time of this report; another was alive with a recurrent disease and still another was lost to follow-up. The remaining three patients were in good condition, although the follow up period was still too short to establish any conclusions. In four of seven cases, it was possible to remove the neoplasia, even when some of the tumors were fairly large (Table 1). This high percentage of resectability is in agreement with information gathered from other series (1). As a group, symptoms in these patients were also very similar to previous information found in the literature (1), except in two cases that were associated with jaundice. This symptom has been reported only occasionally (36, 43) and appears due to direct invasion or migration of tumor tissue into the biliary system.

Although the etiology of FLHCC is unknown and has not been associated to administration of drugs or viral infections, it must be emphasized that two of the four women in this series took oral contraceptives for periods of six months and one year respectively, and another was seropositive for the hepatitis B virus.

Radiologic studies (CT scan and MR) made it possible to suspect the diagnosis of FLHCC in three of the seven cases. In one series of 31 patients (13) at CT scan, the margins of the tumors were well defined in 24 (77%) cases, calcifications were depicted in 21 (68%), a central scar in 22 (71%), and abdominal lymphadenopathy was found in 20 (65%).

Frequency of FLHCC in our hospital (5.8%) is similar to that reported by Dunk (34) in England (Table 3). However, we must be mention that the frequency of this

neoplasia can vary considerably from a series even within a single country. Thus, Chedid (4) in the U.S. found four fibrolamellar carcinomas in a series of 224 hepatocellular carcinomas (1.8%), while Wood (5), also within the U.S. population, found 15 cases of FLHCC in 77 hepatocellular carcinomas (19.4%). Review of other series in other populations also revealed variations in the frequency of this tumor. In most populations FLHCC represents less than 5% of the primary carcinomas of the liver (Table 3). A review of the literature for a period of 20 years suggests that FLHCC is predominant in the U.S. The predominance of FLHCC in the U.S. (Table 2) could be explained by a number of reasons, including the following: a) FLHCC is diagnosed and reported more frequently in the U.S. than in other countries, b) FLHCC is reported primarily in the British literature and in U.S. journals, which are widely distributed, c) fibrolamellar hepatocarcinoma is diagnosed and reported only sporadically in poorer countries; d) the low frequency of this neoplasia in some Oriental countries in Asia, including Korea, China, and Japan seems to be real (20, 35) and, e) although the reasons are unknown, the frequency of FLHCC in the U.S. it could be really high. While FLHCC has been noted outside the U.S. it probably is true that it is rare in countries in which the usual type of hepatocellular carcinoma is common. Several series of HCC from endemic areas have specifically noted the absence of FLHCC (45). The seven patients reported here were born and lived in Mexico, and none was were immigrant or of Caucasian descent.

There are still many questions concerning FLHCC that need to be answered including those related to its etiology and epidemiology. As has been suggested, an international case registry of the neoplasm in this field is necessary to better understand these etiologic and epidemiologic aspects (45).

Table 1. Clinical features of fibrolamellar hepatocellular carcinoma in Mexican patients

Case	Sex/Age	Symptoms	Radiology	Treatment	Follow up
1	F/26	Resection of the tumor 8 years previously. Readmission due to abdominal pain, palpable mass, weight loss, and ascitis	CT scan: LHL (8 cm). Extension to retroperitoneum, mesentery, and lymph nodes.	Recurrent tumor not resectable Chemo-therapy	AWD, 1 year
2	F/17	Abdominal pain, nausea, weight loss, and palpable mass (7 months)	CT scan: RHL (18cm). Well-defined limits. Adenoma vs FLHCC	Resection	AFD, 1 year
3	M/21	Nausea, vomiting, weight loss and palpable tumor (6 months)	MR: LHL (14 cm). Non-resectable tumor.	Chemotherapy	DOD, 3 weeks
4	M/25	Resection of the tumor 3 years previously. Admitted with abdominal pain and dyspepsia.	CT scan: RHL (7.4 cm). Well-defined limits.	Resection of recurrent tumor.	AWD, 1 month
5	F/19	Abdominal pain, jaundice, and weight loss (10 days)	CT scan and MR: RHL (17 cm). Calcifications and well defined limits. Probable FLHCC.	Resection	AFD, 1 week
6	F/19	Epigastric pain, vomiting, diarrhea, fever, weight loss and palpable mass (3 months)	CT scan: RHL (14cm). Extension to mesentery and retroperitoneum.	Non-resectable tumor	DOD, 1 year
7	M/24	Fever, astenia, jaundice, palpable mass (4 months).	CT scan and MR: LHL (26 cm). Probable FLHCC	Resection	Unknown

CT: computed tomography; MR: magnetic resonance; LHL: left hepatic lobe; RHL: right hepatic lobe; AFD: alive free of disease; AWD: alive with disease; DOD: dead of disease; FLHCC: Fibrolamellar hepatocellular carcinoma.

Table 2. Geographic distribution of fibrolamellar hepatocellular carcinoma obtained from 44 reports of the international literature.(1980-1999).

Geographic area	Number of cases	%
U.S.	100	60.6
Europe	40	24.2
Asia	15	9.0
Latin America	5	3.0
Australia	2	1.2
Middle East	2	1.2
Africa	1	0.6
Total	165	99.9

Table 3. Frequency of fibrolamellar hepatocellular carcinoma among hepatocellular carcinomas.

Author	Country	HCC No. Cases	FLHCC No. cases (%)
Chedid[4]	U.S.	224	4 (1.8)
Wood[5]	U.S.	77	15 (19.4)
Kaczynski[10]	Switzerland	532	2 (0.3)
Van Leeuwen[18]	The Netherlands	61	2 (3.3)
Dunk [34]	England	41	2 (4.9)
Ashraf [39]	Saudi Arabia	75	1 (1.3)
Present report	Mexico	121	7 (5.8)

HCC: Hepatocellular carcinoma. FLHCC: Fibrolamellar hepatocellular carcinoma

Figures

1. Macroscopic aspect of a fibrolamellar hepatocellular carcinoma. The neoplasia shows well-defined limits and an irregular central scar.
2. Fibrolamellar hepatocellular carcinoma. Neoplastic hepatocytes are arranged in nests and cords divided by bundles of fibrous tissue (HE, x 100).

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