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CASE REPORT

Inflammatory Myofibroblastic Tumor of the Mid Common Bile Duct Masquerading as Cholangiocarcinoma

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Introduction

Inflammatory myofibroblastic tumors (IMTs) of the biliary ducts represent an uncommon cause of obstructive jaundice. It mimics cholangiocarcinoma both clinically and radiologically. Only nine reports of the biliary IMT have been reported in the literature [1]. Here, we report a case of biliary IMT presenting with recurrent episodes of obstructive jaundice.

Case Report

A 24-year-old female presented with yellowish eyes and urine for 1 month. She also complained of fever with chills and rigor and abdominal pain. She had associated loss of appetite and significant weight loss. There was no history of abdominal swelling, pedal edema, hematemesis, or encephalopathy. She had past history of recurrent episodes of obstructive jaundice for last 9 years.

Her examination revealed scleral icterus, pruritus and a palpable, firm, non-tender gall bladder. There was no evidence of any other oraganomegaly or lymphadenopathy. Her investigations at the admission revealed mild leukocytosis, total bilirubin 5.8 mg/dL (0.1–1.3), direct bilirubin 2.9 mg/dL (0–0.4) and alkaline phosphatase 204 U/L (35–150), ALT 86 U/L (5–40) and AST 71 U/L (5–40). Viral serology for hepatitis A, B, and C and HIV were negative. Ultrasonography (USG) and computed tomography (CT) abdomen revealed a mass in the hepatic hilum extending up to the mid common bile duct (CBD) and bilateral intrahepatic biliary radicle dilatation (IHBRD) with no ascites or lymphadenopathy. Magnetic resonance cholangiopancreatography (MRCP) and endoscopic retrograde cholangiopancreatography (ERCP) also revealed well defined, asymmetrical, circumferential obstructing mass in the hilum-mid CBD with uninvolved intrapancreatic part of CBD. Patient was suspected as a case of type IV cholangiocarcinoma. Palliative stenting was done to accomplish free flow of bile. Patient underwent exploratory laparotomy and a large mass measuring 10 × 6 cm, arising from bilateral hepatic ducts and extending up to mid CBD was seen adhering to the duodenum and colon. Debulking of the tumor was done and biliary-enteric continuity was restored with Roux-en-Y hepaticojejunostomy. The distal end of CBD was free from tumor. Enlarged regional lymph nodes were excised as well.

Grossly the lesion was grayish-white, firm, and nodular. Attached gall bladder with cystic duct was unremarkable with cystic duct entering the mass. The proximal resection margin was involved by the tumor.

Histopathology revealed a tumor disposed in short fascicular and vague storiform pattern with variable collagenous stroma. The bland tumor cells were plump, spindle with oval to elongated nuclei, minimal nuclear pleomorphism, inconspicuous nucleoli and pale eosinophilic cytoplasm. The spindle cells were intimately mixed with dense inflammatory infiltrate comprising predominantly of mature plasma cells. At places, non-neoplastic glands lined by biliary type columnar epithelium were seen entrapped within the tumor (Fig. 1). On immunohistochemistry, the tumor cells were immunoreactive for vimentin, smooth muscle actin (SMA), and negative for cytokeratin (CK), CD34, CD117, DOG1, and ALK1 (Fig. 2). A final diagnosis of IMT was made. The enlarged lymph nodes revealed reactive lymphoid hyperplasia. The postoperative course was uneventful and the patient was discharged on Etoricoxib.

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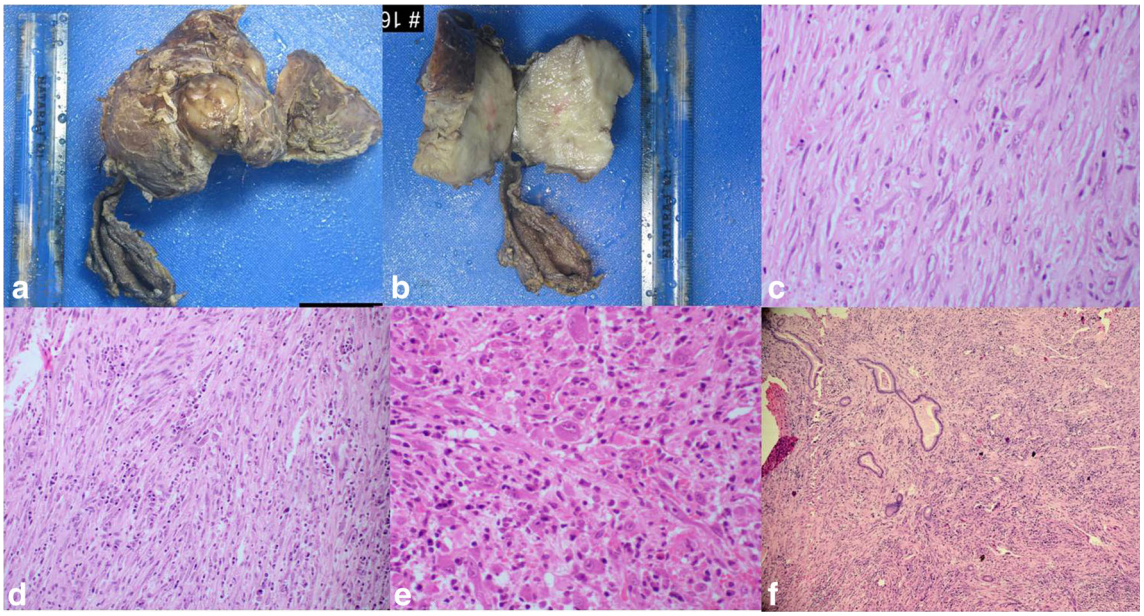

Fig. 1 Gross and cut surface of grayish-white tumor measuring 10 × 5 cm in mid CBD with attached unremarkable gall bladder (**a**, **b**). Inflammatory myofibroblastic tumor of CBD composed of spindle shaped cells arranged in fascicles in a background of chronic inflammatory cells in collagenous stroma (**c**, **d**, **e**). Entrapped benign glands within the tumor (**f**)

Discussion

IMT is rare, intermediate grade rarely metastasizing malignant lesion of mesenchymal origin, which can occur anywhere in the body. It most commonly involves lung, mesentery, and omentum followed by soft tissue, mediastinum, gastrointestinal tract, pancreas, genitourinary tract, oral cavity, skin, breast, nerve, bone, and central nervous system [2]. Common bile duct is rarely involved by IMT [2].

The clinical presentation of IMT of CBD including episodes of recurrent painless jaundice, unintentional weight loss are non-specific and are indistinguishable from cholangiocarcinoma. Despite the advances in imaging techniques, it is difficult to differentiate between the two preoperatively [3]. CT findings of a biliary stricture/intraluminal growth favors more common diagnosis of cholangiocracinoma at that site. IMT can involve any part of the CBD (Table 1).

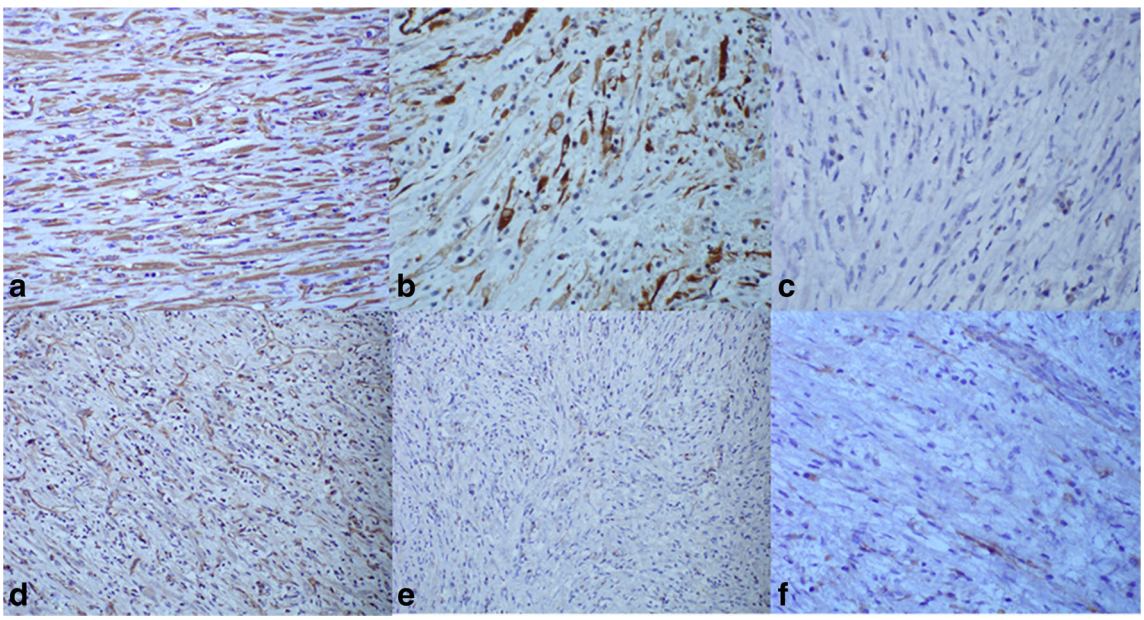

Fig. 2 Tumor cells are positive for vimentin (**a**), SMA (**b**) and negative for ALK1(**c**), CD34 (**d**), desmin (**e**), and DOG1 (**f**)

Table 1 Inflammatory myofibroblastic tumors of reported cases in CBD

	Age/sex	Site	Treatment	Follow-up	Outcome
Haith EE et al. 1964	6/M	Distal CBD	PD & celecoxib	5 months	NR
Stamatakis JD et al. 1979	13/F	Prox. CBD, CD, CHD	EH BD excision	21 months	NR
Ikeda et al. 1990	43/M	IHD, CHD, ProxCBD	Surgery	7 months	Lung mets
Fukushima N et al. 1997	58/F	Mid-lower CBD	PD	–	NR
Walsh et al. 1998	50/M	Proximal CBD	PD	19 years	Metastasis
Fernandez EMLT et al. 2006	55/F	Distal CBD	PD	4 years	R
Martin MA et al. 2006	51/F	Distal CBD	PD	–	–
Sobesky R et al. 2012	51/F	Distal CBD	PD	2 years	NR
Abu-Wasel B et al. 2012	55/M	Distal CBD	EH BD excision	14 months	NR
Vasiliadis K et al. 2013	70/F	Mid-distal CBD	EH BD excision	8 months	NR
D'Cunha A et al. 2016	12/F	Distal CBD	Debulking, corticosteroid	NR	
Present case	24/F	Mid CBD	EH BD excision Etoricoxib	12months	NR

CBD common bile duct, *M* male, *F* female, *PD* pancreatoduodencectomy, *NR* no recurrence, *CD* cystic duct, *CHD* common hepatic duct, *EH BD* extra hepatic bile duct

The etiopathogenesis and biologic behavior of these tumors have not been described in the literature. Numerous theories have been proposed including antecedent infections (bacterial, parasitic, or viral). Another proposed etiology of IMT of biliary tree in adults is attributed to autoimmune or sclerosing lymphoplasmacytic pancreatitis [2]. However, pancreas in our case was normal.

On histomorphology, three types of growth pattern are seen in IMT, (1) cellular compact spindle cell pattern, (2) hypocellular densely collagenous with few spindle cells and inflammatory cells pattern, and (3) loose myxoid stroma with prominent vascular pattern reminiscent of granulation tissue [2]. Necrosis and mitotic figures are occasionally seen. Atypical mitosis is virtually absent [4].

Differential diagnosis of IMT includes spindle cell tumors that can occur in the gastrointestinal tract (Table 2). All these tumors are rare in CBD and usually presents with jaundice and pruritus. Gastrointestinal stromal tumor (GIST) usually involves ampullary/periampullary region and presents with obstructive jaundice, abdominal pain, and melena. They are usually submucosal in location. Leiomyosarcoma of CBD presents with episodes of acute cholangitis. Inflammatory fibroid polyps are usually seen in gastrointestinal tract and such tumors usually presents with intussusception or obstructive features. Schwannoma of bile duct has been described in few case reports presenting with overlapping clinical features of IMT. Immunohistochemistry plays a crucial role in establishing the diagnosis. The tumor cells are characteristically positive for vimentin and SMA. Negativity of tumor cells for CD117 and DOG1 rules out the closest histopathological differential diagnosis of GIST. ALK1 positivity is seen in ~ 50% cases of IMT [2]; however, it was negative in our case. Another important differential diagnosis considered in our case was IgG4 related sclerosing inflammatory lesion as it has been shown in the literature that most of the reported cases of IMT of distal CBD shows strong association with

Table 2 Immunohistochemical panel for differential diagnosis of inflammatory myofibroblastic tumors

Lesion	CD 117	CD34	SMA	Desmin	S100
IMT	–	–	+	+	+/–
GIST	+	+/–	+/–	–	+/–
Inflammatory fibroid polyp	–	+/–	+/–	–	–
Solitary fibrous tumor	–	+	–	–	–
Schwannoma	–	–	–	–	+
Leiomyoma	–	–	+	+	–
Leiomyosarcoma	–	–	+	+/–	–
Fibromatosis	–	–	+	+	–
Synovial sarcoma	–	–	–	–	+/–

sclerosing lymphoplasmacytic pancreatitis or autoimmune pancreatitis. However, serum IgG4 level was normal and on IHC plasma cells were polyclonal in our case.

Cytogenetic or molecular genetic studies have revealed rearrangement of ALK1 gene in chromosome 2p23 leading to constitutional activation of tyrosine kinase [2]. Surgical excision is currently considered the treatment of choice for IMT, although anti-inflammatory drugs and chemoradiotherapy have been used in some cases [2]. Halozaki et al. reported the successful use of anti-inflammatory medications in the treatment of hepatic IMT [5]. Etoricoxib is a non-steroidal anti-inflammatory drug (NSAID) with selective COX2 inhibitor activity. The mode of action remains unknown. However, it has been postulated that it has inhibitory effect on angiogenesis and cell proliferation on angiogenesis and cell proliferation by induction of fibroblast apoptosis [6]. The presence of ganglion-like cells, p53 expression and aneuploidy connotes aggressiveness of the tumor [2]. Local recurrence have been reported in 10–25% and metastasis in < 5% patients [2]. Therefore, a strict follow-up is mandatory to look for local recurrence and to avoid complications specifically at these locations as cholangitis, pancreatitis and liver damage. Steroidal and NSAID medications have been proposed to be therapeutic alternative in cases of incomplete resection, local recurrence or distant metastasis and can also be used as first line therapy for unresectable tumors [7]. As shown by DiFiore et al. [8] and Meis et al. [9], it is believed that IMT occurring in abdomen or retroperitoneum have a propensity for more aggressive behavior with multiple recurrences, invasion into adjacent structures and metastasis. However, this has been contradicted by other studies, which showed that aggressive behavior, rapid infiltration, and multiple recurrences of IMT are not limited to abdominal location [10, 11]. Thus, there is need for long-term follow-up as IMT has an unpredictable course. IMT with ALK1 immunoreactivity has a more favorable prognosis with lower chances for relapse and are potential candidates for anti-ALK treatment with crizotinib [12].

Conclusion

IMT may mimic cholangiocarcinoma on clinical presentation and radiological investigations. The pointers of IMT in our case were young age and prolonged duration of illness. Intraoperative frozen section may be considered to avoid unnecessary major surgical resections. On histopathology, establishing the diagnosis is important by judicious use of immunohistochemistry as GIST can be effectively treated by targeted therapy.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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