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CASE REPORT

Heterotopic Pancreas Mimicking Cholangiocarcinoma. Case Report and Literature Review

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ABSTRACT

Context Majority of the patients developing obstructive jaundice have an underlying malignancy. Identification of a benign pathology like heterotopic pancreas as an aetiology is uncommon and usually occurs only subsequent to a major operation.

Case report We report a case of heterotopic pancreas adjacent to the ampulla of Vater mimicking distal cholangiocarcinoma. A 47-year-old patient presented with abdominal pain and obstructive jaundice. ERCP demonstrated a distal common bile duct stricture suspicious of cholangiocarcinoma. He underwent a pylorus-preserving pancreaticoduodenectomy. Histology showed a nodule of heterotopic pancreatic tissue adjacent to the ampulla.

Conclusion We have reviewed the literature on heterotopic pancreas of the periampullary region presenting with biliary obstruction. This is a rare entity and remains difficult to diagnose, despite advances in radiological and endoscopic imaging techniques. For symptomatic patients with an established diagnosis of periampullary heterotopic pancreas, local excision may be sufficient. However, in the absence of unequivocal imaging or histological confirmation of benign pathology, and when there is a suspicion of underlying malignancy, pancreaticoduodenectomy may be the only treatment option, as in this case.

INTRODUCTION

Heterotopic pancreas is an uncommon developmental anomaly, which may be noted both during operations and post-mortem autopsies. As reported by Hsia *et al*., it has been recognized since 1727 when Jean Schultz found it in an ileal diverticulum during autopsy of a newborn [1]. In 1859, Klob presented histological confirmation of heterotopic pancreatic tissue in two cases [2]. In autopsy series, the reported prevalence of heterotopic pancreas ranges from 0.55 to 13.7% [3]. Clinically, pancreatic heterotopia is identified with an estimated frequency of one in every 500 upper abdominal operations [4]. It usually occurs in the upper gastrointestinal tract, the commonest sites being duodenum (27.5%), stomach (25.5%) and jejunum (15.9%) [5]. Less common sites include the umbilicus, fallopian tube, lymph nodes, mediastinum, tongue and submandibular salivary gland. Only 21 cases of heterotopic pancreas at periampullary region have so far been reported in the literature [3, 4, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23]. We report such a case and review the literature on the diagnosis and management of these lesions.

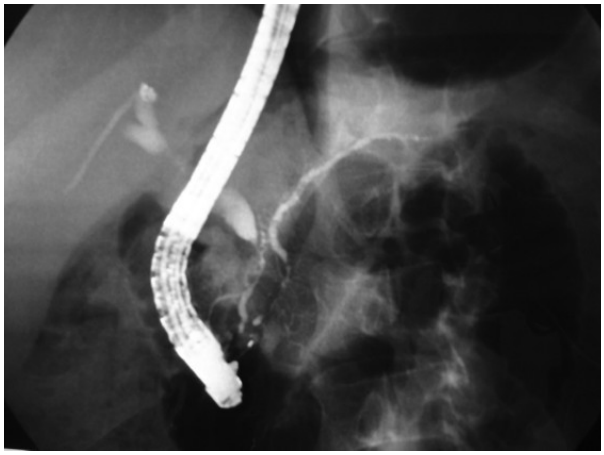

Figure 1. ERCP showing distal common bile duct stricture.

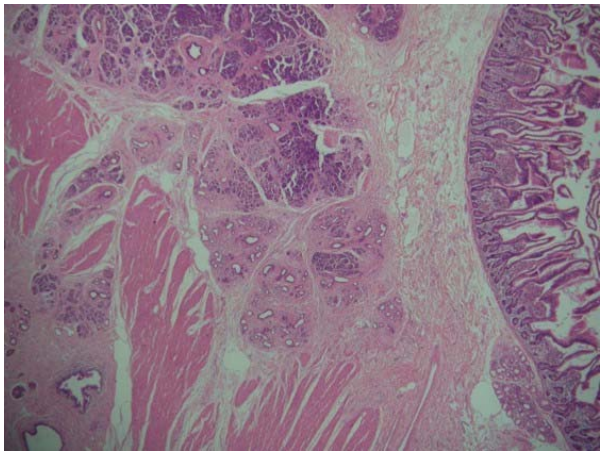

Figure 3. Low magnification view of heterotopic pancreas nodule in duodenal muscularis propria.

CASE REPORT

A 47-year-old man was admitted to his local hospital with a history of progressive jaundice and abdominal pain for three months. An ultrasound did not demonstrate gallstones. Endoscopic retrograde cholangiopancreatography (ERCP) suggested a distal bile duct stricture, suspicious of cholangiocarcinoma (Figure 1). Brushing was not done and attempted stenting was unsuccessful. The patient was then referred for further management to a tertiary hepatopancreatobiliary unit. On admission, his routine blood results were noted to be within normal limits, with the exception of his liver function tests: serum bilirubin 428 μmol/L (reference range: 1-17 μmol/L), alkaline phosphatase 430 IU/L (reference range: 39-117 IU/L), ALT 93 IU/L (reference range: 0-40 IU/L). Serum CA 19-9 was normal. He underwent a percutaneous transhepatic cholangiopancreatography (PTC) and internal-external drainage followed by internalisation of the stent. A contrast-enhanced pancreatic protocol helical CT did not demonstrate a mass in the head of the pancreas (Figure 2). Endoscopic ultrasound was not performed because it was felt that the patient needed surgery in view of highly suspicious ERCP appearance irrespective of endoscopic ultrasound (EUS) findings. So he was explored once his jaundice had resolved. At laparotomy, a 20 mm mass was palpable in the head of the pancreas. There was no evidence of intra-abdominal metastases. A pylorus-preserving pancreaticoduodenectomy was performed. He made an uneventful recovery apart from a superficial wound haematoma, which needed evacuation. He was well, mobile and pain free prior to his discharge on post-operative day 18.

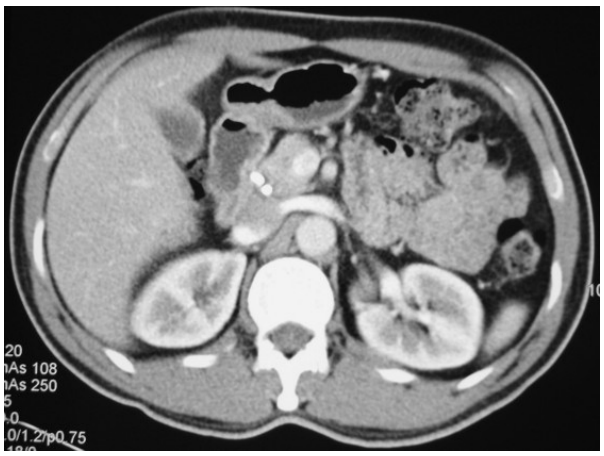

Figure 2. Axial CT scan of the pancreatic head. No mass lesion.

Histopathological Findings

Macroscopic examination revealed a nodule measuring 15x14x7 mm immediately adjacent to the ampulla of Vater in the wall of the duodenum. The nodule had a homogenous, yellow cut surface with no areas of haemorrhage or necrosis. Histologically, it was composed of pancreatic tissue, including ducts, acini, and well-formed islets. It lay in the muscularis propria of the periampullary duodenum, immediately adjacent to the ampulla of Vater, but did not communicate with the ampulla (Figures 3 and 4). It was

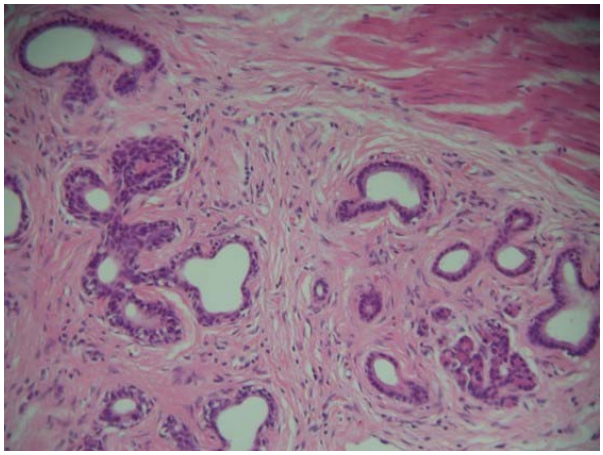

Figure 4. High magnification view of heterotopic pancreas nodule showing variably dilated ducts, acini and islets.

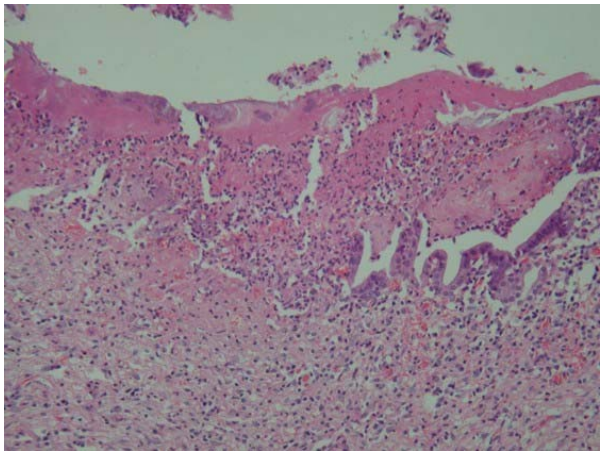

Figure 5. Distal common bile duct showing ulcerated mucosa and inflammation.

completely separate from the native pancreas. The common bile duct showed acute and chronic inflammatory changes consistent with distal obstruction (Figure 5). The native pancreas showed foci of chronic pancreatitis. There was no dysplasia or malignancy.

DISCUSSION

Pancreatic heterotopia is defined as histologically normal pancreatic tissue outside its usual location, showing no anatomic or vascular continuity with the main body of the pancreas [4]. Heterotopic pancreas has been found in all age groups, with a peak incidence in the fourth, fifth and sixth decades of life. The male-to-female ratio is 3:1.

Several hypotheses have been advanced to explain the origin of heterotopic pancreas.

1. The pancreas is formed by two buds of endodermal cells arising from caudal part of

Table 1. Summary of the reported cases of heterotopic pancreas in the ampulla of Vater (AV) or the common bile duct (CBD).

No.	Author, year	Age (years)	Sex	Symptoms (duration)	Location	Size (mm)	Biliary dilatation
1.	Hoelzer, 1940 [8]	54	F	Pain, mass abdomen, jaundice (1 year)	AV	12	Yes
2.	Mitchell *et al*., 1943 [9]	68	F	N/a	AV	5	No
3.	Varay, 1946 [10]	44	F	Jaundice (5 weeks)	AV	3	Yes
4.	Barbosa *et al*., 1946 [4]	55	M	Pain, jaundice (3 months)	CBD	2	Yes
5.	Barbosa *et al*., 1946 [4]	61	F	Gas indigestion (15 years)	CBD	N/a	Yes
6.	Pearson, 1951 [3]	43	F	Pain, intermittent jaundice (5 years)	AV	25	Yes
7.	Weber *et al*., 1968 [11]	46	F	Pain, jaundice (6 weeks)	AV	8	Yes
8.	Sabini *et al*., 1970 [12]	54	F	Pain, jaundice	CBD	5	Yes
9.	Bill *et al*., 1982 [13]	64	M	Depression, pain abdomen (“months”)	AV	40	Yes
10.	O’Reilley *et al*., 1983 [14]	61	M	Jaundice (3 weeks)	AV	8	Yes
11.	Laughlin *et al*., 1983 [15]	54	F	Pain (3 months)	AV	5	Yes
12.	Coupland *et al*., 1987 [16]	58	M	Jaundice (8 weeks)	CBD	30	Yes
13.	Tsunoda *et al*., 1990 [17]	77	F	None	CBD	4	Yes
14.	Kubota *et al*., 1996 [18]	71	M	Pain (N/a)	AV	N/a	Yes
15.	Hammarstrom *et al*., 1999 [19]	N/a	F	Acute pancreatitis	AV	4	No
16.	Molinari *et al*. (2000 [7]	42	M	Pain, jaundice, weight loss (3 months)	AV	4	Yes
17.	Chen *et al*., 2001 [6]	59	F	Pain (6 months)	AV	12	Yes
18.	Contini *et al*., 2003 [20]	72	F	Pain, jaundice (2 weeks)	AV	8	Yes
19.	Obermaier *et al*., 2004 [21]	46	M	Jaundice (N/a)	AV	2	Yes
20.	Maisonnette *et al*. , 2004 [22]	N/a	N/a	Jaundice (N/a)	CBD	N/a	No
21.	Wagle *et al*., 2005 [23]	70	F	Pain, jaundice (2 weeks)	AV	N/a	Yes
22.	Biswas *et al*., 2007 (Present study)	47	M	Pain, jaundice (3 months)	AV	15	Yes

N/a: not available
F: female; M: male

the foregut - anterior and posterior pancreatic buds [24]. Prior to fusion of these buds, small branches from them may become attached to the gut wall at various locations. These branches remain anchored to the gut wall and as the pancreatic gland pulls away from the gut, these remain grafted in its new location on the gut wall and develop as heterotopic pancreatic tissue [25].

2. The stomach, duodenum and pancreas have a common origin from the embryonic foregut. The origin of heterotopic pancreatic tissue may be the result of abnormal differentiation of multipotent regional endoderm. This may explain why heterotopic pancreatic tissue is most often located in the wall of the stomach, duodenum or proximal small bowel [26].

3. Persistence or incomplete regression of the left ventral pancreatic bud, which is normally destined to atrophy [27].

When discussing heterotopic pancreas, Pearson [3] grouped the common bile duct and ampulla of Vater as one topographical site, partly because pancreatic heterotopia in

Table 1. Continues.

No.	Radiologic/ultrasonographic/endoscopic investigations	Treatment	Outcome
1.	N/a	Inoperable	Death
2.	N/a	N/a	Death
3.	N/a	Pancreaticoduodenectomy	Death
4.	Abdominal X-ray: negative	Pancreaticoduodenectomy	Death
5.	Oral cholecystogram: non-functioning gallbladder	Pancreaticoduodenectomy	Cured
6.	N/a	Pancreaticoduodenectomy	Cured
7.	N/a	Pancreaticoduodenectomy	Cured
8.	None	Resection of CBD	Cured
9.	OGD: inconclusive; Abdominal US: gallstones, dilated CBD; ERCP: narrowing of distal CBD; selective angiography: increased vascularity	Pancreaticoduodenectomy	Cured
10.	Abdominal US: mild dilatation of CBD; ERCP: narrowing of CBD and PD	Pancreaticoduodenectomy	Cured
11.	Abdominal X-ray: recurrent hiatus hernia and gallstones	Ampullectomy	Cured
12.	Abdominal US: dilated IHBD, EHBD, CHD, and gallbladder; PTC: same with complete obstruction of CBD	Pancreaticoduodenectomy	Cured
13.	Abdominal US: dilated IHBD, EHBD; ERCP: same with filling defect in distal CBD; cholangioscopy: polypoid lesion distal CBD	Resection of CBD	Cured
14.	Abdominal US: dilated IHBD, EHBD, and PD; OGD: red swollen ampulla; biopsy: adenoma; cholangiography through PTBD: obstruction of distal CBD by a polyp; cholangioscopic biopsy: mucosal hyperplasia	Pancreaticoduodenectomy	Cured
15.	OGD: small lesion in ampulla of Vater	Endoscopic sphincterotomy + biopsy	Cured
16.	ERCP: failed; PTC: dilated IHBD, stricture of CBD	Pancreaticoduodenectomy	Cured
17.	OGD: unremarkable; abdominal US: dilated CBD, IHBD; ERCP: dilated CBD and PD; EUS: hypoechoic tumour in muscularis propria, leiomyoma (?)	Ampullectomy	Cured
18.	Abdominal US/CT: dilated CBD; ERCP: same with nodular lesion in major papilla; biopsy: inconclusive	Ampullectomy	Cured
19.	OGD: unremarkable; CT/ MRI: tumour in pancreatic head; MRCP: obstruction of the PD	Pancreaticoduodenectomy	Cured
20.	N/a	Pancreaticoduodenectomy	Cured
21.	Abdominal USG/CT: dilated CBD with tapered distal end; ERCP: ampullary nodularity with dilated and abruptly narrowed CBD	Pancreaticoduodenectomy	Cured
22.	Abdominal USG/CT: unremarkable; ERCP/PTC: narrowing of distal CBD	Pancreaticoduodenectomy	Cured

N/a: not available

CHD: common hepatic duct; EHBD: extrahepatic bile duct; EUS: endoscopic ultrasound; IHBD: intrahepatic bile duct; OGD: oesophagogastroduodenoscopy; PD: pancreatic duct; PTBD: percutaneous transhepatic biliary drainage; PTC: percutaneous transhepatic cholangiopancreatography

both areas produces common bile duct obstruction. To our knowledge, only 22 cases of heterotopic pancreas, including the present case, have been reported in the literature (Table 1). Nineteen of these 22 patients had some degree of biliary dilatation. The two most common symptoms were jaundice and abdominal pain present in 14 (64%) and 12 (55%) patients, respectively. The maximum size of the lesions ranged from 2 to 40 mm. Development of jaundice was independent of lesional size. The mechanism of biliary tract obstruction by heterotopic pancreas is believed to be due to [28]:

1. secondary irritation as a result of a foreign body effect and excessive irritative secretion producing spasm and hyperirritability of local duodenal and biliary segment.

2. production of some degree of intermittent obstruction to biliary flow due to pressure, tissue oedema leading to acute or chronic cholangitis.

Heterotopic pancreas was present in the common bile duct in 6 (27%) patients and in the ampullary region in 16 (73%). The gross appearance of aberrant pancreatic tissue was similar to that of normal pancreas and was typically described as irregularly shaped yellow nodules. In about half the cases, heterotopic pancreas was located entirely within the submucosa and less frequently involved the muscularis propria. The histological appearance varied from that of perfectly formed and organized pancreatic lobules with ducts, acini, and islets of Langerhans, to that of pancreatic tissue demonstrating only a few widely separated acini with minimally developed ducts.

Accurate preoperative diagnosis of heterotopic pancreas in the periampullary region using endoscopy and radiological imaging is difficult. The presence of central umbilication on endoscopy, though a characteristic finding in heterotopic pancreas, is quite infrequent [6]. The diagnosis was successfully made endoscopically in only one of the previously reported cases. As most of the lesions are submucosal, endoscopic biopsy is also unhelpful in most cases. Contrast-enhanced CT does not appear to be helpful in establishing the diagnosis of heterotopic pancreas pre-operatively either. EUS may have an important role to play in the diagnosis. At EUS, heterotopic pancreas in the upper gastrointestinal tract is usually hypoechoic and heterogeneous with indistinct margins and is most commonly seen to arise from the submucosa [6]. However, EUS was performed in only one of the 22 patients with periampullary heterotopic pancreas in this series. Although EUS suggested benign pathology, it misdiagnosed the heterotopic pancreas as a leiomyoma [6]. Magnetic resonance imaging or cholangiopancreatography (MRI/MRCP) was done only in one other case [21] where it was not helpful in making the diagnosis.

Local excision of heterotopic pancreas when feasible, rather than radical operation, may be the treatment of choice [7]. However, given the difficulties with accurate preoperative diagnosis and the suspicion of an underlying periampullary malignancy, pancreaticoduodenectomy was performed in 14 (64%) of the 22 patients. Five patients were successfully managed by local excision - three by ampullectomy and two by excision of the common bile duct. Among three patients who had ampullectomy, the benign nature of the pathology was suggested by either EUS [6] or pre-operative endoscopic biopsy [20] or per-operative frozen section biopsy [15]. Similarly, out of two patients who had excision of common bile duct done, benign pathology was suggested by intra-operative cholangioscopy in one case [17] and per-operative frozen section biopsy in the other [12]. One patient had endoscopic sphincterotomy done and the endoscopic biopsy revealed heterotopic pancreas [19].

CONCLUSION

Heterotopic pancreas in the periampullary region presenting with biliary obstruction is a rare entity and remains difficult to diagnose, despite advances in radiological and endoscopic imaging techniques. The role of EUS and MRI in clarifying the diagnosis of

heterotopic pancreas of the periampullary region remains unclear. Frozen section biopsy at the time of operation definitely helps in pathologic diagnosis. The problem is that even if a biopsy specimen shows non-cancerous findings, it cannot be confirmed whether the whole lesion is benign and there seems to be a relationship between heterotopic pancreatic tissue and pancreatic carcinoma [14]. For symptomatic patients with an established diagnosis of periampullary heterotopic pancreas, local excision may be sufficient. However, in the absence of unequivocal imaging or histological confirmation of benign pathology, and when there is a suspicion of underlying malignancy, pancreatico-duodenectomy may be the only treatment option, as in this case.

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Keywords Cholangiocarcinoma; Choristoma; Jaundice, Obstructive; Pancreas

Abbreviations CBD: common bile duct; CHD: common hepatic duct; EHBD: extrahepatic bile duct; EUS: endoscopic ultrasound; IHBD: intrahepatic bile duct; OGD: oesophagogastroduodenoscopy; PD: pancreatic duct; PTBD: percutaneous transhepatic biliary drainage; PTC: percutaneous transhepatic cholangio-pancreatography

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