PRIMARY LIVER CANCER

A Review of the Clinical Features, Blood Groups, Serum Enzymes, Therapy, and Survival of 65 Cases

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A review of 65 patients with primary liver cancer was made. Of these, 53 had hepatocarcinoma. Primary cancer of the liver was most frequently found in patients aged 50 to 80 years, and was observed in three times as many males as females. There was an increased incidence of hepatocarcinoma in Negroes, especially those with blood group B. The most common symptoms with primary liver cancer were upper abdominal pain, weakness, and weight loss, while the most commonly found signs were hepatomegaly or an abdominal mass. Jaundice and ascites were also commonly found. Serum alkaline phosphatase, SGOT, SGPT, and LDH were elevated in most of these patients. In patients with hepatocarcinoma, 66% had histologically confirmed liver cirrhosis at autopsy. Serial alphafetoprotein tests were performed on 19 patients with hepatoma, in 14 of whom (73.6%) AFP was detectable. No Australia antigen was detected in 12 patients with hepatoma. In this study, 9 out of 16 patients (56%) had subjective and objective tumor responses with continuous 5-FUdR hepatic artery infusion. None of 18 patients treated with systemic cytotoxic agents responded. The difference in response between hepatic artery infusion and systemic therapy is statistically significant ($P < .0002$). There was a statistically significant lengthening in survival of patients who responded to intrahepatic artery infusion as compared to non-responders and patients who received systemic chemotherapy. In reviewing the autopsy findings on 30 patients with hepatocarcinoma and 9 with cholangiocarcinoma, there were differences in the incidence of metastases to the lungs or bones between these two types of primary liver cancer.

PRIMARY LIVER CANCER IS A RARE TUMOR IN the United States. The autopsy incidence of primary liver cancer ranges from 0.19% to 0.57% found by different authors.[41,56,64,72,79] In most cases, by the time the diagnosis is made, the patient is beyond the stage of resectability. In five different series, metastases from cancer of the liver had occurred in from 42% to 70% of the patients at the time of diagnosis,[32,41,45,78,88] and in Gall's survey of the literature, the incidence ranged from 20% to 65%.[35]

Systemic chemotherapy using a variety of cytotoxic agents did not produce any appreciable effect.[66,69] Nelson et al.[66] reported no significant tumor response in a series of 21 patients with hepatocarcinoma treated by different chemotherapeutic drugs.

In 1962, Clarkson et al.[22] reported on the utilization of the hepatic artery catheterization by way of the brachial artery for the treatment of malignant lesions in the liver. Later, Reed et al.[76] reported successful treatment of carcinoid tumor metastatic to the liver by hepatic artery infusion. At the present time, chemotherapy through hepatic artery infusion has been utilized with good response in patients with primary liver cancer, and

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metastatic cancer to the liver from gastrointestinal tumors.[8,9,16,21,27,28,33,47,49,75–77,90,91,93,96,98]

This is a review of 65 cases with primary liver cancer that were diagnosed and treated in Grace Hospital and the Darling Memorial Center in Detroit. The present review includes clinical evaluation, blood group studies, studies of alphafetoprotein, Australia antigen (Au ag), serum enzymes, and survival. Also, a comparison is made of hepatocarcinoma patients who were treated by hepatic artery infusion, to those treated by systemic chemotherapy.

MATERIALS AND METHODS

The records of primary liver cancer which were diagnosed in Grace Hospital for the period of 1960 to 1971 were reviewed. Only those cases with available histologic diagnoses are included in this report. The histologic diagnosis was confirmed either by percutaneous needle biopsy, or wedge biopsy during laparotomy or postmortem. History, physical examination, and all available laboratory data as well as autopsy findings were reviewed.

Serum alphafetoprotein (AFP) was evaluated in some of these patients by the Ouchterlony test. Australia antigen (Au ag) was tested in the sera of 12 patients with hepatocellular carcinoma.

Eighteen patients with hepatoma were treated systemically with different cytotoxic agents, while 16 patients had continuous hepatic artery infusion with 5-FUdR. In the latter group, the catheter was inserted either through the brachial artery (and after an objective response changed to transabdominal), or was inserted directly after laparotomy.[49] Eleven patients had laparotomy and the insertion of a hepatic artery catheter. Continuous 5-FUdR was given through a Watkin's Pump; the bag was changed weekly. The dosage of 5-FUdR ranged from 0.3–0.5 mg/kg per day in distilled water with heparin. 5-fluorouracil dosage was 15 mg/kg per day I.V. bolus for 5 days, repeated every 4 weeks. The dosage of the combination of 5-FU and Velban was: 5-FU, 10 mg/kg; Velban, 0.1 mg/kg I.V. bolus weekly. Initial workup of each patient included complete blood and platelet count, serum alkaline phosphatase, LDH, SGOT, and SGPT, metastatic bone survey, and chest roentgenogram. The liver size was measured clinically, or by other means such as liver scan. Prior to each weekly visit, complete blood count and serum enzymes were obtained. Also, clinical liver measurement was done and recorded on each visit. Liver scans were repeated every 1 to 2 months and compared. Objective tumor regression was accepted when a shrinkage of 50% or more occurred in the product of two diameters of all lesions measurable by physical examination, x-ray, or isotopic scan, and if this change lasted 2 months or more. If the measurable lesion was liver size (by palpation or percussion) an objective remission was considered if the sum of the measurements at both mid clavicular lines and the xiphoid had decreased 30% or more. Subjective improvement was defined as improvement in the patient's clinical symptoms or laboratory tests. A 2-week minimum intrahepatic artery infusion was considered as adequate therapy.

This was not a randomized selection between hepatic artery infusion and systemic chemotherapy; most of the cases treated systemically were before 1967. All patients in both groups had localized disease confined within the liver, except for one patient who had localized metastases to the right iliac bone at time of diagnosis. Nineteen patients with hepatoma were not known to receive chemotherapy, either because they had been diagnosed at autopsy, or because of early death after diagnosis.

A comparison of survival from the time of first therapy of patients who had intra-arterial infusion to those who had systemic therapy was made. In 30 cases with hepatocarcinoma, and in 9 with cholangiocarcinoma, an autopsy was performed and the findings were reviewed.

RESULTS

Sixty-five patients with primary liver cancer were found between the period of 1960 and 1971 in our hospital. Of these, 53 had hepatocellular carcinoma, 9 had cholangiocarcinoma, 2 had a mixed type (hepatocholangio-carcinoma), and 1 patient had hemangiosarcoma of the liver.

Age and sex incidence (Table 1): The ages ranged from 13 to 85 years old. The majority of patients with hepatocarcinoma were in their fifth to seventh decade. Only two non-Caucasian patients with hepatocellular carcinoma were below the age of 40 years, while the majority had an age range between 50 and

TABLE 1. Primary Liver Cancer: Sex and Age Incidence

	Sex		Age					
	Male	Female	<40	41–49	50–59	60–69	70–79	>80
Hepatocarcinoma (53)	39	14	4	4	13	13	15	4
Cholangiocarcinoma (9)	4	5		2		5	2	
Mixed type (2)	0	2		1			1	
Hemangiosarcoma (1)	1	0				1		
TOTAL (65)	44	21	4	7	13	19	18	4

80 years. The same was true for patients with cholangiocarcinoma.

We found 39 males and 14 females with hepatocellular cancer, giving us a ratio of 3:1 male to female. There was no notable difference because of sex in those patients with cholangiocarcinoma.

Racial incidence (Table 2): In this series there were 41 (63%) Caucasian and 24 (37%) non-Caucasian patients. In the period reviewed, of the patients with neoplastic diseases admitted to our hospital, 86% were Caucasian and 14% were non-Caucasian. The higher incidence of primary liver cancer in non-Caucasian was statistically significant ($p < 0.0007$). In reviewing the race incidence together with the sex distribution, there seems to be a higher incidence of hepatocarcinoma in patients who are Negro and male.

Blood groups: In 44 cases the blood groups were determined and recorded. Of these, out of 36 patients with hepatocarcinoma, 14 (38%) had blood group O, 12 (33%) group A, 9 (25%) group B, and 1 belonged to group AB. In studying the race and sex distribution in relation to blood group, it seems that group B is more common in males and Negroes. The majority of patients with cholangiocarcinoma (5/8) had blood group A. The Rh factor was positive in 37 of the 44 cases tested.

Symptoms and signs (Tables 3 and 4): The symptoms most commonly present in patients with hepatocarcinoma were abdominal discomfort (62%), weight loss (34%), and abdominal swelling (30%). Three patients were completely asymptomatic. The majority of these patients presented with hepatomegaly (75%) and ascites (30%). No abnormal findings were reported on physical examination in seven patients.

Laboratory results: Serum alkaline phosphatase (N = 9–35 U) was elevated in 88% of 51 patients with primary liver cancer. While 78% had an elevated SGOT (N = 8–40 U.), 66% had an elevated LDH (N = 24–78 I.U.). SGPT was elevated in only 34% of 32 patients in which it was performed (N = 5–35 U). The degree of these enzymes' elevation was 2–5 times the normal level for the majority of these patients. Serum alkaline phosphatase was elevated 2–3 times normal in 23 patients, 4–5 times normal in 12, and in 9 patients greater than 8 times the normal level.

Paraneoplastic syndromes: Four patients with hepatocarcinoma were found to have paraneoplastic syndromes. These disorders were: polycythemia, thrombocytosis, hypoglycemia, and hypercalcemia (possibly due to ectopic hyperparathyroidism). The patient with hypercalcemia had persistently low serum phosphorus and no evidence of osseous metastases on a skeletal survey. In the patient with hypoglycemia and hepatoma, there was no evidence of insulin-like activity (ILA) in the serum, and no increase in the serum insulin.

Liver cirrhosis: Liver cirrhosis diagnosed by tissue examination at autopsy was present in 20 of 30 (66%) patients with hepatocarcinoma. Most of these patients gave a history of previous excessive ethanol intake.

Alphafetoprotein (AFP): Serum AFP was tested by the immunodiffusion technique on serial sera from some of the hepatocarcinoma patients.[3,5] Of the 19 patients tested, 14 (73.6%) had AFP found in the serum before starting on chemotherapy. In 2 patients with cholangiocarcinoma, no AFP was found by the Ouchterlony test.

Australia (Au) antigen: Twelve patients with hepatocarcinoma had their serum tested for the presence of Au antigen.[4] No Au ag was found by immunodiffusion and the counter-

TABLE 2. Primary Liver Cancer: Racial Incidence and Sex Distribution

Race	Hepato Ca Male/Female	Cholangio Ca Male/Female
Caucasian	22/9	5/2
Negro	16/4	0/2
Other	1/1	0/0

TABLE 3. Hepatocarcinoma: Presenting Symptoms in 53 Patients

Symptoms	No.	%
Abdominal discomfort	33	62
Weight loss	18	34
Weakness & fatigability	15	30
Abdominal swelling	15	30
Anorexia	10	19
Nausea & vomiting	2	4
Others	14	27
Asymptomatic	3	6

electrophoresis techniques using human anti-Au antigen. However, 8 out of 12 patients had detectable alphafetoprotein in their sera.

Therapy and survival: Eighteen patients with hepatocarcinoma received systemic chemotherapy. The agents used are shown in Table 5. The majority of these patients had either 5-fluorouracil alone or a combination of 5-fluorouracil and vinblastine as was described before.[2] None of these patients had objective tumor regression. The survival of these hepatocarcinoma patients who received systemic chemotherapy ranged from 1–36 weeks from the time of first therapy. The mean survival was 11.1 weeks, the median was 9 weeks (Table 6).

Of the 16 patients who were treated by continuous chemotherapy of 5-FUdR through intrahepatic artery catheter, 15 were considered to have received adequate therapy. The duration of infusion ranged from 3–74 weeks with a mean of 22 weeks. One patient died 1 week after the starting of the intra-arterial infusion. Nine patients (56%) had objective tumor response. All those patients with objective response also experienced subjective response with improvement of clinical symptoms and liver function tests. Of the responders, four patients had mild nausea or vomiting, and four needed a decrease in drug dosage because of mild to moderate increase in the serum enzymes. Only one patient had mild leukopenia.

TABLE 4. Hepatocarcinoma: Presenting Signs in 53 Patients

Signs	No.	%
Hepatomegaly	39	75
Ascites	15	30
Jaundice	9	16
Splenomegaly	5	10
Indefinite mass	5	10
Metastases	7	13
No abnormal findings	7	13

TABLE 5. Type of Drugs Given Systemically to 18 Patients with Hepatoma

Drugs	No.
5-FU	8
5-FU & Velban	5
Cytoxan	2
TEM	1
Alkeran	1
Porfiromycin	1

One had thrombosis of the catheter after 40 weeks of infusion (the therapy was discontinued while she remained in remission for an additional 156 weeks). None of the patients without objective tumor response experienced subjective improvement. This difference in response between continuous hepatic artery infusion and systemic therapy is statistically significant ($p < .0002$).

The survival of responders from the time of therapy ranged from 16–196 weeks, with 62.2 weeks mean survival (Table 6). The survival times in weeks were: 16, 28, 31, 34, 40, 59, 74, 82, and 196. The patients who did not respond to such therapy had a mean survival of only 5.1 weeks. There is a definite correlation between the duration of infusion and survival. The cause of death in the responders was due to progression of the disease without further response to systemic chemotherapy.

Autopsy study: Of the 53 patients with hepatocarcinoma, only 30 were autopsied. The sites of metastases in these patients are shown in Table 7. The majority of hepatocarcinoma patients had metastases to the lungs and lymph nodes. Portal vein involvement was found in 23%, metastases to adrenal glands in 20%, and to the bone in 20%. Table 8 shows the sites of metastases in 9 patients with cholangiocarcinoma. In these patients, 55% had metastases to the bone. Next in frequency were metastases to the lymph nodes and lungs.

DISCUSSION

Primary carcinoma of the liver is an uncommon malignancy in the United States among different neoplastic tumors and au-

TABLE 6. Survival from Time of Therapy in Weeks

Type of therapy	Range	Mean	Median
Hepatic artery infusion (16)	1–196	37.2	25
Responder (9)	16–196	62.2	54
Non-responder (7)	1–12	5.1	4
Systemic therapy (18)	1–36	11.1	9

TABLE 7. Site of Metastases at Autopsy of 30 Cases with Hepatocarcinoma

Site	Percent
Lungs and pleura	57
Lymph nodes	
Portal	33
Parapancreatic	33
Retroporitoneal	30
Mediastinal	10
Cervical	3
Portal vein	23
Adrenal glands	20
Bone	20
Hepatic veins	13
Peritoneum	13
Gall bladder	10
Diaphragm	10
Kidneys	10

TABLE 8. Site of Metastases at Autopsy of 9 Cases with Cholangiocarcinoma

Site	Percent
Bone	55
Lymph nodes	
Portal	33
Parapancreatic	33
Mediastinal	33
Mesenteric	22
Lungs and pleura	22
Peritoneum	22
Inferior vena cava	22

topsy incidence reported.[41,56,64,72,79] Gall[36] states that primary liver cancer occurs in 0.25% of all autopsies, with a much higher incidence in parts of Africa, the Orient, and South America. The reported incidence of primary liver cancer in autopsies from Africa ranged from 1.3–5.7%.[24,85] Perhaps the most extreme example of this has been reported by Berman,[13] who found up to 86.8% of all cancers in young Bantu miners in South Africa were hepatic primary. The high incidence in this part of Africa was also confirmed by others.[68] The reported autopsy incidence of liver carcinoma in Greece was 2.2%,[92] Japan 2.36%,[62] and in Singapore 5.3%.[83] Lopez-Corella et al.[55] found only 37 (0.56%) cases of primary hepatic carcinoma among 6558 autopsies performed in the General Hospital of Mexico City. In their review of the literature they found that the incidence of primary liver cancer in Latin America is low.

Primary cancer of the liver usually affects middle-aged men in the fifth, sixth, and seventh decades of life, although no age group is exempt. Parker et al.[71] found the ratio of males to females was 3.6:1. This increased incidence of hepatocarcinoma in males has been supported by others.[23,29,38,41,72,87] With cholangiocarcinoma the sex predominance is less striking. In Chinese and Africans, the peak incidence of hepatocarcinoma is in the third and fourth decade.[2,14] Alpert et al.[2] reported that the age peak of primary hepatoma in Uganda was from 25 to 45 years, and the ratio of male to female was 2:1.

The majority of the patients in this series, with hepatocarcinoma or cholangiocarcinoma, had age incidence between the fifth and seventh decade. There was no difference in peak age between Caucasian and non-Caucasian patients. Patients with hepatocarcinoma had a ratio of 3:1 male to female. There were 5 males and 4 females who had a diagnosis of cholangiocarcinoma.

There is strong evidence pointing to the association of blood group A and gastric carcinoma.[20] Senkale et al.,[80] in a study of the A, B, and O blood groups and Rh factors of 120 African patients with primary carcinoma of the liver, did not show any relationship between this disease and any particular blood group.

It was reported by Buckwalter[20] that blood group B incidence was 20% in Negroes from St. Louis as compared to Caucasions from Iowa (10%). The incidence of this blood group was reported to be higher in Bantu or Indians from South Africa than in Caucasians of the same country.[20]

In our study, blood group B was more frequent among Negro males with hepatocarcinoma. Nine of 36 patients (25%) with hepatoma were found to have blood group B. The incidence of non-Caucasians with primary liver cancer in this series was 37%, as compared to 14% of all patients with neoplastic diseases admitted to our hospital in the same period.

The most common complaints with primary liver cancer are upper abdominal discomfort, weight loss, and abdominal swelling,[2,30,32,45,46,51,55–57,59,63,71,72,79] The most common finding on physical examination is hepatomegaly or an abdominal mass. Jaundice and ascites are also common.[2,40,51,55–57,63,71,72,76,79] The presenting symptoms and signs in our patients with hepatocarcinoma are shown in Tables 3 and 4.

San Jose et al.[79] reported that in 90% of

patients with primary liver carcinoma the alkaline phosphatase was elevated. Other enzymes, such as SGOT, SGPT, and LDH were elevated in 66% to 70% of these patients. The same findings were reported by others.[2,46,56,64,72] The incidence of elevated serum enzymes was the same in our study. The degree of elevation was two to five times the normal level in the majority of the cases.

Many paraneoplastic syndromes have been reported in patients with hepatocarcinoma.[11,12,44,48,50,52,61,65,74,81,82,94] The most common associations reported were hypoglycemia, polycythemia, or hypercalcemia due to parathyroid hormone-producing tumors, either alone or in combinations. An unexplained hypercholesterolemia was noted by Alpert et al.[2] in approximately one third of the patients with primary hepatoma in Uganda.

In our study, out of 53 patients with hepatoma we found 4 with paraneoplastic syndromes. These were: polycythemia, thrombocytosis, hypoglycemia, and hypercalcemia (possibly due to ectopic hyperparathyroidism). In the patients with hypoglycemia, there was no increase in insulin or insulin-like activity in the serum.

The majority of the cases of primary liver cancer reported were of hepatocarcinoma types. Cholangiocarcinoma usually constitutes about 5–30% of primary liver carcinoma.[30,55,72,79,88,95] Very few patients have the mixed type malignant lesion.

It has been reported that cirrhosis of the liver accompanies about 75% of the cases of hepatocarcinoma and 30% of those of cholangiocarcinoma.[29,31,35,41,56,62,71,72,78,79,86] Lopez-Corella et al.[55] found that in two-thirds of their patients, liver cell cancer co-existed with cirrhosis, and 0.26% of all cases of proven liver cirrhosis were complicated by primary liver carcinoma. Postnecrotic cirrhosis was the most common type reported associated with hepatoma.[71] There is also an increased incidence of hepatic cancer in hemochromatosis of the liver[23] and following the administration of Thorotrast.[45,67,89]

Alphafetoprotein (AFP), a protein normally found in fetal serum, was not detectable in human adults by the immunodiffusion test. AFP was found to be present in patients with hepatocarcinoma, embryonal tumors of the gonads, and occasionally in other tumors, especially those of the gastrointestinal tract.[3,5] In reviewing the reported major series,[5] we found the incidence of detectable AFP in the sera of patients with hepatocarcinoma ranged from 40–79% with an average of 67%. A higher incidence as well as a higher level of AFP was detected in African and Southwest Asian patients with primary liver cancer than was found in Caucasian patients of European or U.S. origin. There was also a higher incidence of detection in reported cases in which a definite histologic diagnosis of hepatoma had been made. In our study we were able to detect AFP in 14 patients out of 19 with hepatocarcinoma. AFP was not detectable by the immunodiffusion test in 2 patients with cholangiocarcinoma.

No Australia (Au) antigen was found in 12 patients tested with hepatocarcinoma by the immunodiffusion and the counter-electrophoresis technique.[4] In our review of the literature[4] we found that Au ag was reported present in patients with hepatocarcinoma from Uganda, Kenya, Senegal, Greece, and Great Britain, although it was reported not detectable in patients with hepatoma from East Africa, Hong Kong, Singapore, or the United States. These differences in the incidences of Au ag in patients with hepatoma may be related to different techniques used, age of patients, or different incidence of Au ag in different regions.

Patton and Horn[72] found that the average survival from time of diagnosis was 6.5 months, with a range of 1–21 months. Warvi[95] reported the survival in cholangiocarcinomas was 6 weeks, and in hepatomas, 8 months, from the time of diagnosis. Lemmer[53] found the average time from onset of symptoms to death only 7 months, and Epstein[32] found a similar figure of 29 weeks.

Jaffe et al.[43] found in their review that only 7% of 390 patients with untreated hepatic metastasis lived more than 1 year. The over-all median survival time was 75 days. However, there have been reports of patients with a resected hepatoma surviving for 5 years or longer.[7,18,19,26,97]

Hepatic lobectomies have been performed for the treatment of benign tumors of the liver, unilateral hepatomas, hepatoblastomas in infants and children, cancer of the gallbladder or hepatic duct, solitary or localized metastasis, and trauma to the liver.[7,15,17–19,26,37,54,58,60,73,97] Long survival has also been reported for hepatic lobectomy for metastatic carcinoma[18,26,73] or cancer of the gallbladder.[17,18] Unresectable hemangioma of the liver has been treated successfully either with cor-

ticosteroids,[39] radiotherapy,[42,66] or hepatic artery ligation.[25]

Partial hepatectomy remains a formidable operation, with a mortality rate of up to 30%.[18,54] In many cases, resection is not possible because both lobes of the liver are involved by the tumor.

The use of systemic chemotherapy for the treatment of unresectable primary cancer of the liver had been disappointing. Papac and Calabresi[69] found no response in patients with hepatocarcinoma to intravenous infusion of floxuridine. Nelson et al.[66] had the same experience in 21 patients who were treated with different drugs.

Since the report of Clarkson et al.[22] of the utilization of the hepatic artery catheterization for the treatment of malignant lesions of the liver, more reports have appeared with good responses.

Continuous chemotherapy infusion through the hepatic artery, or intra-aortic infusion, are now being used with good tumor responses with definite increase in average survival in patients with primary or secondary liver cancer.[8–10,16,21,27,28,33,34,47,49,75–77,84,90,91,93,96,98]

Hepatic artery infusion has been utilized for the treatment of primary cancer of the liver.[8,30,75,77,96] Of the six patients treated by hepatic artery infusion reported by El-Domeiri et al.,[30] two exhibited a marked regression of the lesion and survived more than 2 years. Rochlin and Smart[77] noted regression in two out of four hepatomas treated by hepatic artery infusion with fluorouracil.

In our study, we have 9 of 16 (56%) patients with hepatocarcinoma who responded to hepatic artery infusion with 5-FUdR, while none of the 18 patients responded to systemic chemotherapy.

There was definite and statistically significant improvement in the length of survival in the responders as compared to non-responders to hepatic artery infusion ($p < .03$) or those treated by systemic chemotherapy ($p < .001$) (Table 6). We believe that intrahepatic artery continuous infusion of chemotherapy is the treatment of choice for patients with unresectable primary liver cancer.

Both types of primary liver cancer tend to spread rapidly within the liver and both also demonstrate a high incidence of extrahepatic metastasis. The lungs are the most common site of metastasis, which is probably related to the tendency to invade and spread by venous channels. In four different series pulmonary metastasis occurred in 41–82% of the cases.[32,56,59,72] Patton and Horn[72] reported 70% metastasis to the lungs from hepatocarcinoma, and 54% by cholangiocarcinoma. Lymph nodes at the liver hilus were commonly involved. Patton and Horn[72] reported only 13% metastasis to bone in patients with hepatoma, while 47% bone metastasis occurred in cholangiocarcinoma patients. The incidence of adrenal gland metastasis found at autopsy ranged from 17–30% of the cases.[32,72]

Albacete et al.[1] found portal vein thrombosis six times more frequently in patients with hepatoma as compared to patients with cirrhosis or metastatic carcinoma of the liver.

In our series, metastasis to regional lymph nodes was common. The same incidence occurred in both types of primary liver cancer. Patients with hepatocarcinoma had 57% metastasis to lungs and 20% to bone, as compared to patients with cholangiocarcinoma, who had 22% to lungs and 55% to bone (Table 7 and 8).

Twenty percent of hepatoma patients had involvement of the adrenal glands. Portal vein involvement and thrombosis were found in 23% of these patients.

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