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Tumor in the liver: Six inflammatory pseudotumor patients

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ABSTRACT

Inflammatory pseudotumor (IPT) is a rare liver disease confused with liver tumors. It is a disease that should be known in the differential diagnosis for clinicians as the correct diagnosis of IPT will prevent unnecessary surgery. Demographic datas, diagnoses and imaging modalities of six patients with radiologically and/or histopathologically diagnosed hepatic IPT between 2016 and 2023 were retrospectively analyzed. Four out of six patients were female and median age was 57.5 (47-66). C-reactive protein was higher in four patients, and carbohydrate antigen 19.9 level was higher in one patient. We used magnetic resonance imaging (MRI) for diagnosis in five patients. Only in one patient computed tomography was enough for diagnosis. Tumor locations were segment 5 for two patients, segment 7-8 in two patients, segment 7 in one patient, and 8 in one patient. Liver biopsy was performed in five patients because it could not be distinguished from malignancy by imaging methods. Histopathological results of all these biopsies defined as IPT. Initial tumor median size was 31 (17-55) mm. Two patients were operated on. The first one underwent right hepatectomy due to a 2-fold increase in size within 11 months. The second one had a mass indistinguishable from hepatic adenoma by MRI and underwent nonanatomic resection. In one patient, IPT disappeared completely in the 18th month of follow-up period while it regressed in size in two patients. Two of our patients had a history of recurrent endoscopic retrograde cholangiopancreatography, which we noticed incidentally before IPT was diagnosed. IPTs are liver masses with low malignant potential and may shrink spontaneously during follow-up. We suspected that biliary tract interventions may be the cause of IPT.

Keywords: Inflammatory pseudotumor, hepatic mass, IgG4, biliary tract intervention

INTRODUCTION

Inflammatory pseudotumor (IPT) is a rare disease characterized by fibrosis and chronic infiltration of inflammatory cells (1). It may affect many organs including the biliary tract, lung, lymph nodes, pancreas, retroperitoneum and liver (2,3). IPT localized in the liver may be confused with liver tumors (1). In the etiology infections (mostly bacterial), immunology, allergy or malignancies are blamed (4). It has also been reported that there may be a relationship between immunoglobulin G4 (IgG4)-related sclerosing disease and IPT (5). It is mostly observed in men between the ages of 30-40 years, and its symptoms include nonspecific findings including fever, abdominal pain and weight loss (6). Computed tomography (CT) of the liver and magnetic resonance imaging (MRI) with liver-specific contrast are recommended for differential diagnosis (1) .

IPT has a good prognosis and it has been reported in the literature that spontaneous regression in tumor size may occur spontaneously or with anti-inflammatory drugs or steroid treatment (7). Since unnecessary surgery will be prevented with the correct diagnosis of IPT, it is a disease that should be known in the differential diagnosis for clinicians. Our aim was to raise awareness about this disease by sharing our clinical experience with you.

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MATERIAL and METHODS

This study was approved by the institutional review board (Approval number: 19). When the admissions to our clinic between 2016 and 2023 were analyzed retrospectively, we found that a total of six patients were diagnosed with IPT radiologically and/or histopathologically. Demographic data, diagnosis and screening parameters were analyzed retrospectively. Continuous variables were defined as median (range), and categorical data were defined as frequencies and percentages. Patients were followed up clinically and radiologically until March 2024.

RESULTS

Demographic and preoperative biochemical results of six patients are analyzed in Table 1. Four (66.6%) out of six patients were female and median age was 57.5 (47-66). White blood cell (normal level is between 4.4-12.6 x 10^3/Ul), and alpha fetoprotein (AFP) (normal level is between 0.5-5.8 IU/mL) levels were between normal values. C-reactive protein (CRP) (normal level is between 0-5 mg/L) was higher in four patients, and carbohydrate antigen (CA) 19.9 (normal level is between 0-27 U/mL) level was higher in one patient. Viral markers (hepatitis B, C, and anti-HIV) were between normal levels for all of the patients.

Diagnosis and follow-up outcomes are shown in Table 2. We used MRI for diagnosis in five patients. Only in one patient, CT was enough for diagnosis. Tumor locations were segment 5 for two patients, segment 7-8 in two patients, segment 7 in one patient, and 8 in one patient. Liver biopsy was performed in five patients because it could not be distinguished from malignancy by imaging methods. Histopathological results of all these biopsies were defined as IPT. The pathological results of three patients were related with IgG4. Anaplastic lymphoma kinase (ALK) was negative for five patients.

Table 1. Demographic data and preoperative biochemical test results of the patients

Patient Number	**1**	**2**	**3**	**4**	**5**	**6**
Gender	F	M	F	F	M	F
Age (year)	55	47	60	63	66	48
WBC (10^3/uL)	4.4	9.4	5	7.6	11.9	7.9
CRP (mg/L)	**13.8**	**76.6**	**14.6**	**22.8**	2.3	0.7
CA 19.9 level (U/mL)	2.9	9.48	0.6	4.43	**41.1**	-
AFP level (IU/mL)	4.2	-	1.86	1.69	3	-
Viral markers	N	N	N	N	N	N

F: Female, M: Male, WBC: White blood cell, AFP: Alpha fetoprotein, CRP: C-reactive protein, CA: Carbohydrate antigen, N: Normal.

Table 2. Diagnosis and follow-up outcomes of the patients

Patient Number	**1**	**2**	**3**	**4**	**5**	**6**
Imaging methods	CT	MRI	MRI	USG-MRI	MRI	MRI
Tumor location in the liver (segment)	5	5	7	7-8	8	7-8
Liver biopsy (+/-)	+	+	+	+	+	-
IgG4	-	+	-	-	+	+
ALK	-	-	NA	-	-	-
Initial tumor size (mm)	50	17	55	40	22	20
Tumor number (n)	1	1	1	1	1	1
O/F	F	F	F	F	O	O
Last tumor size (mm)	50	10	22	0	-	-
Follow up period (month)	12	33	4	18	11	6
Survival status	E	A	E	A	A	A

CT: Computed tomography, USG: Ultrasonography, MRI: Magnetic resonance imaging, IgG4: Immunoglobulin G4, ALK: Anaplastic lymphoma kinase, NA: Non-available, O: Operation, F: Follow up, A: Alive, E: Exitus.

Initial tumor median size was 31 (17-55) mm, and a tumor focus was detected in all patients using imaging methods. Two patients were operated. Patient 5 was diagnosed as IPT by preoperative liver biopsy but underwent right hepatectomy due to a 2-fold increase in size within 11 months. Patient 6 had a mass indistinguishable from hepatic adenoma by preoperative MRI and underwent nonanatomic resection.

In one patient, IPT disappeared completely in the 18th month of follow-up period while it regressed in size in two patients (Figure 1). One of the patients with tumor size regression died in the fourth month of follow-up period due to intracranial hemorrhage. One patient died in the 12th month of follow-up period because of heart failure; no progression in tumor size was noted during this 12-month follow-up period. The follow-up periods of the two patients who survived and did not have surgery were 33 month and 18 month, respectively.

Two of our patients had a history of recurrent endoscopic retrograde cholangiopancreatography (ERCP), which we noticed incidentally before IPT was diagnosed. Patient 1, who had pancreatic head malignancy, underwent preoperative ERCP three times. Postoperatively, three percutaneous transhepatic cholangiographies were performed, followed by the placement of a percutaneous biliary stent. A liver mass developed after the biliary tract interventions, and the pathological result was IPT. Patient 2 has a history of nine ERCP procedures performed over five years due to acute biliary pancreatitis.

DISCUSSION

IPT, also known as inflammatory myofibroblastic tumor and plasma cell granuloma, is a rare inflammatory soft tissue lesion (2). IPT is also known as inflammatory myofibrohistiocytic proliferation, fibrous histiocytoma, etc. in the literature (8). IPT usually affects the right lobe of the liver, but it has been rarely reported to be found in the spiegel lobe and hilar region or bilobar multifocal (6,9). IPT was localized in the right lobe in all of our patients in accordance with the literature. We thought that the reason of IPT for two patients may have been related to repeated biliary tract interventions. Similarly, our hypothesis is supported by a case series including three patients, in which it has been reported that biliary tract manipulation may be the cause of IPT (10).

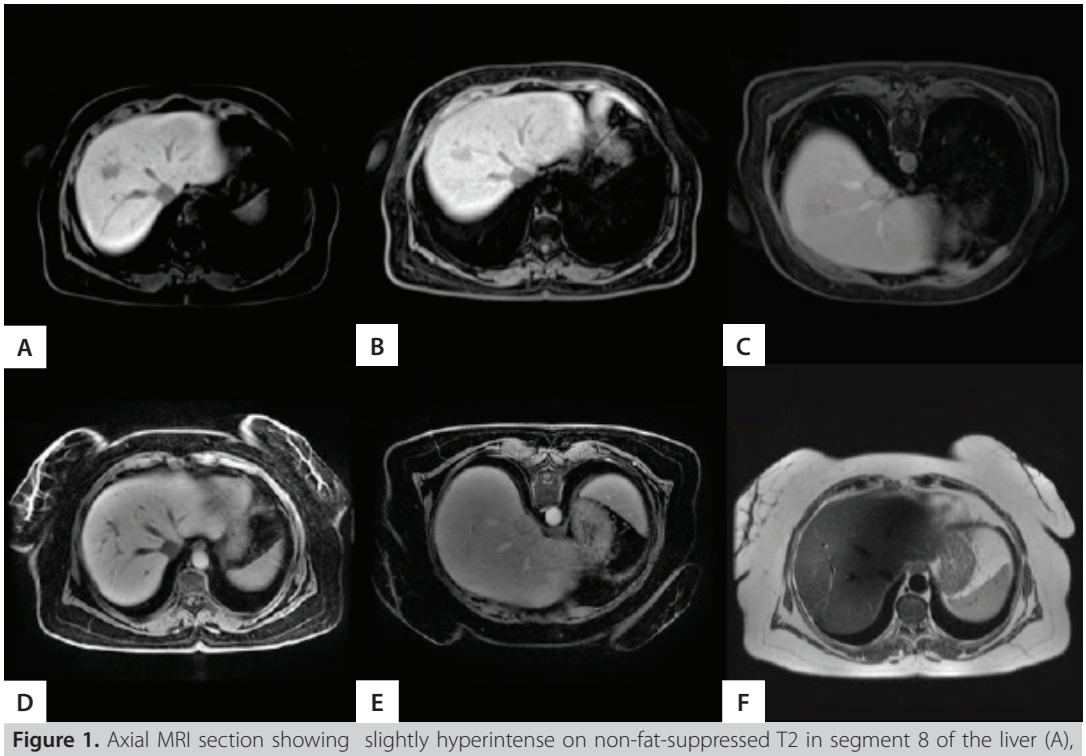

Figure 1. Axial MRI section showing slightly hyperintense on non-fat-suppressed T2 in segment 8 of the liver (A), hypointense on precontrast T1 (B), centrally stained in postcontrast portal phase images and becomes isointense with the parenchyma (C). In control imaging, the lesion has completely regressed. T2AG without fat suppression (D), post-contrast portal phase images (E) and hepatobiliary phase images (F).

Laboratory findings include leukocytosis, increased erythrocyte sedimentation rate and CRP, polyclonal hypergammaglobulinemia, and mildly elevated liver enzymes. AFP, one of the tumor markers, is mostly normal, whereas CA 19.9 has been found at high values in some patients (6). ALK overexpression is observed in 50% of patients with IPT, and positivity has been associated with high local recurrence and increased mortality (8).

Similar contrast enhancement patterns on CT and MRI can also be observed in other lesions such as atypical hepatocellular carcinoma, intrahepatic cholangiocarcinoma, metastatic tumors and abscesses (1). CT findings for IPT exhibit significant variability. The most frequently observed features are hypoattenuating, ill-defined masses with a range of contrast enhancement levels. Delayed enhancement, particularly in septal and peripheral regions, is noted and is believed to be associated with fibrous components (11). MRI reveals a variable presentation of these tumors; they are generally hypointense relative to skeletal muscle on T1-weighted images, hyperintense on T2-weighted images, and show heterogeneous enhancement after contrast material is administered (12). It has been reported that IPT should be suspected if Ig G4 is also positive in the presence of targetoid-like aspect of hepatic mass on MRI (4).

Nevertheless, because of uncertainty in the imaging diagnosis, histologic diagnosis is important to accurately diagnose IPT (8). It is known that the clinical course and prognosis of IPT are favorable with conservative treatment (1). While we diagnosed IPT in five patients with biopsy and followed four of them, right hepatectomy was performed in only one patient in consequence of of rapid growth. On histopathological examination, IPT is characterized by proliferation of fibroblasts or myofibroblasts and inflammatory cell infiltration consisting of lymphocytes and plasma cells (6,9). Two histologic forms have been reported for IPT in the liver. These are fibrohistiocytic and lymphoplasmocytic forms (13). Lymphoplasmocytic form has been associated with Ig G4. It has been reported that this form is mostly observed in the hepatic hilus (13). In the fibrohistiocytic form, the tumor is found as a mass located in the periphery of the liver (14).

It has been reported that spontaneous regression may occur with conservative treatments such as nonsteroidal antiinflammatory drugs after pathologic diagnosis (8). In a case series of three patients in the literature, spontaneous regression has been reported for liver localized IPT (7). Although the recurrence rate has been reported to be approximately 25%, it has also been reported that surgical procedure may be required (8). No conservative treatment was given to the patients in our study group, and no progression in the size of the mass was observed except in one patient and even regression was found.

CONCLUSION

IPTs are liver masses with low malignant potential and may shrink spontaneously during follow-up. As long as they are closely monitored with imaging methods and there is no suspicion of malignancy, there is no need for surgical intervention. Finally, we doubt that development of IPT may be associated with biliary tract interventions.

Ethics Committee Approval: This study was approved by the Eskişehir Osmangazi University Non-Invasive Clinical Research Ethics Committee (Decision no: 19, Date: 21.03.2023).

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OLGU SERİSİ-ÖZET
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Karaciğerde tümör: Altı enflamatuvar psödotümör hastası

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ÖZET

Enflamatuvar psödotümör (EPT), karaciğer tümörleriyle karıştırılan nadir bir karaciğer hastalığıdır. Enflamatuvar psödotümörün doğru tanısı gereksiz cerrahiyi önleyeceğinden klinisyenler için ayırıcı tanıda bilinmesi gereken bir hastalıktır. 2016-2023 yılları arasında radyolojik ve/veya histopatolojik olarak hepatik EPT tanısı almış altı hastanın demografik verileri, tanıları ve görüntüleme yöntemleri retrospektif olarak analiz edildi. Altı hastanın dördü kadındı ve ortanca yaş 57,5'ti (47-66). C-reaktif protein dört hastada yüksekti ve karbohidrat antijeni 19,9 seviyesi bir hastada yüksekti. Beş hastada tanı için manyetik rezonans görüntüleme (MRG) kullanıldı. Sadece bir hastada tanı için bilgisayarlı tomografi yeterli oldu. Tümör yerleşimi iki hastada segment 5, iki hastada segment 7-8, bir hastada segment 7 ve bir hastada 8 idi. Beş hastaya görüntüleme yöntemleriyle maligniteden ayırt edilemediği için karaciğer biyopsisi yapıldı. Tüm bu biyopsilerin histopatolojik sonuçları EPT olarak tanımlandı. Başlangıçtaki tümör medyan boyutu 31 (17-55) mm idi. İki hasta ameliyat edildi. İlk hastaya 11 ay içinde tümör boyutunda iki kat artış olması nedeniyle sağ hepatektomi yapıldı. İkinci hastada MRG ile hepatik adenomdan ayırt edilemeyen bir kütle vardı ve anatomik olmayan rezeksiyon yapıldı. Bir hastada EPT, takip süresinin 18. ayında tamamen kaybolurken, iki hastada boyut olarak geriledi. Hastaların ikisinde EPT tanısı konulmadan önce tesadüfen fark edilen tekrarlayan endoskopik retrograd kolanjiyopankreatografi öyküsü vardı. Enflamatuvar psödotümörler düşük malignite potansiyeline sahip karaciğer kütleleridir ve takip sırasında kendiliğinden küçülebilmektedir. Safra yolu müdahalelerinin EPT'ye neden olabileceğinden şüphelenilmektedir.

Anahtar Kelimeler: Enflamatuvar psödotümör, karaciğerde kütle, IgG4, safra yolu girişimi

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