ORIGINAL ARTICLE

CLINICOPATHOLOGICAL FEATURES OF LIVER TUMOURS: A TEN-YEAR STUDY

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Background: Various diseases affect the liver, among them, malignant and benign tumours with hepatic nodules are the most important. We aimed to evaluate the clinicopathological findings related to hepatic tumours and nodules. **Methods:** This retrospective study was carried out during November 2014 to August 2015 by reviewing the hospital medical records of 164 registered patients with liver biopsies referred to Shahid Sadoughi educational General Hospital, Yazd, Iran, between 2004 and 2014. The samples were selected through the census method. Age, gender, clinical symptoms, initial clinical diagnosis, pathology reports and ultrasound results were considered as variables. Data were analysed by using SPSS-17. **Results**: There were 87 (53%) men and 77 (47%) women. The mean ages of presentation for malignant and benign tumours were 57.9±17.2 and 44.9±19.4 years, respectively. Seventy benign tumours and 147 malignant tumours were recorded. The most frequent chief complaint was abdominal pain (54.9%) in both malignant (56.50%) and benign tumours (41.20%). Hepatocellular carcinoma (HCC) and hemangioma were the most prevalent malignant and benign hepatic tumours, respectively. In our study, correlation between pathology reports and primary diagnoses was 40.9%, and a significant relationship was found between sonography and pathological findings (p=0.038). **Conclusions**: We found that only when primary clinical diagnosis and sonography were in favour of malignancy, they were correlated with pathology results. Clinicopathological assessments can help physicians in their diagnosis in order to facilitate the management of hepatic tumours.

Keywords: liver, neoplasms, ultrasound, biopsy

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INTRODUCTION

The liver is an important organ in the human body developed for various vital functions, from protein production, metabolism of cholesterol, glucose and trace elements such as iron to detoxification of various metabolites. Liver affects by variety of illnesses, among them hepatic tumours are especially important because of their high prevalence with high mortality and morbidity rates.[1,2] These tumours can be asymptomatic or present with symptoms such as abdominal pain, hepatomegaly, weight loss, jaundice, etc; some are even found accidentally.[3,4]

There are various reports showing different incidences of hepatic tumours such as, tumour-like lesions (3.5%), benign tumours (15.8%), and malignant tumours (80.7%), respectively. Most tumour-like lesions, benign tumours, and malignant tumours were inflammatory pseudo-tumours (73.2%), cavernous hemangioma (73.4%), and hepatocellular carcinoma (96%), respectively.[5] In pediatrics, knowing patient's age, laboratory findings, and knowledge of specific type of malignant tumours in this group with their imaging characteristics can help radiologists propose better differential diagnosis for the patient's workup.[6] Diagnosis of hepatocellular nodules in liver cirrhosis and predicting their progression from regenerative nodules to hepatocellular carcinoma were better done by correlation of contrast-enhanced ultrasound findings and pathologic diagnosis.[7] Considering the various presentations of hepatic tumours and nodules, and the lack of recent and more comprehensive studies on relation between ultrasound findings and primary clinical diagnosis with histopathological findings, as well as the difference between the prevalence of hepatic masses in different countries, causes delay in definitive diagnosis. So we aimed to determine the clinicopathological characteristics of hepatic tumours in Yazd, Iran. Therefore, by evaluating the relationship between age, sex, clinical and radiological symptoms and the frequency of malignant and benign tumours, correct and accurate decision making can be facilitated.

MATERIAL AND METHODS

This retrospective study was conducted during November 2015, on medical records of all registered patients with liver biopsy results in the pathology department of Shahid Sadoughi educational General Hospital (referral center for Shahid Sadoughi University of Medical Sciences and Health Services in Yazd, Iran) between 2004 to 2014. The samples were selected through the census method. The

patient's informations such as age, gender, clinical symptoms, initial clinical diagnosis, pathology reports and ultrasound results were extracted from their pathology and hospital records according to the prepared checklist.

Medical records from patients, whom had biopsied for other reasons such as; staging and grading for different types of chronic hepatitis (alcoholic, viral and autoimmune), patients with inherited metabolic, copper and iron metabolism disorders and also liver biopsies after transplantation were excluded from the study.

The study protocol was in accordance to Declaration of Helsinki for investigation with human subjects and was approved by the ethics committee of Yazd University of Medical Sciences.

Data were analyzed using SPSS-17. Chi-square and ANOVA tests were used as appropriated. In all tests, $p<0.05$ was considered as the threshold to reject the null hypothesis. The coefficient of agreement between radiological and pathological diagnosis was determined in order to compare primary clinical and pathological findings.

RESULTS

In this study 164 hospital medical records from 77 (47%) women and 87 (53%) men were evaluated. We found no significant relationship between sex and pathological findings (malignant or benign) (p=0.098, table-1). The mean±SD ages of presentation of benign and malignant tumours were 44.9±19.4 and 57.9±17.2 years, respectively (p=0.018, Table-1). The frequency distribution of benign and malignant hepatic tumours based on the chief complaints and physical exam is shown in table-2. The most frequent chief complaint was abdominal pain (54.9%) in both malignant (56.50%) and benign tumours (41.20%). We found a significant relationship between pathology results and the patients' chief complaints (p=0.025).The most frequent clinical symptom was tenderness (42.7%) in both malignant (44.2%) and benign tumours (29.4%) (Table-3).We found a significant relationship between clinical symptoms and pathological findings in the studied patients (p=0.021).The initial clinical diagnoses based on the patients history and physical examination were as follows: malignant tumour in 42 (25.60%) patients, liver mass in 26 (15.9%) patients, and metastasis in 16 (9.8%) patients. The other 80 (48.78%) patients were discharged with other diagnoses such as liver cirrhosis, hepatitis, cholecystitis, etc.

Radiological (sonographic) findings included mass without specific diagnosis in 51 (31.1%) patients, metastasis in 48 (29.3%) patients, primary malignant hepatic tumour in 5 (3.0%) patients, and primary benign hepatic tumour in 1 (0.6%) patient. Five patients (3.0%) had normal reports and in 11 patients (6.7%) other findings such as hepatomegaly, ascites, hepatic echogenicity alterations and etc were reported. Also, 43 records (26.2%) were incomplete. In 44 cases (26.8%) the sonography results were correlated with primary diagnosis, while in 51 cases (31.1%) these results were not correlated.

We could not assess the correlation of sonogrpahy findings and primary diagnosis in 69 cases (42.1%) because of incomplete records. In the obtained pathology results, 17 cases (10.4%) were benign and 147 cases (89.6%) were malignant. Of the 147 malignant cases, 19 (12.9%) were hepatocellular carcinoma (HCC), 5 (3.4%) cholangiocarcinoma, 2 (1.4%) hepatoblastoma, 115 (78.2%) metastasis and 6 (4.1%) were others. No case of angiosarcoma was reported. The underlying diagnosis of metastasis was unknown in 85 patients. In other patients, the origin of metastasis were uterine cervix squamous cell carcinoma (n=5), malignant lymphoma (n=5), renal cell carcinoma (n=3), GI neuroendocrine tumours (n=2), skin malignant melanoma (n=2), stomach (n=3), colon (n=1), esophagus (n=1), breast (n=1), pancreas (n=5), small intestine (n=1), and anal basaloid carcinoma (n=1). Therefore, gastrointestinal tract malignancies were the most frequent metastatic origin. Benign lesions included hemangioma (n=11, 64.7%), focal nodular hyperplasia (n=4, 23.5%), and fibro fatty vascular connective tissue in two patients. No case of hyper-regenerative nodule was found.

The pathology results were correlated with primary diagnosis in 67 (40.9%) cases, while we did not find such as correlation in 75 (45.7%) cases. Such a correlation could not be assessed in 22 cases (13.4%) because of incomplete records. The initial diagnosis of metastasis was 100% correlated with pathology results. Regarding malignant tumours, the clinical diagnosis correlated with pathology reports in 95.2% of the cases. However, for benign tumours, such a correlation was observed in only 23.1% of the cases.

A significant relationship was found between sonography and pathological findings (p=0.038, Chi-square test). With respect to the coefficient of agreement between the sonography and pathology findings, by omitting the incomplete records and sonographic findings without any specific diagnosis, we found a significant relationship between these findings using the Chi-square test (p=0.049, table 4). Moreover, a significant relationship was found between primary clinical diagnosis (including history and physical exams without using sonography or radiology) and pathology (p=0.049, table-5).

Table-1: Frequency (%) of the patients with malignant and benign tumours according to age and sex

Variable		Malignant tumours (n=147)	Benign tumours (n=17)	*p*-value
Age	1–10	2	1	0.018
	11–20	3	0	
	21–30	6	5	
	31–40	14	5	
	41–50	18	1	
	51–60	29	5	
	61–70	33	2	
	71–80	37	2	
	81–90	5	2	
Sex	Women	66 (85.7)	11 (14.3)	0.98
	Men	81 (93.1)	6 (6.9)	

Table-2: Frequency (%) of the patients' chief complaints and their relation to pathology results

Chief Complaints	Malignant tumours (n=147)	Benign tumours (n=17)	Total (n=164)
Abdominal pain	83 (56.5)	7 (41.2)	90 (54.9)
Palpable abdominal mass or distention	7 (4.8)	5 (29.4)	12 (7.3)
Icter	9 (6.1)	0 (0)	9 (5.5)
Fever	5 (3.4)	2 (11.8)	7 (4.3)
Loss of weight and appetite	6 (4.1)	0 (0)	6 (3.7)
Nauseas and vomiting	6 (4.1)	0 (0)	6 (3.7)
Weakness	5 (3.4)	0 (0)	5 (3.0)
Itching	1 (0.7)	0 (0)	1 (0.6)
Other	6 (4.1)	1 (5.9)	7 (4.3)
Incomplete record	19 (12.9)	2 (11.8)	21(12.8)

Table-3: Frequency (%) of the patients' main clinical symptoms

Symptoms	Malignant tumours (n=147)	Benign tumours (n=17)	Total (n=164)
Tenderness	65 (44.2)	5 (29.4)	70 (42.7)
Hepatomegaly or Hepatoslenomegaly	23 (15.6)	0 (0)	23 (14)
Ascites	8 (5.4)	0 (0)	8 (4.9)
Palpable mass	12 (8.2)	4 (23.5)	16 (9.8)
Other (icter, etc.)	9 (6.1)	0 (0)	9 (5.5)
Normal	4 (2.7)	2 (11.8)	6 (3.7)
Incomplete record	26 (17.7)	6 (35.3)	32 (19.5)

Table-4: Comparison between sonography and pathology findings in patients with benign and malignant hepatic tumours

Sonography	Pathology		*p*-value	Coefficient of agreement
	Malignant	Benign		
Metastasis	46 (31.3%)	2 (11.8%)	0.038	0.049
Primary malignant mass	4 (2.7%)	1 (5.9%)		
Mass without specific diagnosis	43 (29.3%)	8 (47.1%)		
Normal	5 (3.4%)	0 (0%)		
Benign tumour	0 (0%)	1 (5.9%)		
Incomplete	39 (26.5%)	4 (23.5%)		
Others	10 (6.8%)	1 (5.9%)		

Table-5: Comparison between primary clinical evaluation and pathology findings in patients with benign and malignant hepatic tumours

Primary clinical evaluation	Pathology		*p*-value
	Malignant	Benign	
Metastasis	16(10.9%)	0 (0%)	0.049
Liver mass	20 (13.6%)	6 (35.3%)	
Others	71 (48.3%)	9 (52.9%)	
Malignant mass	40 (27.2%)	2 (11.8%)	

DISCUSSION

Biopsy along with radiological findings and clinical impression are necessary for definitive diagnosis of liver space occupying lesions and it is not possible regardless of considering all of them. So we aimed to evaluation the clinicopathological characteristics of patients with liver mass that underwent needle biopsy in Yazd, Iran.

The medical records along with histopathological evaluation of 164 patients were reviewed. The impact of several factors including the patients' age, sex, clinical symptoms, chief complaints, primary clinical diagnosis, radiological findings and pathological diagnosis were investigated in order to identify determinant variables. Among these, we found a significant relationship between the frequency distribution of benign and malignant hepatic tumours based on chief complaint and physical exams. We also found a significant relationship between pathology results (benign or malignant tumour) and radiology (sonography) findings. The relationship between primary clinical diagnosis and pathology findings and frequency distribution of benign and malignant tumours was also significant. However, no significant relationship was found between the frequency distribution of benign and malignant tumours and sex. In our study, the mean age of the patients was 56.25 years.

In UK study the mean age of patients was 40–44 years. However, in that study hepatic cancer was raised in 55–59 years and peak in 85 years old.[8] In present study primary malignant liver tumours were more prevalent in men than women which were in accordance with other studies.[3,8,9] In our study, the most prevalent chief complaints were abdominal pain, palpable mass or distention and icter. With respect to benign tumours, the most prevalent chief complaint was abdominal pain and palpable mass or abdominal distention. Nausea, vomiting, malaise, loss of weight and appetite were not observed in patients with benign tumours. These symptoms were the specific complaints of patients with malignant tumours. In a study in Pakistan on 82 patients suspected of having HCC, the most important reported symptom was right hypochondrial pain.[10] Consistently abdominal pain was the most frequent symptom in our study as well.

In present study, abdominal pain was the most prevalent chief complaint in various benign tumours, so our findings were different to other studies done on benign tumours, that most of the patients were asymptomatic and also called as incidentalomas.[4,11,12] In our study, the most prevalent clinical complaint for benign tumours was tenderness, followed by palpable mass. In patients whose clinical exam was normal but had hepatic mass, the possibility of a malignancy was higher (66.7% vs 33.3%). In general, it can be concluded that no clinical symptom is more specific in benign tumours. Tenderness, followed by hepatomegaly, was the most prevalent symptoms in malignant tumours. Ascites and hepatomegaly were specific to malignancy. Chiche *et al* 2013. found that hepatomegaly was the main clinical finding[12] while in our study it was the second most prevalent symptom. Based on present study, it can be stated that, if the primary diagnosis of a malignant mass was made, the possibility of malignancy was very high (96.55%). Regarding benign tumours, only 23.1% of the diagnosis was correct. With respect to the correlation between primary sonographic diagnosis and pathology reports, among the 95 assessed records, a 46.31% correlation was observed. We did not find any studies reporting any correlations in this regard. It can be stated that if sonography showed a mass without stating whether it was malignant or benign, there was an 84.3% possibility of malignancy in pathology. If sonography reports had stated a malignant mass (metastasis or primary malignancy) there was a 94.33% possibility of malignancy in pathology reports. In our study sonography was able to diagnose all hemangiomas. We found four cases of focal nodular hyperplasia (FNH) that all of them were in young adults and as mentioned in prior studies, solid lesions such as FNH and hepatocellular adenoma mostly found in young adults and differentiation these lesions from each other may be difficult by sonography alone, but using contrast-enhanced ultrasound and magnetic resonance imaging may be useful, but for definitive diagnosis biopsy should be done.[3,13]

In our study, 10.4% of the hepatic tumours were benign and 89.6% were malignant. Among the malignant tumours, metastatic masses were the most prevalent (82.3%). HCC was the most prevalent primary malignant hepatic tumour, which was consistent with previous reports.[14,15] Intrahepatic bile duct carcinoma was low in our study in contrast to other studies that in time, the incidence was increased, and this difference may be due to lower sample size, or variation in risk factors such as lower incidence of viral or parasitic infections in our city.[16,17] The most common origin of metastatic tumours in present study was gastrointestinal tract malignancies which are in concordance with other studies.[8] Moreover, hemangioma was the most prevalent benign hepatic tumour in our study, which was similar to previous studies.[18,19]

CONCLUSION

This study showed that in cases which the primary clinical diagnosis and sonography were in favour of malignancy, they were correlated with pathology results. However, in cases with a sonographic or clinical primary diagnosis of benign tumour, the results did not correlate with pathology reports. It can be stated that the results of clinicopathological assessments can help physicians in their diagnosis in order to facilitate the management of hepatic tumours. In patients suspected of having hepatic neoplasms considering their age, chief complaints and clinical symptoms, primary clinical diagnosis can be made even before performing sonography in some cases.

Conflict of interest: The authors have not declared any conflicts of interest.

AUTHOR'S CONTRIBUTION

SHT: Conceived the study design, supervised the study, write up and proof reading, EA, MV: Data collection, Statistical analysis and Literature review.

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