

Inflammatory pseudotumor of the liver diagnosed by needle biopsy: Report of three cases (one with neuroendocrine tumor of the rectum and lung)

Karaciğer iğne biopsisi ile tanı konan: bir olguya rektum ve akciğerin nöroendokrin tümörünün eşlik ettiği; üç inflammatuar psödotümör olgusu

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Inflammatory pseudotumor of the liver is a rare disorder that can histologically and radiologically resemble malignant neoplasms. The prognosis of the patients with hepatic inflammatory pseudotumor is usually good with conservative therapy. Most of the reported cases are diagnosed in the surgical resection specimens; only very few reported cases have been diagnosed by needle biopsy. We report three additional cases of inflammatory pseudotumor of the liver diagnosed by liver biopsy. Two of these cases were treated successfully with antibiotics. The other case, who was resistant to medical treatment, had coexisting neuroendocrine neoplasms of the rectum and the lung. Since her general condition did not allow an extensive surgery, the mass of the liver could not be resected and she died approximately five months after she was voluntarily discharged from the hospital. Many of the inflammatory pseudotumor of the liver are found to be associated with variable neoplasms, but to our knowledge, the latter case is the first case of inflammatory pseudotumor associated with a neuroendocrine tumor.

Key words: Inflammatory pseudotumor, liver

INTRODUCTION

Inflammatory pseudotumor (IPT) is a rare benign neoplasm found in almost every organ of the human body (1, 2). Involvement of the liver is rare (3). IPT of the liver can histologically and radiologically resemble various malignant neoplasms. Most of the reported cases were diagnosed after surgical resection (3-5); only very few reported cases have been diagnosed by needle biopsy (3). It is important to diagnose IPT on liver biopsy because IPT can be cured with medical treatment including nonsteroidal antiinflammatory drugs (NSAID), antibiotics or steroids. There are a few cases of IPT of the liver with disea-

İnflammatuar psödotümör histolojik ve radyolojik olarak maligniteyi taklit edebilen nadir bir karaciğer tümörüdür. Konservatif tedaviyle prognozu genellikle iyidir. Rapor edilmiş olguların çoğunda olgu cerrahi rezeksiyon materyallerinde tanı almış olup, iğne biopsisiyle tanı konmuş çok az sayıda olgu bulunmaktadır. Biz bu makalede iğne biopsisi ile hepatik inflammatuar psödotümör tanısı almış üç olgu sunmayı amaçladık. Bu olgulardan ikisi antibiotik ile başarılı bir şekilde tedavi edildi. Medikal tedaviye direnç gösteren diğer olgunun rektum ve akciğerinde ise eşlik eden nöroendokrin tümör mevcuttu. Bu olgunun genel durumu cerrahi girişimi kaldıramayacak durumda olduğundan, karaciğerdeki tümör cerrahi olarak çıkarılamadı ve hasta kendi isteğiyle taburcu olduktan yaklaşık beş ay sonra eks oldu. Hepatik inflammatuar psödotümör'ün farklı neoplazmlerle birlikte bulunabildiği bildirilmiştir. Söz konusu olgumuz literatür taramalarımıza göre nöroendokrin tümör ile birlikte ilk gösteren ilk olgu olma özelliğini taşımaktadır.

Anahtar kelimeler: İnflammatuar psödotümör, karaciğer

se progression and mortality (1, 6-8). In this report, we present three cases of IPT of the liver diagnosed by liver biopsy. Two of the cases were treated successfully with antibiotics. The other case, who was resistant to medical treatment, had coexisting neuroendocrine neoplasms of the rectum and the lung.

CASE REPORTS

Case 1

A 65-year-old woman presented with abdominal pain, nausea, and weight loss that persisted for

more than three months. Laboratory tests disclosed increased C-reactive protein (CRP) (43.3; normal range (NR) 0-5 mg/L), erythrocyte sedimentation rate (ESR) (107; NR 0-20 mm/h) and white blood cell (WBC) ($12500/\text{mm}^3$ with a differential count of 75% neutrophils) values. Other laboratory data including tumoral markers were within normal ranges. Hepatic markers were also negative. Computed tomography (CT) of the abdomen revealed a heterogeneous solid hepatic mass of 18x17 cm on the left lobe (Figure 1). Upper gastrointestinal endoscopy was normal but colonoscopic examination

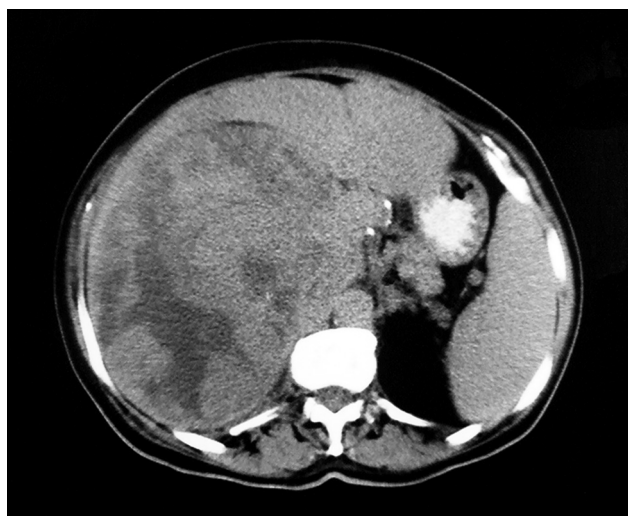


Figure 1 (Case 1): Computed tomography shows a solid mass with heterogeneous pattern measuring 18x17 cm in the left lobe of the liver.

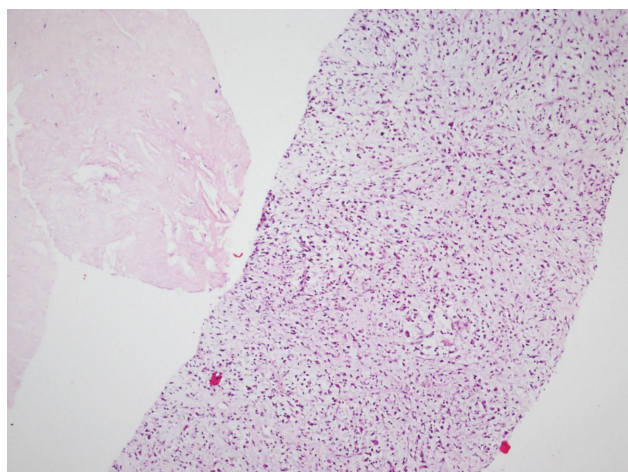


Figure 2-a (Case 1): Stellate-shaped fibroblast-like cells intermixed with polymorphous inflammatory infiltrate in a background of myxoid stroma. The tumor is composed of hypocellular hyalinized stroma in one part of the core biopsy (hematoxylin-eosin X100).

on disclosed an 8 mm polyp in the rectum, which was diagnosed as a well-differentiated neuroendocrine tumor. Percutaneous needle core biopsy of the liver mass showed stellate, spindle-shaped fibroblast-like cells admixed with polymorphous inflammatory infiltrate in a background of myxoid to collagenous and hyalinized stroma (Figure 2-a). There was no cellular atypia, necrosis or mitotic activity. Immunohistochemically, smooth muscle actin (SMA) was positive in stellate, spindle cells, whereas desmin, CD34, S100 protein, and anaplastic lymphoma kinase (ALK) were negative. After the diagnosis of IPT, the patient was given antibiotics. On follow-up CT scan, the mass showed no regression so antibiotics were stopped and prednisolone with NSAID was initiated. During this follow-up, thorax CT was performed and a 2 cm peripheral solid mass with irregular contours in the inferior lobe of the right lung was detected. CT-guided transthoracic aspiration biopsy, which was performed in another institution, revealed features consistent with neuroendocrine tumor with the possibility of a pulmonary carcinoid (Figure 2-b).

The next follow-up CT scan of the liver showed no regression in the mass. Meanwhile, the patient's condition worsened dramatically (progressive shortness of breath, intolerance of minimal physical activity, myalgia, low-grade fever, and significant fatigue). She ceased taking all her medication voluntarily and was discharged from the hospital. It was learned that she died approximately five months after discharge from the hospital.

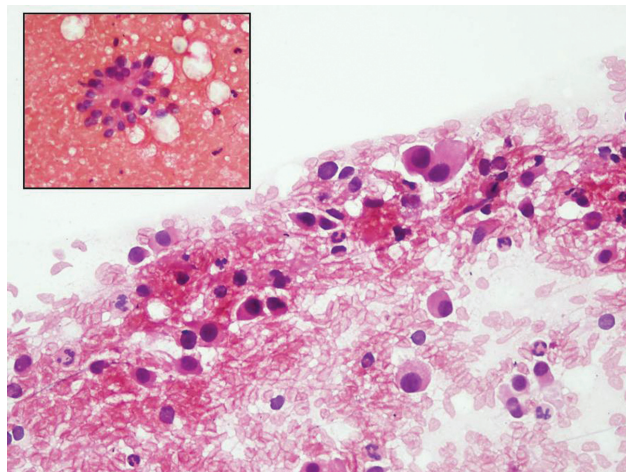


Figure 2-b (Case 1): Dis-cohesive single tumor cells with uniform, round eccentrically placed nuclei have moderate amount of eosinophilic cytoplasm and inset is rosette formation (hematoxylin-eosin X200).

Case 2

A 74-year-old man presented with fever, epigastric pain and nausea that started five days prior to his admission. Physical examination showed mild epigastric tenderness on palpation. Laboratory evaluation was remarkable for elevated WBC ($16600/\text{mm}^3$ with 80% neutrophils). Abdominal ultrasonography (USG) revealed a solid hepatic mass lesion and further CT scan showed an 8 cm hypodense, solid hepatic mass with irregular contours on the right lobe. Biopsy of the lesion revealed a mixture of chronic inflammatory cells on a background of collagenous and fibrous stroma (Figure 3). Immunohistochemically, SMA and CD68 were positive. ALK was negative. Diagnosis of IPT was made and antibiotic therapy was started. He was invited for a follow-up CT at one month but was lost to follow-up. Four years after his discharge from the hospital, he was contacted by telephone and reported that he was in good health.

Case 3

A 70-year-old man presented with severe epigastric pain, nausea, vomiting, and loss of appetite. These symptoms started 10 months prior to his admission, and he lost nearly 10 kilograms. He had abdominal pain that was moderate in intensity, and intermittent at the beginning, which became severe and constant in the last month. Physical examination revealed right upper quadrant tenderness without rebound. His body temperature was normal. Laboratory findings revealed increased alkaline phosphatase (ALP) (225 u/L; NR 40-140), gamma-glutamyl transpeptidase (GGT) (137 U/L, NR 9-64), ESR (98 mm/h), and normochromic normocytic anemia. Serologic markers for viral hepatitis were negative. Tumoral markers were within normal limits except for CA19-9 (46.69 U/ml, NR 0-30). The rest of the laboratory data was normal. CT scan of the abdomen showed a 5 cm solid and necrotic mass on the left lobe of the liver. Liver biopsy was performed with the initial diagnosis of metastatic carcinoma. Microscopic examination revealed polymorphous inflammatory infiltrate admixed with bland spindle cells in a loose and myxoid hypocellular stroma. Spindle cells were positive with SMA and negative with ALK. A diagnosis of IPT was made and treatment with antibiotics was started. Follow-up CT scan performed three weeks after the antibiotic therapy showed that the mass had markedly reduced in size (Figure 4a-b). Unfortunately, this patient was also lost to follow-up. Two years

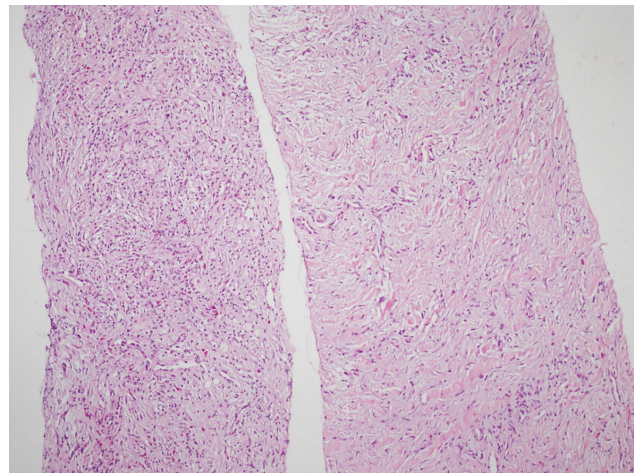


Figure 3 (Case 2:) Spindle-shaped fibroblasts with a mixture of chronic inflammatory cells on a background of collagenous and fibrous stroma (hematoxylin-eosin X100).

after his last follow-up visit, he was contacted by telephone and it was learned that he had no symptoms and was in good health.

DISCUSSION

Inflammatory pseudotumor (IPT) of the liver is a rare benign hepatic lesion that clinically and radiologically mimics malignancy (4, 5). One-third of the patients are male with a mean age of 56 years (9). Histopathologically, IPT is characterized by bland spindle cells admixed with polymorphous inflammatory cells in a background of collagenous, hyalinized or myxoid stroma (3). The spindle cells are in the form of fibroblasts and myofibroblasts. Mitosis is absent or scanty and cellular atypia is generally mild, but atypical ganglion-like cells can sometimes be seen. Spindle cells are usually positive with SMA and muscle specific actin (MSA). ALK expression is highly specific for IPT but sensitivity is low depending on the primary site (10). ALK is found to be positive mostly in atypical ganglion-like cells and in patients under the age of 40 (11).

The pathogenesis and etiology of IPT of the liver are still unclear (5). Some IPTs of the liver are found to be associated with systemic inflammatory disorders, autoimmune diseases or neoplasms (3, 9, 12, 13). There have been 12 case reports in the literature associated with malignant tumors (13, 14). Three types of cancer patients have been documented in IPT of the liver: gastrointestinal tract cancer patients including gastrointestinal stromal tumor (GIST) (12), biliary tract cancer patients



Figure 4-a (Case 3:) Computed tomography demonstrates a slightly heterogeneous and hypodense 4 cm diameter mass adjacent to the gallbladder within the right lobe of the liver.

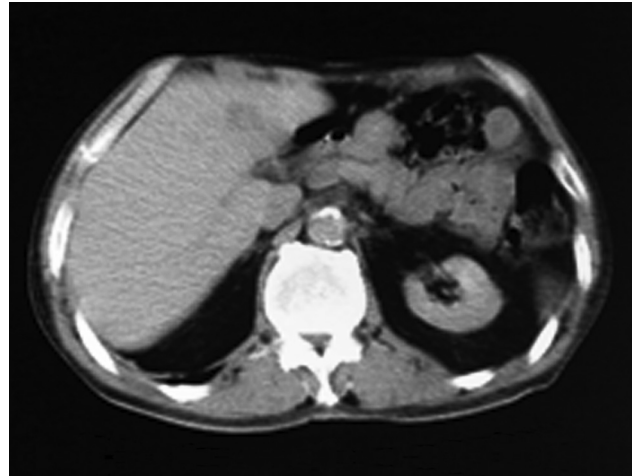


Figure 4-b. CT scan performed 3 weeks later shows a regression of the mass to approximately one- third of its initial size.

and patients who received systemic chemotherapy (13). Probable septic origin, hepatic abscess or infection through the portal vein causing IPT of the liver has been widely suggested, but no definitive microorganisms could be isolated from the specimens in most cases (12, 15). Also, in our first case, it would be hard to suggest that an 8 mm polypoid-shaped neuroendocrine tumor of the colon could have assisted the entry of the enteric microorganisms into the portal vein to support an infectious etiology.

Most of the cases reported have systemic symptoms such as fever, epigastric pain, vomiting, malaise, or weight loss (5). Laboratory findings might reveal evidence of inflammation, hypergammaglobulinemia and mildly elevated serum aminotransferases (3, 9). All of our cases had some of these symptoms and laboratory findings.

The radiologic features of IPT are nonspecific and mimic malignant neoplasms, such as hepatocellular carcinoma, metastatic adenocarcinoma or hepatic abscess, making it essential to obtain a tissue diagnosis (3, 5).

Differential diagnosis of IPT of the liver is broad and depends on the predominant histologic pattern present (16). Angiosarcoma, inflammatory malignant fibrous histiocytoma, and metastatic GIST should be differentiated from IPT. The presence of cellular atypia and frequent mitotic figures supports the diagnosis of the former tumors. Immunohistochemistry may also aid in diagnosis; angiosarcomas react with vascular endothelial markers whereas metastatic GISTs stain positive

with CD117 and/or CD34 (16, 17). Differential diagnosis of IPT with follicular dendritic cell tumor of the liver is difficult. Presence of pleomorphism and lack of plasma cells with the positivity of CD21, CD23 and CD35 in tumor cells support the latter (16, 17). In our case, there was no mitotic activity or atypia, and the spindle cells were positive for SMA. Solitary fibrous tumor, peripheral nerve sheath tumor and inflammatory type of angiomylipoma might also cause problems in the differential diagnosis, but immunohistochemistry assists in the diagnosis with the expression of CD34, S100 and HMB45, respectively (16, 18).

The prognosis of the patients with hepatic IPT is generally excellent (5). Spontaneous regression or regression after conservative treatment with antibiotics, NSAID and corticosteroids has been reported (1-3, 5, 12). On the other hand, as in our first case, there are cases with mortality, recurrences and disease progression in IPT of the liver (1, 6-8). Such malignant transformation and cases ending in mortality challenge the assumption that hepatic IPTs are totally benign lesions (7).

Although no standard treatment guidelines for IPT of the liver are available, once the diagnosis of IPT of the liver is established, follow-up or conservative therapy should be the first line of treatment (1, 5, 12). Surgical treatment, which is generally regarded as over-treatment, should be considered if IPT does not respond to medical therapy (1, 12), causes major complications such as biliary obstruction and portal hypertension (12), or when the definitive diagnosis cannot be made by needle bi-

opsy (15). Hence, the diagnosis of IPT on percutaneous needle biopsy is important to avoid unnecessary exploratory laparotomy or hepatectomy (1). Unfortunately, needle biopsy leads to the diagnosis of IPT in only a few cases (3).

All three cases in this report were diagnosed by needle biopsy and two of them responded well to antibiotics. The first case with a huge mass of the liver did not respond to medical treatment. The mass in the liver did not regress and since her general condition did not allow an extensive surgery, resection of the tumor was not possible. She died one year after the diagnosis. To our knowledge, this case

is the only reported case of IPT of the liver associated with a neuroendocrine tumor and one of the few cases of IPT of the liver with a fatal outcome.

In conclusion, diagnosis of IPT of the liver by needle biopsy is very advantageous but not always possible since the differential diagnosis of IPT is extensive (1, 9). IPT should be kept in mind in the differential diagnosis of mass lesions of the liver. Medical treatment should be preferred initially, and continued long-term follow-up is recommended for all patients due to the reported risk of malignant transformation, late disease recurrence and mortality.

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