Rare disease

Benign inflammatory pseudotumour mimicking extrahepatic bile duct cholangiocarcinoma in an adult man presenting with painless obstructive jaundice

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Summary

Inflammatory pseudotumours (IPTs) of the biliary tract are extremely rare and heterogeneous by aetiology and clinical presentation. They might cause biliary obstruction and mimic cholangiocarcinomas and their final diagnosis is usually achieved only after surgical excision. The most characteristic feature of IPT is the presence of chronic inflammatory cell infiltrates with variable degree of proliferating fibrous tissue. IPTs have the potential for recurrence even after resection and if untreated they can grow causing a variety of symptoms due to compression of the surrounding structures and organs. Despite the significant improvement of modern imaging techniques, preoperative distinction between IPTs of the biliary system and malignancies is extremely difficult. Histological diagnosis poses a clinical challenge because sampling is often suboptimal. Although rare, IPTs should be in the differential diagnosis of patients who present with painless jaundice and no other clinical symptoms or signs characteristics of cholangiocarcinomas.

BACKGROUND

Inflammatory pseudotumour (IPT) of the biliary tract is a very rare benign disease that mimics cholangiocarcinoma. We describe the clinical presentation, investigations, treatment and surgical pathology findings of a 55-year-old Caucasian man, who presented with painless jaundice due to the development of an extrahepatic bile duct stricture caused by a pseudotumour. The patient underwent surgical resection and his final diagnosis consisted in a biliary stricture caused by an IPT with prominent fibrous component that caused an extrinsic compression on the extrahepatic bile duct. On histopathological exam, it presented as a conglomerate of inflammatory cells, enlarged lymph nodes, neuronal hyperplasia and proliferating fibrous tissue around the spared bile duct. Cases of intrahepatic bile duct compression by IPTs have been described in the past, but to the best of our knowledge, there is lack of reports on extrahepatic bile duct IPTs. In addition, the presence of enlarged lymph nodes and neuronal hyperplasia characteristics of this patient's IPT, make this case very unique as no other similar cases have been previously published in the scientific literature.

CASE PRESENTATION

A 55-year-old Caucasian man was admitted at a tertiary university centre with painless jaundice. His medical history was unremarkable. His physical examination revealed a mildly obese patient without any distress and no other abnormalities except for his sclero-icterus. He denied any weight loss or other constitutional symptoms and he did not take any conventional or alternative medications. His liver, spleen and superficial lymph nodes were not enlarged and there was no sign of any palpable mass.

INVESTIGATIONS

Serum tumour markers CEA and CA-19.9 were in the normal limits as well as his tests for viral A, B and C hepatitis. Blood and urine cultures were negative for infections and his haematological and biochemistry profiles were unremarkable except for the total serum bilirubin level that was 357 $\mu\text{mol/l}$ (normal range 0–20 $\mu\text{mol/l}$) and alkaline phosphatases that was 672 IU/l (normal range 30–140 IU/l) at the time of presentation.

A trans-abdominal ultrasound (US) revealed dilatation of the intrahepatic and extrahepatic bile ducts with tapering of the mid-common hepatic duct. The gallbladder as well as the common bile system did not contain any visible stones. Subsequently, an endoscopic retrograde cholangiography (ERC) (figure 1) was requested to palliate his pruritus, and a temporary stent was deployed across the stricture after brushing of the stricture was performed to obtain a cytological specimen. The ERC revealed the presence of a stricture measuring approximately 3 cm in the mid-common bile duct. There were no other abnormalities of the intrahepatic biliary system. Cytology specimen was negative for malignant cells. Endoscopic US revealed a mass in the area of the porta hepatis and triphasic contrast multidetector CT of the abdomen and pelvis (figure 2) revealed the presence of a hypoattenuated mass located in the hepato-duodenal ligament adjacent to the strictured extrahepatic bile duct. There was no evidence of metastatic disease and magnetic resonance cholangiopancreatography (figure 3) confirmed the presence of a single stricture in the mid-common bile duct with no involvement of the intrahepatic biliary system or intrapancreatic tract. Both the portal vein and hepatic arterial systems were not involved by the suspected malignant stricture and therefore the patient was considered for

Figure 1 Endoscopic retrograde cholangiopancreatography image showing the presence of a stricture in the mid-common bile duct (white arrow).

surgical resection of a suspected cholangiocarcinoma involving the extrahepatic bile duct.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis of common bile duct strictures includes:

1. Benign causes:
  - ▶ Choledocholithiasis
  - ▶ Iatrogenic (surgical injury)
  - ▶ Primary sclerosing cholangitis
  - ▶ Pancreatitis
2. Malignant causes:
  - ▶ Pancreatic cancer
  - ▶ Cholangiocarcinoma

Figure 2 CT of the abdomen and pelvis showing a low-density area adjacent to the strictured extrahepatic bile duct (white arrow).

Figure 3 Magnetic resonance cholangiopancreatography showing the presence of stricture in the mid-common bile duct with no involvement of the intrahepatic biliary system (white arrow).

TREATMENT

Intraoperative frozen sections of the resection margins of the biliary system were negative for malignant involvement and the patient underwent an extended right hepatic resection with en-bloc excision of the gallbladder and extrahepatic bile duct with a Roux-en-Y biliary-enteric anastomosis to left intrahepatic bile duct.

The permanent pathological examination of the surgical specimen revealed an IPT with prominent fibrous component adjacent but not infiltrating the common bile duct. Macroscopically, the cut surface of the specimen in the common bile duct region demonstrated a mottled appearance. Histologically, the focus of fibrosis was centred on the hepatic artery and adjacent lymph nodes. One node had focal sclerosis with hyaline vascular structures and focal neutrophilic collections. Other nodes were enlarged and congested but without sclerosis. The adipose tissue in this area was largely replaced by hyalinised and cellular inflammation rich in plasma cells and small lymphocytes. No atypical lymphoid cells were seen. There was a prominent neuronal hyperplasia in the fibrotic region. The adjacent bile ducts were spared from the fibrotic reaction. There was no duct fibrosis to suggest primary sclerosing cholangitis and no dysplasia or malignancy related to the ducts. The liver tissue was normal apart from effects of partial duct obstruction.

OUTCOME AND FOLLOW-UP

The patient had an uneventful postoperative course and recovered well after surgery with normalisation of his serum bilirubin on the eighth postoperative day. At 14 months from his surgery, the patient is doing well and there are no radiological findings of recurrent disease.

DISCUSSION

IPT are extremely rare benign lesions of unknown aetiology. They have been described in many organs and the most common location is the respiratory system.^{1 2} Hepatic IPTs were first reported by Pack and Baker³ in

1953. They account for 0.4% of all focal liver lesions treated by hepatectomy and approximately 82 cases are reported to date in the literature.¹ IPTs of the biliary tree are less frequent and, to the best of our knowledge, only 12 cases have been reported (table 1).

The clinical presentation of biliary IPTs is non-specific and obstructive jaundice represents the most common clinical finding. Other symptoms may include abdominal pain, nausea, vomiting and fever. In all previously reported IPT cases, surgical resection was the treatment of choice. This can be attributed to the radiological findings that are suspicious for cholangiocarcinoma in addition to inconclusive cytology and in some cases even on histological inspection.

The histopathological characteristics of IPTs include a non-specific inflammatory infiltrate mainly consisting of lymphocytes and eosinophils, and collagen tissue composed of fibroblasts and myofibroblasts.⁴ Someren⁵ classified IPTs into three histological groups: (a) xanthogranuloma-type, (b) plasma cell granuloma type and (c) sclerosing type. The current case is very unusual in terms of location, and histopathology as extrahepatic duct involvement by IPT is extremely uncommon in both adult and paediatric populations.³ Furthermore, lymphadenopathy was identified on histopathological

examination of the present case. This might represent primary lymphadenitis with reactive chronic inflammatory reaction or reactive lymphadenitis secondary to a primary inflammatory process.

The aetiology and pathogenesis of IPTs remain unknown.² Infectious agents are often suspected, yet not always proven. The most common causative microorganisms are *Bacteroides caccae*, actinomyces, klebsiella, *Escherichia coli*, Gram-positive cocci and B-haemolytic streptococcus.⁴ The association between Epstein-Barr virus and IPT of the spleen and the liver has been well established.⁶ Some authors believe that autoimmunogenic processes represent the underlying aetiology of IPT.⁷⁻⁸ Furthermore, IgG4-related IPTs of the liver,⁹⁻¹¹ which are characterised by dense infiltration of IgG4-positive plasma cells and lymphocytes intermixed with fibrosis and obliterative phlebitis, have been recently reported in patients with or without autoimmune pancreatitis.

In summary, the diagnosis of biliary tree IPTs is challenging as both its clinical presentation and radiological features are similar to biliary tract malignant neoplasms. The final diagnosis of the tumour relies mainly on the pathological examination of the surgical specimen. Surgical resection of hepatic and biliary tract IPTs represents the treatment of choice, ensuring a satisfactory prognosis.

Table 1 Characteristics of patients with inflammatory pseudotumours of the biliary system

Authors	Year of publication	Age at presentation and symptoms	Location	Therapy	Follow-up
Haith <i>et al</i> ¹²	1964	6-year-old, boy, vomiting, diarrhoea, fever and obstructive jaundice	Distal common bile duct	Surgical resection	5 months, no recurrence
Stamatakis <i>et al</i> ¹³	1979	13-year-old girl, abdominal pain and obstructive jaundice	Proximal common bile duct, cystic duct, common hepatic duct	Surgical resection	21 months, no recurrence
Ikeda <i>et al</i> ¹⁴	1990	43-year-old man, fever, weight loss and obstructive jaundice	Intrahepatic ducts, common hepatic duct, common bile duct	Surgical resection	7 months, no recurrence
Pokorny <i>et al</i> ¹⁵	1991	43-year-old man, nausea, epigastric pain and obstructive jaundice	Right intrahepatic duct, anterior right hepatic lobe, porta hepatis, proximal common bile duct	Surgical resection	5 year, no recurrence
Ozeki <i>et al</i> ¹⁶	1993	73-year-old man, obstructive jaundice	Bile duct bifurcation	Surgical resection with an extended right hepatic and caudate lobe resection	n.a.
Fukushima <i>et al</i> ¹⁷	1997	58-year-old woman, obstructive jaundice	Mid and distal common bile duct	Surgical resection with duodenopancreatectomy	n.a.
Walsh <i>et al</i> ¹⁸	1998	50-year-old man, obstructive jaundice	Proximal common bile duct	Surgical resection	19 years, recurrent disease submandibular gland, pancreatic tail, kidney
Walsh <i>et al</i> ¹⁸	1998	69-year-old woman, obstructive jaundice	Bile duct bifurcation	Chemotherapy followed by surgical resection	21 years, recurrent disease left intrahepatic bile duct. Treated with resection and multiple endoscopic stents
Saint-paul <i>et al</i> ¹⁹	1999	53-year-old man, jaundice and weight loss	Intrahepatic bile duct	Surgical resection: partial hepatectomy	n.a.
Sobesky <i>et al</i> ²⁰	2003	51-year-old woman	Distal common bile duct	Surgical resection: duodenopancreatectomy	No recurrence
Ashcroft <i>et al</i> ¹	2009	50-year-old woman, epigastric pain, obstructive jaundice and significant weight loss	Common hepatic duct	Stent placement followed by surgical resection	8 years, no recurrence
Ashcroft <i>et al</i> ¹	2009	61-year-old man, right upper quadrant abdominal pain and obstructive jaundice	Common hepatic duct and cystic duct	Stent placement followed by surgical resection	6.5 years, no recurrent disease
Current case	2012	55-year-old man, obstructive jaundice	Common bile duct, common hepatic duct	Stent placement, right portal vein embolisation, right extended hepatic and extrahepatic bile duct resection	16 months, no recurrent disease

n.a., not applicable.

Learning points

- ▶ Inflammatory pseudo tumours of the biliary system are very rare.
- ▶ Their clinical presentation and radiological characteristics mimic cholangiocarcinomas.
- ▶ Surgical resection is recommended as preoperative diagnosis is very challenging, and often both histology and cytology specimens are insufficient for proper diagnosis.

Competing interests None.

Patient consent Obtained.

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