Inflammatory Myofibroblastic Tumor of Liver Masquerading as Focal Nodular Hyperplasia in a Patient with Non-Cirrhotic Portal Hypertension and Biliary Pancreatitis

Vivek Kasana · S. Rajesh · Udit Chauhan ·
Chhagan Bihari · Ashok Choudhury · Shiv K. Sarin

Received: 8 May 2014 / Accepted: 3 February 2015 / Published online: 20 February 2015
© Indian Association of Surgical Oncology 2015

Abstract Inflammatory myofibroblastic tumor (IMT) is a rare lesion of undetermined pathogenesis characterized by proliferation of spindled myofibroblast cells in a collagenized inflammatory background. It is usually benign but may show local infiltration or, in rare cases, metastasis. IMT has been observed in almost all solid organs; however, involvement of liver is exceptional. Its symptoms and radiological findings can mimic malignancy and pose diagnostic difficulties. The authors report the case of a 43-year-old woman with non-cirrhotic portal hypertension and gall stone induced acute pancreatitis having a mass in the right lobe of the liver which was initially diagnosed as focal nodular hyperplasia on imaging but proved to be inflammatory myofibroblastic tumor on pathological and immunohistochemical examination. The lesion resolved with conservative management without the need for surgical intervention.

Keywords Inflammatory myofibroblastic tumor · Focal nodular hyperplasia · Non-cirrhotic portal hypertension · Biliary pancreatitis

Introduction

Inflammatory myofibroblastic tumor (IMT) is an abnormal proliferation of mesenchymal spindle cells admixed with variable inflammatory component [1, 2]. Its exact etiology remains obscure and multiple factors including infection, chemo-radiotherapy, vascular diseases, chronic inflammation and autoimmune disorders have been hypothesized in the pathogenesis [3]. Traditionally considered to be a benign lesion arising as a result of exaggerated response to tissue injury, it is now generally accepted that IMT represents a distinctive neoplastic entity which may demonstrate a locally aggressive behavior [1, 4]. Originally described in the lung, IMT has since been encountered in multiple other locations, most commonly the mesentery of the small intestine and omentum predominantly in children and young adults [2]. Although hepatic involvement was first described way back in 1953 by Pack and Baker [5], literature is sparse on the subject and limited to a few anecdotal case reports and retrospective reviews signifying its rarity [1–16]. Herein, we present a case of hepatic IMT in a patient with non-cirrhotic portal hypertension (NCPH) and biliary pancreatitis masquerading as focal nodular hyperplasia (FNH) which showed spontaneous regression on follow-up imaging.

Case Report

A 43-year-old woman presented to our out-patient department with complaints of intermittent upper abdominal pain, fever and generalized weakness for one and a half months. She had an episode of acute right upper quadrant pain radiating to back 2 months back for which she was evaluated at another institute. An ultrasound at that stage had revealed features of acute calculus cholecystitis with associated mild acute

V. Kasana · S. Rajesh (✉) · U. Chauhan
Department of Radiology, Institute of Liver and Biliary Sciences,
D-1, Vasant Kunj, Off Abdul Gaffar Khan Marg,
New Delhi 110070, India
e-mail: rajesh387@gmail.com

C. Bihari
Department of Pathology, Institute of Liver and Biliary Sciences,
New Delhi 110070, India

A. Choudhury · S. K. Sarin
Department of Hepatology, Institute of Liver and Biliary Sciences,
New Delhi 110070, India

pancreatitis. In addition there was imaging evidence of extrahepatic portal vein thrombosis with portal cavernoma formation and moderate splenomegaly. This acute episode had subsided within a week with conservative measures but a week later she started having intermittent spikes of moderate to high grade fever with chills and recurrence of upper abdominal pain with which she presented to us. Physical examination was essentially unremarkable. Laboratory investigations revealed a mildly elevated white blood cell count of 12,700/ μL (normal range- 4000–11,000/ μL) with segmental neutrophilia (83 %, normal range- 40–75 %), elevated erythrocyte sedimentation rate (ESR) of 120 mm/h (normal value- 0–20 mm/h), and hemoglobin level of 8.1 g/dl (normal range- 12–15 g/dl). The liver function tests were mildly deranged- total serum bilirubin- 1.7 mg/dl (normal range- 0.3–1.2 mg/dl) with direct bilirubin of 1.09 mg/dl, aspartate aminotransferase and alanine aminotransferase values of 57 IU/L each (normal range- of 5–40 IU/L and 7–35 IU/L respectively), serum alkaline phosphatase value of 135 IU/L (normal range- 32–92 IU/L) and serum albumin of 2.9 g/dl (normal range- 3.5–5.2 g/dl). Serology for hepatitis markers was negative. Magnetic resonance imaging (MRI) of abdomen showed attenuated main portal vein and its second order branches with portal cavernoma formation, multiple perisplenic and peripancreatic porto-systemic collaterals, moderate splenomegaly and normal liver outline consistent with extrahepatic portal venous obstruction (EHPVO) leading to NCPH (Fig. 1). Pancreas

and gall bladder were normal. However, a solitary well-defined lobulated T2-hyperintense lesion showing a central T2-*hypointense* stellate scar was noted in segment VII of right lobe of liver measuring about $6.3 \times 5.1 \times 6.0$ cm (Fig. 2) which was not seen on the previous ultrasound scan done outside. Possibility of FNH was suggested based on imaging features. However, since no evidence of cholecystitis or pancreatitis was seen on the MRI to explain the patient's symptoms of fever and abdominal pain and the fact that the lesion did not have a typical central stellate scar, biopsy of the lesion was performed which revealed dense myofibroblastic proliferation and neovascularization with collagenization and infiltration by mixed inflammatory cells including neutrophils, eosinophils and small lymphocyte cells showing smooth muscle actin positivity (Fig. 3). The findings were consistent with inflammatory myofibroblastic tumor. Her serum tumor markers were within normal range. The patient was managed with conservative measures and on 2-months follow-up there was near-complete resolution of the lesion (Fig. 2).

Discussion

IMT is an entity with uncertain etio-pathogenesis and biological behavior. A reflection of this is the various names by which it has been referred to in the literature including inflammatory pseudotumor, pseudosarcomatous myofibroblastic, or

Fig. 1 Axial FIESTA (a) and T2W fat saturated image at TR-1440 ms and TE-83.07 ms (b) and axial and coronal T2WI at TR-1449 ms and TE- 79.3 ms (c, d). Attenuated main portal vein (arrow in a) and its second order (right posterior division) branch (arrow in b) with portal cavernoma formation (horizontal arrow in c) associated with splenomegaly and multiple peripancreatic and perisplenic collaterals (vertical arrows in c and d). Note the smooth and regular outlines of liver without any features of volume redistribution to suggest cirrhosis

Fig. 2 Axial T1WI (a) at TR-4.4 ms and TE-2 ms and axial T2WI (b) at TR-1449 ms and TE-79.3 ms show a well defined round mass lesion (*arrowheads*) in segment VII of liver depicting diffuse hypointense signal on T1WI and heterogeneously hyperintense signal with central hypointense areas on T2W sequences. Follow-up MRI after two months. Axial T2W (c) and T2 fat sat (d) images shows marked reduction in size of the lesion (*arrows*)

fibromyxoid lesion, and plasma cell granuloma [4]. The common denominator in all these lesions is abnormal spindle cell proliferation intermingled with a variable inflammatory component [1]. It is controversial as to whether these are neoplastic or reactive pseudotumoral lesions. A review of recent literature indicates that these should best be considered benign

neoplasms with a potential for local invasion and in rare cases metastases [1, 4]. In up to 60 % of cases, IMTs are associated with a gene rearrangement involving the anaplastic lymphoma kinase (ALK) gene at chromosomal locus 2p23 [2].

IMT is most commonly described in the lung and abdomen of children and young adults, but it can also be found in the

Fig. 3 Histopathological findings a. Dense myofibroblastic proliferation with inflammatory cells infiltrate (HE, 100X) b. Inflammatory cells include eosinophils, lymphoplasmacytic cells on a compact myofibroblastic proliferated background with collagenization (HE, 200X) c. Collection of histiocytic cells with acute inflammatory cells (HE, 200X) d. Smooth muscle actin (SMA) positivity (100X)

central nervous system, salivary glands, larynx, bladder, breast, spleen, skin and liver [1, 2]. Although multicentricity has been described, hepatic IMTs are usually solitary and occur predominantly in the right lobe of the liver. Rarely, other hepatic locations such as the Spiegel lobe and hilar region have been reported [3].

Patients with hepatic IMT may be asymptomatic or may present with right upper quadrant pain, fever, jaundice, and, occasionally, obliterative phlebitis [1]. Laboratory findings include leukocytosis, anemia, thrombocytosis, polyclonal hypergammaglobulinemia, and elevated ESR and C-reactive protein [14]. Occasionally slight elevation of liver enzymes may also be noted.

Radiological features are non-specific and it can mimic hepatic abscesses, benign hepatic tumors (FNH, adenoma), malignant liver tumors (hepatocellular carcinoma, cholangiocarcinoma, lymphoma, metastases) and granulomatous lesions (tuberculosis and sarcoidosis) [2]. Computed tomographic scan usually reveals isodense to hypodense lesion relative to skeletal muscle with variable contrast enhancement and occasional calcification. Variety of enhancement patterns have been noted including early peripheral, with delayed central filling; heterogeneous; homogeneous; and no enhancement. Larger lesions may have central necrosis. MRI usually shows a T1-hypointense and T2-hyperintense lesion with a thick-fibrotic rind that may show delayed enhancement [7, 9].

Owing to the non-specific clinical presentation and radiographic and laboratory features, diagnosis by non-invasive means is often challenging. Percutaneous tumor biopsy can usually suggest the diagnosis in the appropriate clinical setting. Macroscopically, the lesion may be single or multiple with dimensions up to 25 cm. Histologically, it is characterized by the presence of proliferating fibrovascular stroma consisting of spindled myofibroblasts variably infiltrated by a heterogeneous population of acute and chronic inflammatory cells mainly consisting of plasma cells, lymphocytes and occasionally histiocytes [1–3].

Multiple factors have been implicated in its pathogenesis including infections, immunosuppression, radiotherapy, trauma, vascular and autoimmune disorders, chronic inflammation and malignancies [3]. Certain bacteria including *Escherichia coli*, *Staphylococcus aureus*, and Gram-positive cocci have been proposed as the causative agents of IMT of the liver. It has also been suggested that micro-organisms could seed the hepatic parenchyma through the portal vein, thus creating an inflammatory reaction with obliterating phlebitis and granuloma formation [1]. Intraparenchymal hemorrhage secondary to trauma or coagulopathy has also been propagated as a possible mechanism [1]. The high content of plasma cells in these lesions has led some authors to suggest an immunological origin of this disease [1]. The precise etiology, however, remains uncertain.

The association of cholelithiasis and pancreatitis and hepatic IMT has been described in only a handful of case reports

[15, 16]. It has been proposed that the presence of gall stones could facilitate entry of enteric bacteria into the portal circulation, which might then result in an inflammatory response and possibly an IMT.

Another point of interest in the current case was that the patient was suffering from NCPH due to EHPVO. FNH is commonly associated with NCPH [17]. The lesion seen in our case was hypointense on T1-weighted sequence with a central hypointense scar and hyperintense on T2-weighted sequences (Fig. 2). However, the central area was not hyperintense on T2-weighted sequences as is expected in cases of typical FNH. With these findings in background of NCPH a provisional diagnosis of FNH was made. But, since the clinical picture (fever and abdominal pain) and MRI findings were not typical of an FNH we went ahead with a biopsy of the lesion which revealed the lesion to be IMT.

Because partial hepatectomy in non-cirrhotic livers carries low morbidity and mortality, surgical resection is considered by many as the treatment of choice for IMT [1, 10]. However, few recent studies have emphasized that these patients can be managed medically and surgical resection should be reserved for cases where diagnosis is unclear or the patient is not responding to medical treatment with progression of disease or symptoms. [6, 7, 14]. Our case was also managed conservatively and a follow-up MRI after 2 months showed marked reduction in the size of the lesion with an area of capsule retraction.

In conclusion, definite diagnosis of IMT on imaging may be difficult; however, it should not prevent radiologists from considering IMT in the differential diagnosis of solitary liver lesions in patients presenting with clinical and laboratory features of active inflammation. The current case also illustrates that although clinical and molecular features may not predict biological behavior, indications for surgery must be carefully assessed in each case and a trial of conservative therapy is worthwhile as the tumor may regress spontaneously. Thus, early and accurate recognition of this entity with either clinico-radiological features or image guided biopsy can help individualize management of patients and avoid unnecessary radical surgery.

Conflict of Interest All authors state that there are no conflicts of interests.

References

1. Tang L, Lai EC, Cong WM, Li AJ, Fu SY, Pan ZY, Zhou WP, Lau WY, Wu MC (2010 Feb) Inflammatory myofibroblastic tumor of the liver: a cohort study. *World J Surg* 34(2):309–313
2. Solomon GJ, Kinkhabwala MM, Akhtar M (2006 Oct) Inflammatory myofibroblastic tumor of the liver. *Arch Pathol Lab Med* 130(10):1548–1551

3. Sürer E, Bozova S, Gökhan GA, Gürkan A, Elpek GO (2009 Jun) Inflammatory myofibroblastic tumor of the liver: a case report. *Turk J Gastroenterol* 20(2):129–134
4. Kovach SJ, Fischer AC, Katzman PJ, Salloum RM, Ettinghausen SE, Madeb R, Koniaris LG (2006 Oct 1) Inflammatory myofibroblastic tumors. *J Surg Oncol* 94(5):385–391
5. Pack GT, Baker HW (1953) Total right hepatic lobectomy; report of a case. *Ann Surg* 138:253–258
6. Yamaguchi J, Sakamoto Y, Sano T, et al (2007) Spontaneous regression of inflammatory pseudotumor of the liver: report of three cases. *Surg Today* 37:525–529
7. Goldsmith PJ, Loganathan A, Jacob M, Ahmad N, Toogood GJ, Lodge JPA, Prasad KR (2009) Inflammatory pseudotumours of the liver: a spectrum of presentation and management options. *Eur J Surg Oncol* 35(12):1295–1298
8. Lupovitch A, Chen R, Mishra S (1989) Inflammatory pseudotumour of the liver. Report of the fine needle aspiration cytologic findings in a case initially misdiagnosed as malignant *Acta Cytol* 33(2):259–262
9. Yu JS, Park C, Kim JH, Chung JJ, Kim KW (2007 Aug) Inflammatory myofibroblastic tumors in the liver: MRI of two immunohistochemically-verified cases. *J Magn Reson Imaging* 26(2):418–421
10. Chen HW, Lai EC, Huang XJ, Chen FN, Lu RL, Pan AZ, Lau WY (2008 Jan) Inflammatory myofibroblastic tumours of the spleen and liver. *Asian J Surg* 31(1):25–28
11. Firat O, Ozturk S, Akalin T, Coker A (2009 Jun) Inflammatory myofibroblastic tumour. *Can J Surg* 52(3):E60–E61
12. Kim SJ, Kim WS, Cheon JE, Shin SM, Youn BJ, Kim IO, Yeon KM (2009 Nov) Inflammatory myofibroblastic tumors of the abdomen as mimickers of malignancy: imaging features in nine children. *AJR Am J Roentgenol* 193(5):1419–1424
13. Yu JS, Park C, Kim JH, Chung JJ, Kim KW (2007 Aug) Inflammatory myofibroblastic tumors in the liver: MRI of two immunohistochemically-verified cases. *J Magn Reson Imaging* 26(2):418–421
14. Liu XF, He BM, Ou-Yang XH, Wang ZZ, Su JG (2012 Oct 28) Different imaging findings of inflammatory myofibroblastic tumor of the liver. *World J Gastroenterol* 18(40):5821–5825
15. Al-Jabri T, Sanjay P, Shaikh I, Woodward A (2010 Aug 18) Inflammatory myofibroblastic pseudotumour of the liver in association with gall stones - a rare case report and brief review. *Diagn Pathol* 5:53
16. Ueda J, Yoshida H, Taniiai N, Onda M, Hayashi H, Tajiri T (2009) Inflammatory pseudotumor in the liver associated with intrahepatic bile duct stones mimicking malignancy. *J Nippon Med Sch* 76(3): 154–159
17. Ibarrola C, Colina F (2003 Mar) Clinicopathological features of nine cases of non-cirrhotic portal hypertension: current definitions and criteria are inadequate. *Histopathology* 42(3):251–264