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Evaluation of Cases Presenting with a Liver Mass

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ABSTRACT

The diagnostic approach to liver masses is important in treatment planning. The aim of this study was to determine the histopathological diagnoses of patients presenting with liver masses and the distribution of organs from which metastases originated.

A retrospective evaluation was performed on 106 patients who presented to the Internal Medicine Clinics between 2016 and 2020, were diagnosed with liver masses, and underwent biopsy.

Hepatocellular carcinoma was diagnosed in 9 patients (8.4%), while metastasis was detected in 97 patients (91.6%). Benign pathology was detected in 2 patients (1.8%). Among the metastatic patients, 19 (17.9%) had pancreatic cancer, 15 (14.2%) had colorectal cancer, 14 (13.2%) had lung cancer, 9 (8.2%) had breast cancer, and 9 (8.2%) had gastrointestinal stromal tumors.

When histological diagnoses were evaluated, adenocarcinoma metastasis was detected in 65 patients (61.6%), neuroendocrine tumor in 12 patients (11.2%), hepatocellular carcinoma in 9 patients (8.4%), and 15 patients (14.2%) had unknown primary tumors.

The majority of liver masses are composed of metastases. Hepatocellular carcinoma is the most common primary tumor of the liver. The diagnostic evaluation of patients with liver masses is important for treatment purposes

Keywords: Liver, Mass, Metastasis, Primary

Introduction

Liver mass lesions are a common condition encountered in clinical practice and have a wide range of benign lesions to aggressive malignancies (1). Malignant liver masses can be primary cancers or can develop through metastasis to the liver from other organs. These lesions can be detected as a single focus or as multiple lesions.

In recent years, the increased use of imaging methods such as ultrasonography (USG), computed tomography (CT), and magnetic resonance imaging (MRI) has increased the diagnosis rate of liver masses (2). Most of these lesions are incidentally discovered during routine imaging examinations of asymptomatic individuals. The most common primary malignant tumor of the liver is hepatocellular carcinoma (HCC), followed by intrahepatic cholangiocarcinoma.

The liver is an organ where metastases are frequently seen due to its high blood supply (3). Additionally, the close proximity of the liver to other abdominal organs can lead to the development of liver mass lesions through direct spread (4). Approximately 40-50% of all malignancies develop liver metastases. The most common cancers that metastasize to the liver are gastrointestinal, breast, and lung cancers, as well as malignant melanoma. Adenocarcinomas constitute approximately 60% of metastatic liver tumors of unknown primary (PBMT) (5).

Accurate diagnosis of liver masses is of great importance for treatment and prognosis. Early diagnosis, appropriate treatment methods, and regular follow-up can improve the quality of life of patients.

In this study, the clinical evaluation and diagnostic methods of 106 patients who presented to the Internal Medicine outpatient clinic between 2018-2020 and were found to have a liver mass were retrospectively evaluated.

Materials and Methods

The study included patients who presented to the Internal Medicine outpatient clinic between 2018-2020, were found to have a liver mass, and underwent biopsy. The patient files were reviewed retrospectively. A total of 106 patients were included in the study. Epidemiological factors such as age and gender, and etiological factors such as chronic viral hepatitis, metabolic liver diseases, alcohol use, and history of oral contraceptive use were investigated.

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In order to investigate the primary focus, examinations related to breast diseases in women and prostate diseases in men were performed. All patients underwent upper and lower gastrointestinal system endoscopy, whole abdominal ultrasonography, abdominal and thoracic tomography, and tumor marker tests. For histological diagnosis, biopsy was performed using semi-automatic liver biopsy needles through the appropriate intercostal space under ultrasound guidance. Patients also underwent positron emission tomography (PET) scans.

SPSS 23.0 software was used for the statistical analysis of the data. The normality of distribution for continuous variables was assessed using the Kolmogorov-Smirnov test. Variables with normal distribution were expressed as mean ± standard deviation (SD), while those without normal distribution were expressed as median (minimum–maximum). Categorical variables were presented as numbers and percentages (%).

In the comparison between patients with solid and multiple lesions, the Chi-square test or Fisher's exact test was used for categorical variables. For continuous variables, the Independent Samples *t*-test or the Mann-Whitney *U* test was applied, depending on the distribution of the data.The level of statistical significance (p-value) was accepted as 0.05.

The study was approved by the Non-Interventional Clinical Research Ethics Committee of Recep Tayyip Erdogan University with the decision number 2018/118 dated 06/07/2018.

Result

A total of 106 patients were included in the study. Of these, 44 (41.5%) were female and 62 (58.4%) were male. The mean age of the patients was 69.5±10.6 years. The mean age of the female patients was 68.4±12.7 years, and the mean age of the male patients was 69.7±11.3 years.

Single masses were detected in 17 cases (16.0%), and multiple masses were detected in 89 cases (84.0%).

When patients with single and multiple masses were compared, there was no statistically significant difference in terms of gender and age. When the laboratory values were examined, gamma-glutamyl transferase (GGT) was significantly higher in the group with multiple lesions ($p<0.001$). There were no significant differences in other laboratory parameters.

In summary, the majority of patients (84%) had multiple liver masses, and higher GGT levels were associated with multiple lesions compared to single lesions. No other significant differences were found between the two groups in terms of age, gender, and other laboratory parameters. Of the patients with a single mass, 12 (11.3%) were female and 5 (4.7%) were male. Of the patients with multiple masses, 32 (30.1%) were female and 57 (53.7%) were male (Table 1).

104 (98.2%) of the cases were found to be malignant, and 2 (1.8%) were benign.

Primary liver cancer was detected in 9 (8.4%) patients, and metastasis was detected in 97 (91.6%) patients.

When the patients with metastasis were evaluated, pancreatic cancer was detected in 19 patients (17.9%), colorectal cancer in 15 patients (14.2%), lung cancer in 14 patients (13.2%), breast cancer in 9 patients (8.2%), gastrointestinal stromal tumor in 9 patients (8.2%), biliary tract tumor in 7 patients (6.6%), and kidney tumor in 3 patients (2.8%). In 15 patients (14.2%), the primary site could not be detected (Table 2).

When the histological diagnoses were evaluated, adenocarcinoma metastasis was detected in 65 patients (61.6%), neuroendocrine tumor metastasis in 12 patients (11.2%), hepatocellular carcinoma in 9 patients (8.4%), metastatic mesenchymal tumor in 8 patients (7.4%), carcinoma metastasis in 6 patients (5.6%), benign lesion in 2 patients (1.8%), nodular hyperplasia in 1 patient, and hepatic adenoma in 1 patient (Table 3).

When the patients with PBMT (primary biliary malignant tumor) were evaluated, adenocarcinoma metastasis was detected in 8 patients (53.3%), neuroendocrine carcinoma metastasis in 4 patients (26.7%), malignant mesenchymal tumor metastasis in 2 patients (13.3%), and squamous cell carcinoma in 1 patient (6.7%) (Table 4).

Table 1: Changes In Laboratory Parameters According To The Number of Lesions In The Liver

	NUMBER OF LIVER LESIONS						p value*
	SOLID LESION (n:17)			MULTIPL LESION (n:89)			
	Median	Minimum	Maximum	Median	Minimum	Maximum	
Female/Male(n)		12//5			32//57		0,008
Age	68	25	80	71	42	88	0.370
CCI	3	0	5	4	0	7	0.374
WBC	7550	2810	32800	8980	9	21580	0.117
HGB	12.5	8.6	14.7	12.0	7.9	16.6	0.278
PLT	257	83	518	270	81	754	0.901
URE	40	13	191	43	16	204	0.472
Crea	0.79	0.49	5.18	0.85	0.40	9.79	0.431
AST	23	14	352	49	11	421	0.008
ALT	20	10	241	35	8	714	0.026
T.BİL	0.49	0.26	14.20	0.90	0.20	17.07	0.007
D.BİL	0.20	0.09	10.70	0.36	0.04	11.50	0.018
GGT	41	17	225	170	6	1677	<0.001
LDH	243	52	661	357	109	3904	0.001
TP	68.0	54.0	81.0	65.0	40.0	97.0	0.072
ALB	37.0	23.0	44.0	33.0	19.0	47.7	0.106
APTT	29.0	21.4	46.9	30.4	1.2	45.4	0.295
INR	1.04	0.88	1.47	1.10	0.80	94	0.054
CEA	4.95	1.94	16.65	5.04	0.81	1015	0.603
CA19-9	13	2	12000	44	1	12000	0.164
ALP	116	65	299	150	34	1141	0.173
ESR	58	6	83	31	6	105	0.183
AFP	3.67	0.50	36.50	2.35	0.39	20000	0.811
CA125	54	9	376	48	4	10000	0.632
CA15-3	30	12	71	23	3	680	0.876

Mann-Whitney U Test Analysis

CCI: Comorbidity index, WBC: Leukocyte, HGB: Hemoglobin, PLT: Platelet, Crea: Creatinine, AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, T. BIL: Total bilirubin, D.BIL: Direct bilirubin, GGT: Gamma-glutamyl transferase, LDH: Lactate dehydrogenase, TP: Total protein, Alb: Albumin,ESR: Erythrocyte Sedimentation Rate

Discussion

The liver is an organ where benign and malignant tumors are frequently encountered. The increased use of abdominal imaging methods has led to a significant increase in the detection of incidental liver masses, in addition to symptomatic patients (6). The most important point in the evaluation of liver masses is to accurately distinguish between benign and malignant lesions. The main goal is to avoid unnecessary diagnostic procedures and treatments for benign lesions, and to apply the most effective treatment methods for malignant lesions (7).

Benign lesions are among the most commonly diagnosed abnormalities in liver imaging, and most of them are asymptomatic, often detected in middle-aged women. The most common benign liver tumors include hepatic adenoma, focal nodular hyperplasia, cavernous hemangioma, and simple cysts. Hepatic angiomyolipoma, hepatic hemangioendothelioma, hepatic schwannoma, and hepatic mesenchymal hamartoma are examples of rare benign liver tumors (8). In our study, benign tumors were detected in 2 (1.8%) patients.

Liver cancer is the second most common cause of cancer deaths worldwide, and the most common subtype is hepatocellular carcinoma (HCC), which accounts for about 90% of cases. Common risk

Table 2: The Organs From Which The Metastatic Cancers Originated

	n	%
Unknown primary	15	14.2
Breast	9	8.5
Colorectal	15	14.2
Liver	11	10.4
Pancreas	19	17.9
Lung	14	13.2
GIST	9	8.5
Kidney	3	2.8
Biliary tract	7	6.6
Prostate	1	0.9
Thyroid	1	0.9
Skin	1	0.9
Bone marrow	1	0.9

GIST: Gastrointestinal Stromal Tumor

Table 3: Documented Histological Subtypes In All Patients

	n (%)
Adenocarcinoma metastasis	65(61,6)
Neuroendocrine carcinoma metastasis	12(11,2)
HCC	9 (8,4)
Malignant mesenchymal tumor metastasis	8 (7,4)
Carcinoma metastasis	6 (5,6)
Benign lesion	2 (1,8)
SCC metastasis	1 (0,9)
Malignant melanoma	1 (0,9)
Lymphoma (B-cell)	1 (0,9)
Medullary carcinoma	1 (0,9)

HCC: Hepatocellular carcinoma, SCC: Squamous cell carcinoma

Table 4: Histological Distributions of Tumors of Unknown Primary Origin

	n	(%)
Adenocarcinoma metastasis	8	(53.3)
Malignant mesenchymal tumor metastasis	2	(13.3)
Neuroendocrine carcinoma metastasis	4	(26.7)
Squamous cell carcinoma metastasis	1	(6.7)

factors include hepatitis B and C virus infections, cirrhosis, metabolic dysfunction-associated fatty liver disease (MAFLD), and alcohol use. MAFLD has become the leading cause of chronic liver disease worldwide, and the prevalence of MAFLD-related HCC has increased in recent years. Other less common risk factors include hemochromatosis, autoimmune hepatitis, and exposure to environmental toxins. Lesions can be single-focused or multifocal (9-12). In our study, HCC was detected in 9 (8.4%) patients, 7 (77.8%) of which were single lesions, and 2 (22.2%) were multifocal.

Approximately 25% of liver tumors are metastatic tumors. Metastatic liver tumors are 18-40 times more common than primary liver cancers. Due to the high blood supply of the liver, malignant diseases most often metastasize to the liver. The most common tumors that metastasize to the liver are gastrointestinal system tumors, followed by breast, lung cancers, neuroendocrine tumors, and malignant melanoma (13). Metastatic liver masses

can appear as a single lesion or multiple lesions. In our study, metastases were detected in 97 (91.6%) patients, 92 (86.7%) of whom had multiple lesions, and 5 (0.47%) had a single lesion. The most common primary diagnosis in patients with metastases in our study was pancreatic cancer (19 patients, 17.9%), followed by colorectal cancer (15 patients, 14.2%), and then lung cancer, breast cancer, and gastrointestinal stromal tumor.

The distinction between metastatic carcinoma and primary hepatocellular carcinoma in the liver can sometimes be difficult, but it is essential to identify the lesion, as they have different treatment options and prognoses. The next step is to determine the primary focus of the metastatic carcinoma. However, despite comprehensive clinical, laboratory, radiological, endoscopic, and conventional pathological examinations, it may sometimes be unsuccessful to identify the primary carcinoma focus, and these cases are defined as PBMT (metastatic liver tumor of unknown primary origin) (14). The incidence of PBMT ranges from 5-10% among all malignant tumors. A study on the imaging of PBMT patients found that the frequency of adenocarcinoma was 60%, and the frequency of SCC was 18%. In this study, PBMT was detected in 15 patients (14.2%), and the most common metastasis was adenocarcinoma, followed by neuroendocrine carcinoma.

The evaluation of patients presenting with liver masses is of great importance. The increased sensitivity of imaging methods has led to a rise in the frequency of liver lesion diagnoses. The distinction between benign and malignant lesions cannot be overlooked. Accurate diagnosis allows for intermittent follow-up for benign masses, while lesions with malignancy or the risk of malignant transformation can be managed with surgical and oncological treatments. In these patients, even metastatic tumors can have their survival time extended and, in some cases, a curable cancer type may be identified with appropriate treatment. Therefore, determining the histological and primary diagnosis of liver masses is essential for determining prognosis and treatment strategies.

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