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Original Research Article

Clinico-pathological study of primary carcinoma of the liver

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ABSTRACT

Background: Since the incidence of the primary carcinoma of the liver in Warangal is very high when compared to other parts of the country, the possible etiological factors have been studied for the increasing frequency of Primary carcinoma of the liver with a view for further follow up. The objective of the present study was to undertake a thorough study of histopathological changes, typing and its association with cirrhosis.
Methods: A hospital based cross sectional study was carried for a period of three years among 56 cases of primary carcinoma of the liver at MGM hospital. Institutional Ethics Committee permission was obtained. Informed consent was taken from each and every patient. Detailed history, clinical examination and investigations were carried out for each and every included patient. Liver biopsy was done under strict aseptic precautions.
Results: The incidence of Primary carcinoma of the liver was found to be highest in males as compared to females. The highest incidence of Primary carcinoma of the liver was found in the age group of 41-50 years. In only 14.3% of cases the Primary carcinoma of the liver was associated with cirrhosis of liver. The most common type of cell found on histopathology was cylindroids type in 35.7% of cases followed by trabecular type in 28.5% of cases.
Conclusions: Incidence of Primary carcinoma of the liver was found to be very high. This was not associated with corresponding increase in cirrhosis. The cause of their increase was obscure.

Keywords: Cirrhosis, Histopathology, Primary carcinoma of the liver

INTRODUCTION

The frequency of liver cancer as reported from different parts of the world shows striking differences. Primary carcinoma of the liver is endemic in some parts of the globe and it is said to occur with higher frequency in Africa and in the rice eating orient including South East Asia. Similarly, it is quite common in Japanese, Chinese, Philippines and Indians.

In contract, it is decidedly low in the European countries and in the United States. Continued examination of geographic distribution may point to new endemic foci and changes in the incidence of the tumor are worthy of note, for it may focus the attention to new etiological factors.[1]Its widespread occurrence in animal kingdom and various types of carcinogenesis factors connected with its occurrence have added to the charm of the study. The Primary carcinoma of the liver has attracted the interest of clinician, pathologist and experimentalist out of proportion to its incidence and the chance of cure, the rate of experimental production to its incidence and the chance of cure.

The rate of experimental production and study of carcinogenesis resulting from it, the great geographical variation in the incidence and the high incidence of cirrhotic patients have given it to a new look.[2]

In India, several workers have given variable incidence of Primary carcinoma of the liver in the different parts of the country. The present study indicates a relatively high incidence of Primary carcinoma of the liver in and around Warangal region when compared to the incidence from other of the country. Since the incidence of the Primary carcinoma of the liver in Warangal is very high when compared to other parts of the country, the possible etiological factors have been studied for the increasing frequency of Primary carcinoma of the liver with a view for further follow up. The objective of the present study was to undertake a thorough study of histopathological changes, typing and its association with cirrhosis.

METHODS

A hospital based cross sectional study was carried for a period of three years among 56 cases of primary carcinoma of the liver at MGM hospital. Institutional Ethics Committee permission was obtained. Informed consent was taken from each and every patient. Detailed history, clinical examination and investigations were carried out for each and every included patient. Liver biopsy was done under strict aseptic precautions. The patients were studied in detail with special reference to their socio-economic status, food habits, drug intake and addiction for alcohol.

The diagnosis of hepatoma was made by uniformity of symptoms of short duration, positive history of detailed dietary habits, alcohol addiction and massive hepatomegaly and by several routine investigations such as hemogram, ESR, urine examination, stool examination, liver function tests, blood sugar, plain and barium meal X ray of the abdomen and lastly confirmation by liver biopsy. Liver biopsy was done under strict aseptic precautions by routine procedure as described in standard protocol and also in some cases it was done at the site of nodule over the liver. Obtained liver tissue was immediately preserved in formaldehyde. The histopathological study of the liver tissue was done in the department of Pathology. The data was entered in the Microsoft Excel Sheet and analyzed using proportions

RESULTS

The incidence of Primary carcinoma of the liver was found to be highest in males as compared to females. This may be due to increased alcohol consumption among males.

The highest incidence of Primary carcinoma of the liver was found in the age group of 41-50 years followed by 51-60 years. Lowest incidence of Primary carcinoma of the liver was found in the age group of 31-40 years. In only 14.3% of cases the Primary carcinoma of the liver was associated with cirrhosis of liver.

Table 1: Incidence of Primary carcinoma of the liver as per gender.

Primary carcinoma of the liver	Male	Female	Total
Yes	52 (92.86%)	04 (7.14%)	56 (100%)

Table 2: Incidence of primary carcinoma of the liver as per age.

Age (years)	Number	Percentage
21-30	08	14.3
31-40	04	07.1
41-50	24	42.9
51-60	12	21.4
61-70	08	14.3
Total	56	100

Table 3: Association of primary carcinoma of the liver with cirrhosis of liver.

Type of cases	Number	Percentage
Primary carcinoma of the liver alone	48	85.7
Primary carcinoma of the liver with cirrhosis of liver	08	14.3
Total	56	100

Table 4: Distribution of study subjects as per their symptoms.

Symptoms	Number	Percentage
Pain in the right hypochondrium	48	85.7
Swelling in the right hypochondrium	24	42.9
Anorexia	56	100
Jaundice	04	07.1
Weakness and fatigability	56	100
Fever	12	21.4
Backache	16	28.57
Dyspnoea	00	00

Anorexia, weakness and fatigability were found to be the universal symptoms. Pain in the right hypochondrium was present in 85.7% of cases followed by fever in 21.4% of cases.

Among the physical signs, wasting of muscles, hepatomegaly and tenderness in the right hypochondrium were universal i.e. present in all cases. Anemia was found to be present in 50% of cases. Signs of hepatocellular failure like jaundice, ascites, pedal edema, spider angioma and loss of hair were present in 7.1% of cases each.

The most common type of cell found on histopathology was cylindroids type in 35.7% of cases followed by trabecular type in 28.5% of cases.

Table 5: Distribution of study subjects as per their signs.

Physical signs	Number	Percentage
Febrile	12	21.4
Anemia	28	50
Wasting of muscles	56	100
Hepatomegaly	56	100
Tenderness in the right hypochondrium	56	100
Signs of hepatocellular failure		
Jaundice	04	7.1
Ascites	04	7.1
Pedal edema	04	7.1
Spider angioma	04	7.1
Loss of hair	04	7.1

Table 6: Histopathology of primary carcinoma of the liver alone.

Type of cell	Number	Percentage
Cylindroids type	20	35.7
Trabecular type	16	28.5
Liver cell cord pattern	12	21.4
Giant cell type	04	7.1
Combined type	04	7.1

DISCUSSION

The incidence of primary carcinoma of the liver was found to be highest in males as compared to females. This may be due to increased alcohol consumption among males. The highest incidence of Primary carcinoma of the liver was found in the age group of 41-50 years followed by 51-60 years. Lowest incidence of Primary carcinoma of the liver was found in the age group of 31-40 years. In only 14.3% of cases the Primary carcinoma of the liver was associated with cirrhosis of liver. Anorexia, weakness and fatigability were found to be the universal symptoms. Pain in the right hypochondrium was present in 85.7% of cases followed by fever in 21.4% of cases. Among the physical signs, wasting of muscles, hepatomegaly and tenderness in the right hypochondrium were universal i.e. present in all cases. Anemia was found to be present in 50% of cases. Signs of hepatocellular failure like jaundice, ascites, pedal edema, spider angioma and loss of hair were present in 7.1% of cases each. The most common type of cell found on histopathology was cylindroids type in 35.7% of cases followed by trabecular type in 28.5% of cases. Mourad W et al found that in 98 liver transplants, 15 neoplasms (15.3%) were identified.[3] Patient ages ranged from 5 to 63 years (median, 56 years). The primary etiology of hepatic disease was hepatitis C virus in 12 cases, hepatitis B virus in 1 case, cryptogenic cirrhosis in 1 case and congenital hepatic fibrosis in 1 case. Serum alpha-fetoprotein was significantly elevated (>400 U/L) in only 2 cases. CA19-9 was not elevated in any of the cases. The tumors included hepatocellular carcinoma (HCC) in 13 cases, 1 case of choloangio-carcinoma and 1 case of combined HCC and hepatoblastoma. The tumors in size from 0.5 to 5 cm (median 1.4 cm) and were multifocal in 5 of the cases (33%). Tissue alpha-fetoprotein expression was only seen in the cases associated with elevated serum levels.

Caroli-Bottino A et al reported that in 11 patients, 16 HCC had previously been identified in the explants by one or more imaging methods.[4] In the other 19 explanted livers (63.3%), HCC was incidentally found. All HCC identified in 9 patients and some of them in 10 patients were incidentally found, varying from microscopic focuses to 2 cm diameter lesions. They varied from only one (5 cases) to multiple nodules (7 cases).

Terada T et al concluded that the number of cirrhotic livers with AH is increasing gradually, and that cirrhotic livers with Adenomatous hyperplasia atypical are characterized by the association with non-A non-B hepatitis virus as well as simultaneous occurrence of Hepato Cellular Carcinoma.[5] Thus, Adenomatous hyperplasia atypical may be an important preneoplastic lesion in cirrhotic livers associated with non-A non-B hepatitis virus (probably hepatitis C virus).

Kanji K et al found that Hepato Cellular Carcinoma was noted in a few years (follow-up period range, 12-77 months; mean, 31.4 months) in all 3 patients whose resected nodules were classified as FM, in 4 (36%) of 11 with Adenomatous hyperplasia atypical resected nodules, and none of 10 with ordinary Adenomatous hyperplasia resected nodules.[6] The incidence of Hepato Cellular Carcinoma in the patients with FM or Adenomatous hyperplasia atypical nodules was significantly higher than that in those with ordinary Adenomatous hyperplasia nodules.

Kobayashi M et al observed that among the 42 cases, 34 were reported to have died of Adeno-squamous carcinoma and 5 cases were alive at the time of the study.[7] The mean survival of these 34 cases was 8.7 months. Multivariate analysis revealed that lymph node metastasis and the elevation of total bilirubin were associated with poor survival after surgery, and lymph node metastasis, intra-hepatic metastasis, location of tumor in the right lobe, and the pathologic stage were significant factors for all cases.

Maeda T et al reported that most adeno-squamous carcinoma (ASC) had invasive pathologic features, including venous invasion, lymphatic permeation, and intrahepatic metastases.[8] There were lymph node metastases from 7 tumours (88%), and most of the metastases were adenocarcinoma. All adenocarcinoma (AC) components were positive for both CK 7 and CK

19. The squamous cell carcinoma (SCC) components were positive for CK 7 in all cases but were positive for CK 19 in only 5 cases (62.5%). The ACs were positive for CK 903 in only 3 cases (37.5%), whereas all SCCs were positive for CK 903. Almost all ACs were positive for both CK 8 and CK 18, whereas the SCCs were positive for CK 8 in only 3 cases (37.5%) and for CK 18 in no cases. All 6 patients with surgically resected adeno-squamous carcinoma died of the disease within 1 year postoperatively. Their survival curve was significantly worse than that of the 32 patients with common CC ($P < 0.001$). The two patients on whom autopsy was performed also died within 1 year after diagnosis.

Farley JH et al concluded that ASC histology appears to be an independent predictor of poor outcome in women with cervical carcinoma compared with their counterparts who have pure AC.[9] The significant decrease in survival was observed only in patients with advanced-stage cervical carcinoma. This decreased survival may be related mainly to the grade of ASC. Le Bail B et al observed that there was a significant increase in cellular density in AAH and HCC as compared with C and OAH.[10] Proliferative cell nuclear antigen immunostaining similarly showed an increase in proliferation from OAH or C to AAH and HCC. These data suggest that, in Europe as in Japan, one pathway of hepato-carcinogenesis is a multistep process in which AAH should be considered as a premalignant lesion very close to grade I HCC, while OAH seems to correspond to a regenerative nodule with limited proliferative ability.

CONCLUSION

Incidence of primary carcinoma of the liver was found to be very high. This was not associated with corresponding increase in cirrhosis. The cause of their increase was obscure.

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