

Inflammatory Myofibroblastic Tumor of the Liver: A Cohort Study

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Abstract

Background Inflammatory myofibroblastic tumor (IMT) is a rare condition. The aim of the present study was to evaluate the clinical characteristics and surgical outcomes for IMT of the liver in our large cohort of patients.

Methods From January 2001 to December 2007, all patients with a pathological diagnosis of IMT of the liver who underwent partial hepatectomy were retrospectively analyzed.

Results During the study period, 64 patients underwent partial hepatectomy for IMT of the liver in our tertiary referral center. The commonest clinical presentation was abdominal pain (53%), followed by fever (41%); 15.6% of patients were asymptomatic. Preoperative diagnosis of IMT was suspected in only five patients (8%). The indications for surgery included suspicion of malignancy (60.9%), uncertain diagnosis (40.6%), symptomatic disease (26.6%), and spontaneous rupture (3.1%). The postoperative complication rate was low (17.2%). There was no hospital mortality. After a median follow-up of 30 months, no patient developed recurrence.

Conclusions Although there are various treatment options for IMT of the liver, surgical resection for good risk patients is preferred.

Introduction

Inflammatory myofibroblastic tumor (IMT) is a rare condition. There are a variety of synonyms for this tumor including plasma cell granuloma, postinflammatory tumor, xanthomatous pseudotumor, inflammatory pseudotumor, and inflammatory fibrosarcoma [1]. By definition, the tumor is composed of dominant spindle cell proliferation with a variable inflammatory component. These spindle cells are now known to be myofibroblasts, and this is the reason for the current designation for this disease. Inflammatory myofibroblastic tumor may affect individuals of any age, but it has a predilection for children and young adults. It is most commonly found in the lung, but is also reported in the central nervous system, salivary glands, larynx, breast, pancreas, spleen, lymph nodes, skin, and liver [2, 3]. As the synonyms suggest, there has been some confusion as to whether IMT is truly neoplastic or whether it represents a reactive proliferation of myofibroblastic cells. It is now generally accepted that IMT is a true neoplasm. These lesions have a benign behavior, but the possibility of malignant transformation exists [4, 5]. The present study was designed to evaluate the clinical characteristics and surgical outcome based on the largest series of IMT of the liver in the medical literature.

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Materials and methods

From January 2001 to December 2007, all patients with a pathological diagnosis of IMT of the liver who underwent

partial hepatectomy at the Eastern Hepatobiliary Surgery Hospital (Shanghai, China) were retrospectively analyzed. The prospectively maintained database and medical records were reviewed for demographics, characteristics of the tumor, indications for operation, operative variables, length of hospital stay, postoperative complications, and progress.

Preoperative evaluation

All patients had a chest X-ray, ultrasonography (USG) of the abdomen, and either contrast computed tomography (CT) of the abdomen or magnetic resonance imaging (MRI). Laboratory blood tests for hepatitis B surface antigen, antibodies to hepatitis C, serum alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9), serum albumin, serum total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and prothrombin time were obtained. All resected specimens were verified by histopathological examination after the operation.

Surgery

Surgery was performed through a bilateral subcostal incision. During the operation, we carefully searched the abdominal cavity for extent of local disease, extrahepatic metastases, and peritoneal seeding. After mobilization of the liver, intraoperative ultrasound was performed to assess the number and the size of the lesions as well as to assess the relation of the tumor to important vascular structures. The Pringle maneuver was selectively applied to occlude the blood inflow to the liver. Liver resection was carried out by a clamp-crushing method.

Postoperative management

During the early postoperative period all patients received the same postoperative care by the same team of surgeons in the intensive care unit. Need for extending the stay in the intensive care unit was determined by the patient's condition. Liver function test and clotting profile were monitored.

Follow-up

All patients had postoperative follow-up by the same team of surgeons. The follow-up program was similar for all patients and included abdominal USG and a liver function test every year and then at gradually increasing intervals.

Results

During the study period, 64 patients (42 men and 22 women) underwent partial hepatectomy for IMT of the

liver in our center. The patient characteristics are shown in Table 1. The commonest clinical presentation was abdominal pain (53%), followed by fever (41%); 15.6% of patients were asymptomatic. Contrast computed tomography (CT) scan was carried out on 44 patients and magnetic resonance imaging (MRI) with gadolinium-enhanced images was carried out on 28 patients. The radiographic appearance varied, and in the majority of patients it was difficult to make a specific diagnosis based on the findings of the imaging studies. The radiological features are shown in Table 2. Before operation, only five patients (8%) were suspected of having IMT of the liver in the differential diagnoses, whereas 39 patients (60.9%) were diagnosed to have malignant liver tumors. The clinical features of those five patients are shown in Table 3.

The indications for surgery and the surgical details are shown in Table 4. Some patients had more than one indication for surgery. The postoperative complication rate was 17.2%. No patient developed liver failure or postoperative ascites/encephalopathy. There was no hospital mortality. Based on the pathological findings and clinical behavior, all tumors were benign. The tumor and pathological

Table 1 Characteristics of patients with inflammatory myofibroblastic tumor (IMT) of the liver

Age, years (mean \pm SD)	49.1 \pm 12.5
Male:female, <i>n</i>	42:22
Hepatitis status, <i>n</i>	
Hepatitis B carrier	25
Hepatitis C carrier	1
Liver cirrhosis	6
Presentation, <i>n</i> ^a	
Abdominal pain	34
Fever	26
Malaise	13
Incidental finding	10
Epigastric belching	6
Jaundice	4
Weight loss	2
Abdominal mass	1
Past history of gastrointestinal infection, <i>n</i>	
Appendicitis	2
Diverticulitis	0
Ileitis	0
Past history of liver trauma, <i>n</i>	0
History of autoimmune disease, <i>n</i>	
Rheumatoid arthritis	1
Primary sclerosing cholangitis	0
Crohn's disease	0
Ulcerative colitis	0

^a Some patients had more than one presentation

Table 2 Radiological features

Patients with contrast CT scan, <i>n</i>	44
Peripheral enhancement	16
Heterogeneous enhancement	21
Homogeneous enhancement	3
No enhancement	4
Patients with MRI, <i>n</i>	31
T1-weighted image	31
Hypointense	24
Isodense	5
Hyperdense	2
T2-weighted image	31
Hypointense	0
Isodense	3
Hyperdense	28
Gadolinium-enhanced images	28
Peripheral enhancement	8
Heterogeneous enhancement	14
Homogeneous enhancement	2
No enhancement	4

Table 4 Indications for surgery and surgical outcome

Indications for surgery, <i>n</i> ^a	
Suspicion of malignancy	39
Uncertain diagnosis	26
Symptomatic	17
Spontaneous rupture	2
Minor hepatectomy, <i>n</i>	62
Major hepatectomy (≥ 3 Couinaud segments), <i>n</i>	2
Operative time, min (mean \pm SD)	127.8 \pm 43.3
Postoperative complications, <i>n</i>	
Intra-abdominal collection	5
Pleural effusion	3
Hemorrhage	1
Bile leak	1
Wound infection	1
Liver failure	0
Intra-abdominal abscess	0
Hospital mortality, <i>n</i>	0
Postoperative hospital stay, days (mean \pm SD)	10.4 \pm 5.9

^a Some patients had more than one indication for surgery

features are shown in Table 5. After a median follow-up of 30 months (range: 5–96 months), no patient was found to have recurrence.

Discussion

Inflammatory myofibroblastic tumor of the liver is rare. To the best of our knowledge, the present cohort study represents a major proportion of the cases reported in the medical literature. Therefore, our study is important for a better understanding of this unusual tumor.

The etiology and pathogenesis of IMT remain unknown, although the tumors were initially thought to represent a reactive inflammatory process. Factors that have been hypothesized in the pathogenesis include infection, vascular diseases, and autoimmune disorders [6–8]. Some authors have even hypothesized that micro-organisms from

certain conditions such as appendicitis, could seed the hepatic parenchyma through the portal vein, thus creating an inflammatory reaction with obliterating phlebitis and granulomata formation [7]. In our series, two patients (3.1%) had a past history of gastrointestinal infective disease. Some patients in other series have been reported to have Epstein-Barr virus (EBV)-positive inflammatory follicular dendritic cell tumors [8]. However, any association between IMT and infectious organisms is doubtful because in most reported series, including ours, no acid-fast organisms, fungi, parasites, or bacteria could be identified, and EBV has not been detected with in situ hybridization in the tumors in most reported cases. Some authors believe that the etiology of the IMT lesions is vascular, a result of intraparenchymatous hemorrhage secondary to trauma or coagulopathy [8]. The high content of plasma cells in these lesions has led some authors to hypothesize an immunological origin of this disease [9]. In

Table 3 Clinical features of the five patients with preoperative suspicion of IMT in the differential diagnoses

Patients	Sex/age	Presentation	AFP/CEA/CA19-9	Indication for surgery	Tumor location	Tumor size, cm	Type of hepatectomy
1	M/74	Fever	Normal	Symptomatic	Right liver	1.8	Segment V resection
2	F/45	Fever	Normal	Symptomatic	Right liver	1.0	Segment VII resection
3	M/59	Fever and abdominal pain	Normal	Symptomatic	Both lobes	1.5 (IV), 1.0 (VIII)	Segment IV, VIII resection
4	F/53	Abdominal pain	Normal	Symptomatic	Right liver	2.5	Segment V resection
5	M/45	Abdominal pain	Normal	Symptomatic	Right liver	3.3	Segment VI resection

AFP alphafetoprotein, CEA carcinoembryonic antigen, CA 19-9 carbohydrate antigen 19-9

Table 5 Tumor characteristics and pathological features

Tumor size, cm (mean \pm SD)	3.5 \pm 2.4
Tumor location, <i>n</i>	
Right liver	37
Left liver	20
Both right and left liver	6
Caudate lobe	1
Solitary tumor, <i>n</i>	50
Multiple tumors, <i>n</i>	14
Adjacent organ invasion, <i>n</i>	
Greater omentum	5
Diaphragm	3
Peritoneum	2
Transverse colon	1
Metastases, <i>n</i>	0
Macroscopic appearance, <i>n</i>	
White or tan, with a whorled fleshy	59
Variegated appearance with areas of necrosis and hemorrhage.	16
Predominant microscopic appearance, <i>n</i>	
Myxoid, vascular, and inflammatory areas resembling “nodular fasciitis”	34
Compact spindle cells with intermingled inflammatory cells resembling “fibrous histiocytoma”	26
Dense plate-like collagen resembling “a desmoid or scar”	4
Immunohistochemical positivity, <i>n</i>	
Vimentin +	64
Smooth muscle actin +	57
Muscle-specific actin +	53
Desmin +	41
CD68 +	38
Pankeratin +	37
pCEA +	35

pCEA polymorphic carcinoembryonic antigen

our series, one patient (1.6%) had a medical history of autoimmune disease. Based on the findings of our study, there was no single etiological factor that could be identified in all the patients.

The diagnosis of IMT without an operation is difficult, despite the use of modern imaging and laboratory techniques. The lesions are often confused with other tumors, such as primary or secondary neoplasms, because their clinical presentation and morphological appearance are nonspecific. There have been limited radiological descriptions of the appearances of hepatic IMT. In most cases, CT scans and MRI are usually performed to narrow the differential diagnosis and to rule out malignancy [10, 11]. Even fine needle aspiration cytology or core biopsy often just shows a large number of inflammatory cells [3, 12, 13],

thus a definitive diagnosis cannot be reached. As a consequence, most IMT are diagnosed after surgical resection.

On gross examination, IMT tends to be circumscribed or multinodular, firm, white or tan, with a whorled fleshy, fibrotic or myxoid cut surface. The surface, in a minority of cases, has a variegated appearance with areas of necrosis and hemorrhage. Microscopically, three basic histological patterns are recognized: (1) myxoid, vascular, and inflammatory areas resembling nodular fasciitis; (2) compact spindle cells with intermingled inflammatory cells (lymphocytes, plasma cells, eosinophils) resembling fibrous histiocytoma; and (3) dense plate-like collagen resembling a desmoid or scar [2]. There is little pleomorphism or mitotic activity. Immunohistochemistry is a valuable adjunct to light microscopic diagnosis. Vimentin is almost invariably positive in the spindle cells. Smooth muscle actin and muscle-specific actin are present in the majority of cases. Desmin, CD68, pankeratin, and polyclonal carcinoembryonic antigen (pCEA) are positive in some cases, whereas S100, CD21, and myoglobin are uniformly negative.

There are various treatment options for IMT of the liver [3, 12–15]. Surgery, high-dose steroids, irradiation, and chemotherapy have all been suggested. Spontaneous regression has also been reported in IMT [14]. Although some authors suggest observation or conservative therapy with steroids or nonsteroidal anti-inflammatory drugs, if a definitive diagnosis of IMT of the liver can be made, surgical resection is the preferred treatment. The value of resection has been demonstrated in patients in whom a definitive histological diagnosis could not be made preoperatively or intraoperatively by frozen section. The natural course of IMT without resection is unclear. A small proportion of patients with local recurrence or metastases after partial hepatectomy have been recorded [4, 5]. In fact, most patients reported in the medical literature recovered uneventfully after partial hepatectomy. Because the morbidity and mortality of partial hepatectomy in noncirrhotic livers is low, surgical resection with clear margins should be considered as the treatment of choice for IMT in patients with good surgical risk. In our series, partial hepatectomy offered excellent results with low morbidity and zero mortality.

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