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Case report

Primary carcinoid tumour of the common bile duct

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Background

Carcinoid tumours of the extrahepatic biliary tree are exceedingly rare. We report a case of primary carcinoid tumour arising in the distal portion of the common bile duct.

Case outline

A 30-year-old man was admitted with watery diarrhoea and symptoms of biliary obstruction. Abdominal ultrasound scan showed a normal gallbladder without stones, mild dilatation of the intra- and extrahepatic biliary tree and a 2 cm solid lesion in the head of pancreas compressing the distal common bile duct. Computed tomography confirmed these findings and showed that the tumour was hypervascular. Gastrointestinal hormone screening showed an increase in plasma serotonin. The patient underwent a standard pylorus-preserving proximal pancreatoduodenectomy (PPPD).

Results

Pathological examination showed a neuroendocrine tumour (carcinoid) of the distal bile duct. The postoperative plasma serotonin decreased to normal levels. One year later the patient is well without evidence of disease.

Discussion

Primary carcinoid tumours of the extrahepatic biliary tree are rare, accounting for 0.2–2% of all digestive carcinoids. This is the fifth report of a tumour arising from the distal common bile duct. Surgical treatment for neoplasms of the distal common bile duct can be problematic because of the site of the lesion and the difficulty in differentiating them from periampullary neoplasms lesions. Pancreatoduodenectomy (PD) is therefore the treatment of choice.

Keywords

carcinoid tumour, common bile duct.

Introduction

Tumours of the extrahepatic bile ducts are relatively uncommon; the majority are adenocarcinomas (80%), mostly of the well-differentiated type. Carcinoid tumours of the extrahepatic biliary tree are exceedingly rare [1–2]. We describe a case of primary carcinoid tumour originating in the distal portion of the common bile duct. To our knowledge, only 32 cases of biliary carcinoid have been reported and this is the fifth report involving the distal common bile duct.

Case report

A 30-year-old man complained of sudden diarrhoea with pale stools for one month, and the diarrhoea was resistant to treatment. Stool cultures gave negative results. Subsequently, he developed progressive jaundice, pruritus, dark urine and weight loss. Laboratory data revealed abnormal liver function tests indicative of cholestasis. Abdominal ultrasonography showed a normal gallbladder without stones. There was mild dilatation of the intra- and extrahepatic biliary tree, with a 2 cm solid, hypoechoic tumour in the head of pancreas obstructing the distal bile duct.

A multihormonal screen showed an increase in plasma serotonin (350 ng/ml: normal 90–180) and platelet serotonin (1470 ng/10^9 platelets: normal 200–600). All other gastrointestinal hormones were within the normal range. Tumour markers (CEA and CA 19–9) were not elevated. A spiral CT scan confirmed these findings and revealed

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hypervascularity of the tumour (Figure 1). Endoscopic ultrasound demonstrated a well circumscribed mass in the head of pancreas indenting the distal common duct. ^{111}In-pentetreotide scintigraphy at 4 h and 24 h identified a region of abnormal uptake in the head of pancreas.

At laparotomy, a nodular lesion was found in the common bile duct and appeared to invade the head of pancreas, but there was no evidence of metastatic spread. The patient underwent a standard pylorus-preserving proximal pancreatoduodenectomy (PPPD). The postoperative course was unremarkable, with serum bilirubin and plasma serotonin rapidly decreasing to normal values. One year after the operation the patient is well without evidence of disease.

Macroscopic examination of the specimen revealed a firm, yellowish mass measuring 1.8 × 1.0 × 0.7 cm. The mass was located 2.5 cm proximal to the ampulla of Vater and surrounded the common bile duct, partly adhering to the head of the pancreas. It appeared circumscribed with no gross infiltration of the adjacent, loose connective tissue or the pancreas (Figure 2). Histologically, the tumour was composed of nests and sheets of fairly uniform cells in a dense, desmoplastic stroma (Figure 3). The tumour cells displayed lightly eosinophilic cytoplasm, and their nuclei were spherical to ovoid with inconspicuous nucleoli. Mitotic figures were not seen. There was no evidence of necrosis or vascular invasion.

Immunohistochemical studies showed neoplastic cells reactive for general neuroendocrine markers (i.e. neuron-specific enolase, chromogranin A, synaptophysin) and cytokeratin (Figure 4). Stains for gastrin and somatostatin were negative. The assessment of proliferative activity by means of Ki–67 immunodetection showed a labeling index of 6%.

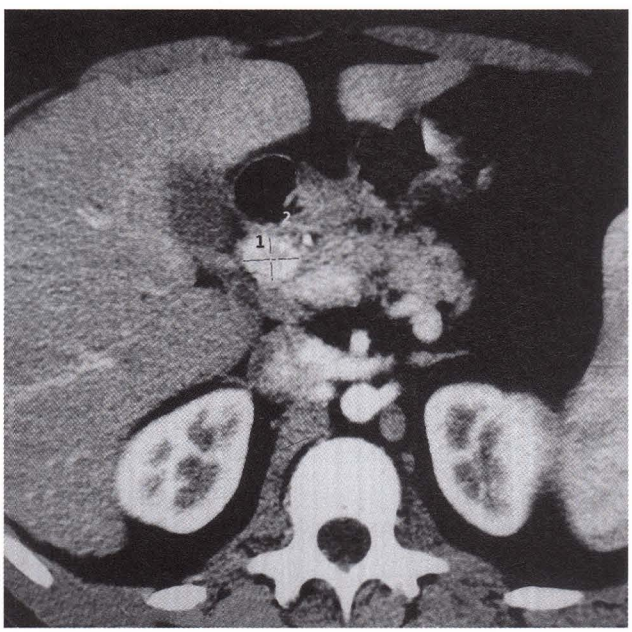

Figure 1. *CT scan showing a solid tumour in the head of pancreas, compressing the distal common bile duct.*

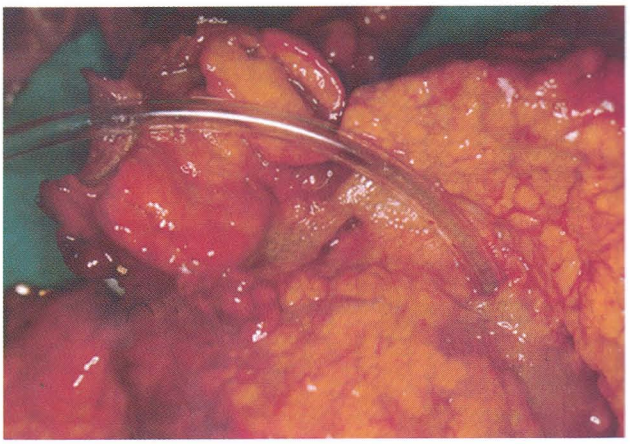

Figure 2. *Gross specimen. The neoplastic lesion appeared as a well circumscribed, yellowish mass encircling the common bile duct and growing within the lumen: (1–2) bile duct, (3) carcinoid tumour, (4) ampullary region.*

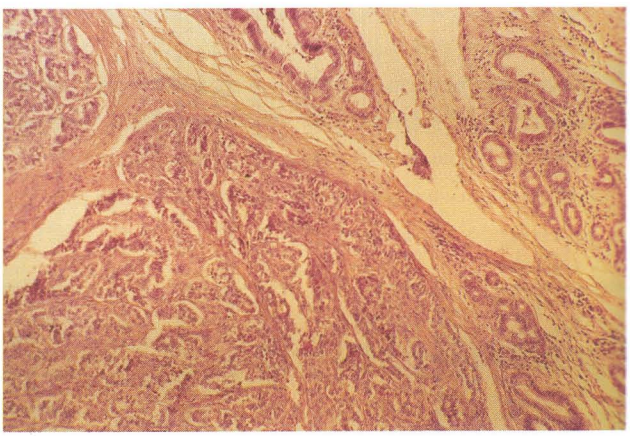

Figure 3. *The tumour exhibited small round cells arranged in nests, separated by dense connective tissue (haematoxylin-eosin ×200).*

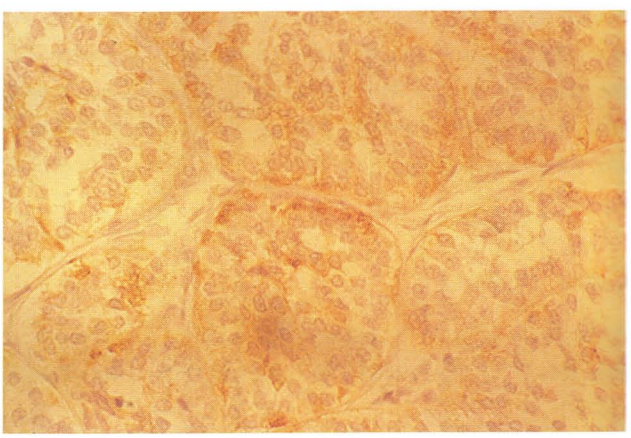

Figure 4. *Cytoplasmic positivity to chromogranin A in the neoplastic cells (avidin-biotin-peroxidase method ×350).*

The final histopathological diagnosis was carcinoid tumour of the common bile duct without lymph node metastasis.

Discussion

Only 32 cases of bile duct carcinoid (including the present one) have been reported since the first description in 1959 [3]. The clinical and morphological features of these tumours are summarised in Table 1. Carcinoids of the extrahepatic biliary tree occur more frequently in women than men (1.8:1). The mean age is two decades less than that of patients with non-endocrine neoplasms of the bile ducts (47 versus 64 years). Outside the gallbladder and the ampulla, the most frequent location of carcinoid is the proximal common bile duct and only five cases have been reported in the distal duct. These tumours do not appear to be associated with cholelithiasis; indeed, only five patients (13%) had gallstones.

The presenting symptoms include jaundice in about (50 % of patients), biliary colic, abdominal or back pain and weight loss and are directly related to the primary tumour or its metastases. In only two previous cases was urinary 5-hydroxyindoleacetic acid (5HIAA) measured, and in each it was slightly elevated [5,10]. One patient had a history of recurrent peptic ulcer; gastrin, serotonin and pancreatic polypeptide were detected by means of immunohistochemistry and electron microscopy [25]. There have been no reports of the carcinoid syndrome.

Although brush cytology can establish the diagnosis, false negative results are common because of the submucosal location of the neoplasm. Most carcinoid tumors of the common bile duct have been found unexpectedly during routine biliary tract operations. Only in the two patients with elevated urinary 5-HIAA was a neuroendocrine tumour suspected preoperatively, though in the present case the diarrhoea and increased plasma serotonin did suggest the diagnosis. Scans and cholangiograms will identify the lesion, but the correct diagnosis generally histological and immunochemical examination of surgical (or autopsy) specimens [34].

Metastases were found at the time of diagnosis in 28 % of patients, usually in the liver, pancreas, gallbladder or regional lymph nodes. Death was attributed to carcinoid tumour invasion in only three patients with liver involvement [6,8,23], and 20-year survival has been described in the presence of extensive metastases [3].

Treatment depends on the location of the tumour and the extent of disease. Proximal duct neoplasms may require en bloc resection of the tumour with regional lymphadenectomy and reconstruction by Roux-en-Y hepaticojejunostomy [35]. Two patients with a small tumour (<1mm in size) in the cystic duct were treated by simple cholecystectomy [30–32]. Hepatectomy may be performed if the liver is involved [22–26]. Excision of distal bile duct tumours is complicated by their site and consequent difficulty in differentiation from other periampullary and pancreatic tumours; PD should then be performed. Only three of the five reported patients were operated, three (including the present case) receiving PD [10,28].

The role of adjuvant therapy is unknown. If radical surgical treatment is not possible, radiotherapy seems to be of no use, but chemotherapy with 5-fluorouracil may be of some palliative value [1,2]. At present, octreotide is the most commonly used drug for disseminated carcinoid tumours at other sites. It has few side effects, it has clearly been shown to decrease urinary levels of 5-HIAA, flushing and diarrhoea and it may cause regression of hepatic metastases [1].

Table 1. *Case review of carcinoid tumours of the extrahepatic bile ducts*

Author	Year	Site	Metastases	Sex/age	Symptoms	Diagnosis	Treatment/follow-up
Davies[3]	1959	CBD	Liver	?	?	At Operation (histology)	Well at 20 years
Pilz[4]	1961	CBD	No	F/55	?	At Operation (histology)	Biopsy
Little[5]	1968	Proximal CBD	Portal vein	F/41	RUQ pain Jaundice ↑ Urinary 5-HIAA	At Operation (histology)	Exploratory laparotomy and biopsy Died of pulmonary embolism 3 wk postop.
Godwin[6]	1975	BD	Liver	?	?	At Operation (histology)	Exploratory laparotomy and biopsy Died at 1 day

Table 1. *Continued.*

Bergdahl[7]	1976	Distal CBD	No	F/79	?	Autopsy	?
Judge[8]	1976	Left HD	Liver LN	M/19	Pain RUQ Jaundice Cholelithiasis	Autopsy	Inoperable Dead at 6 days
Gerlok[9]	1979	Proximal CBD	No	M/32	Painless Jaundice	At Operation (histology)	?
Vitaux[10]	1981	Distal CBD	LN Pancreas	M/30	Jaundice ↑ Urinary 5-HIAA	At Operation (histology)	Pancreatoduodenectomy Well at 48 mo
Goodman[11]	1984	CD	LN	F/28	Pain RUQ	At Operation (histology)	Well at 9 mo
Alexander[12]	1986	BD	No	F/64	Cholelithiasis Haematemesis	?	Well at 8 mo
Jutte[13]	1986	CHD	No	M/62	Back pain	At Operation (histology)	Resection with Roux-en-Y hepaticojejunostomy Well at 24 mo
Nicolescu[14]	1986	CD	No	F/50	Biliary colic cholelithiasis	?	?
Bickerstaff[15]	1987	BD	No	F/57	Jaundice	?	Well at 4 mo
Fujita N[16]	1989	CHD	No	M/55	Jaundice	At Operation (histology)	?
Chittal[17]	1989	CD	No	F/46	Biliary colic	At Operation (histology)	Well at 3 yr
Van Der Wal[18]	1989	CHD/CBD	No	M/55	Abdominal pain	At Operation (histology)	Resection with Roux-en-Y hepaticojejunostomy Well at 12 mo
Bumin[19]	1990	Proximal CBD	No	F/38	Jaundice	At Operation (histology)	Resection with Roux-en-Y hepaticojejunostomy
Brown[20]	1990	HD	No	F/35	Painless Jaundice	At Operation (histology)	Resection with Roux-en-Y hepaticojejunostomy
Angeles-Angeles[21]	1991	Proximal CBD	Hilar Lymph-nodes	F/39	Abdominal pain Jaundice Diarrhoea Acholia	At Operation (histology)	Resection with Roux-en-Y hepatico-duodenostomy and Hilar lymphadenectomy Well at 42 mo
Beszhyak[22]	1991	HD	No	F/13	Jaundice	At Operation (histology)	Hepatic lobectomy Well at 2 yr
Barron-Rodriguez[23]	1991	CHD	Liver	M/36	Pain RUQ Jaundice	Autopsy	Inoperable Dead at 4 days
Rugge[24]	1992	CD/CBD	No	F/64	Biliary colic	At Operation (histology)	Resection with Roux-en-Y hepaticojejunostomy Well at 8 mo
Mandujano[25]	1995	Distal CBD	No	F/53	Peptic ulcer, Jaundice ↑ Gastrin, Serotonin	At Operation (histology)	Resection with Roux-en-Y hepaticojejunostomy Well at 8 mo
Sankary[26]	1995	CHD	No	F/47	Jaundice	At Operation (histology)	Resection with Roux-en-Y hepaticojejunostomy. Trisegmentectomy Well at 4 yr
Belli[27]	1996	Proximal CBD	No	M/78	Jaundice	At Operation (histology)	Resection with Roux-en-Y hepaticojejunostomy Well at 15 mo
Kopelman[28]	1996	CBD distal	Liver	F/44	Jaundice	At Operation (histology)	Pancreatoduodenectomy (pylorus-preserving) Well at 18 mo
Hao[29]	1996	Proximal CBD	No	M/42	End-stage liver disease	At Operation (histology)	Orthotopic liver transplant Resection of tumour Well at 5 mo

Meyer[30]	1997	CD	No	F/56	Abdominal pain Dyspepsia Cholelithiasis	At Operation (histology)	Cholecystectomy Well at 4 yr
Nahas[31]	1998	CHD	No	?	?	?	Resection with Roux-en-Y hepaticojejunostomy Well at 6 mo
Shah[32]	1998	CD	No	F/52	Jaundice Cholelithiasis Abdominal pain	At Operation Histologic Examination	Cholecystectomy
Ross[33]	1999	CBD	No	F/65	Jaundice	At Operation Histologic Examination	Pancreatoduodenectomy Well at 17 mo
Present report	1998	Distal CBD	No	M/30	Jaundice pruritus diarrhoea with pale stools ↑ Plasmatic serotonin	At Operation Histologic Examination	Pancreatoduodenectomy Well at 1 yr

CBD=common bile duct, BD=bile duct (not stated), HD=hepatic duct, CHD=common hepatic bile duct, CD=cystic duct, LN=lymph nodes, RUQ=right upper quadrant, ?=data not reported in the original paper.

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