*The Ulster Medical Journal, Volume 73, No. 1, pp. 59-62, May 2004.*

# Carcinoid tumour of the extrahepatic bile duct - report of a case and literature review

A A C Menezes, A J Diver, D McCance, T Diamond

Accepted 10 March 2004

Carcinoid tumors of the extrahepatic bile duct are rare and account for only 0.2-2% of all gastrointestinal carcinoids [1,2].

*CASE REPORT*

A 30 yr old man presented with obstructive jaundice while on holiday in Australia. Physical examination was otherwise normal. Abdominal ultrasound, CT scan and MRI scan confirmed marked dilatation of the intrahepatic biliary system. ERCP revealed a stricture in the common hepatic duct (Figure 1). A stent was inserted. Brush cytology was inconclusive. CA19-9 and CEA levels were normal. Following return to the UK, laparotomy was performed and revealed a 3cm tumour at the junction of cystic duct and CHD. Excision of the bile duct with portal lymphadenectomy and Roux-en-Y hepaticojejunostomy was performed. He had an uneventful postoperative course.

Histopathology revealed a white firm tumour obliterating the lumen of the CHD. Microscopically, the tumour contained round and polygonal cells arranged in nests and separated by fibrous stroma. Tumour cells were tested for neuroendocrine markers incuding chromogranin S and serotonin, but were positive only for protein gene peptide and neurone specific enolase (Figure 2). Ultrastructural appearances on electron microscopy showed dense-cored neuroendocrine granules consistent with a mid-gut carcinoid tumour. Margins were free of tumour but one out of eleven lymph nodes showed a metastatic deposit.

Postoperatively, gastrointestinal hormone levels including NeurokininA, Gastrin Release Peptide, and Pancreatic Polypeptide were normal. Daily urinary excretion of 5 hydroxyindoleacetic acid (5-HIAA) was also within the normal range. SPECT octreotide scan did not reveal any metastases and he remains well at follow up 18 months later.

**DISCUSSION**

Carcinoid tumours of the bile duct are rare. As with other tumors of the bile duct, these lesions are difficult to diagnose preoperatively and nearly impossible to distinguish from cholangiocarcinoma. They are derived from embryonal neural crest cells (Kulchitsky cells) and have the potential to produce serotonin[3]. These cells are also known as argentaffin cells, because of their affinity for silver staining compounds and are located in the crypts of Leiberkühn.

Most of the information about this malignancy is from case reports. A comprehensive search of Medline and Embase revealed forty two cases of carcinoid of the extrahepatic duct, including our case. In 1959, Davies first published a case of biliary carcinoid although this may have been a periampullary carcinoid[4]. Pilz has been credited with the first reported case of carcinoid of the biliary tract[5]. Clinical characteristics, pathology and follow up data of previously described cases are summarized in Table 1[3-22].

The age of patients ranged from 12 to 79 years with a median of 47 years[12,13]. The female to male ratio was 2:1. The commonest symptom was jaundice (69% of cases), often associated with abdominal pain (30%) and pruritis (21%).

Mater Hospital Trust, Crumlin Road, Belfast BT14 6AB.

AAC Menezes, FRCS, Surgical research Registrar

AJ Diver, MB, BCh, BAO, Senior House Officer

T Diamond, BSc, MD, FRCS, FRCSI, Consultant Hepatobiliary Surgeon

Royal Victoria Hospital, Grosvenor Road, Belfast, BT12 6BJ.

D McCance, MRCP, Consultant Endocrinologist

Correspondence to Mr Diamond.

E-mail: tdiamond-stc@mater.n-i.nhs.uk

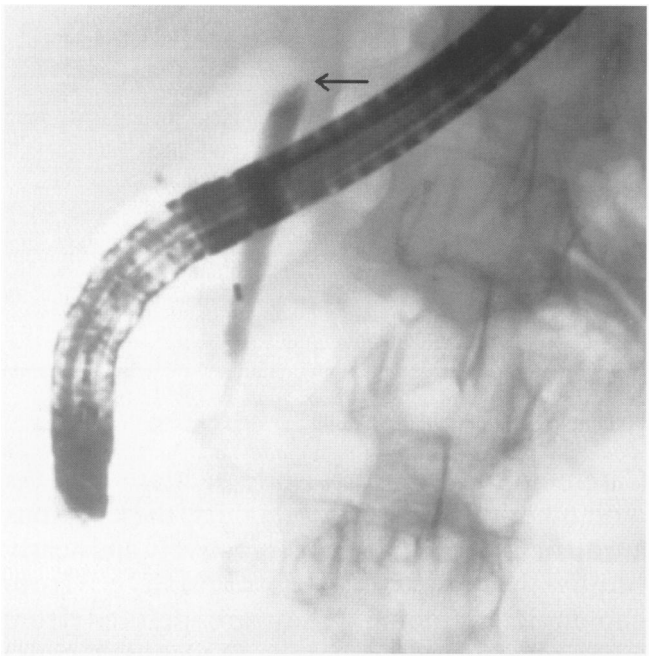

*Fig 1.* ERCP showing a stricture in the common hepatic duct (arrow)

Investigations ranged from abdominal ultrasonography to endoscopic retrograde pancreaticography and more recently CT scan and Magnetic Resonance Cholangiography. However, a preoperative diagnosis of carcinoid tumour was made in just one case [5] and in only 11 cases was a diagnosis of primary CBD tumour suspected. In three cases the diagnosis was made at autopsy[13].

The commonest site of malignant stricture was the common bile duct (55%) followed by the hilar confluence of the bile ducts and the common hepatic duct (33%). Notably, pain in the right upper quadrant was a predominant symptom of tumours in the cystic duct.

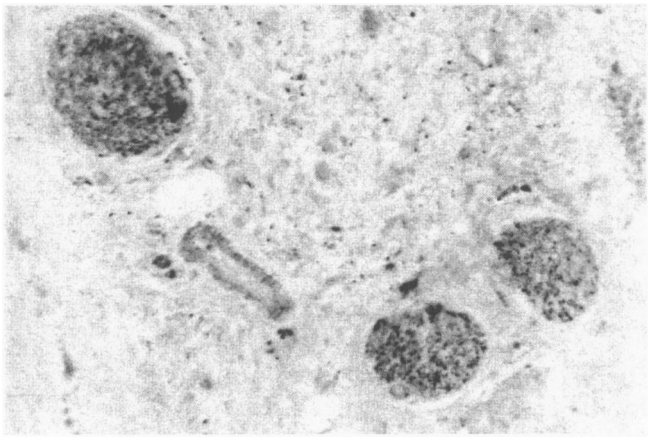

*Fig 1.* (200x magnification) Shows large malignant cells with neuroendocrine granules positive for Neurone Specific Enolase by immunohistochemistry. (Image inverted for clarity)

Metastatic spread was present in 14 cases (33%) in which lymph node involvement was most common site. Immunomarkers were not performed in any case preoperatively and even after diagnosis not all cases were tested. Positive immunomarkers neurokinin, cromogranin, gastrin, serotonin or argyroffin were detected in 10 cases and normal levels found in three, including the present case.

Follow up varied from 6 to 72 months but was not recorded in all cases. Survival in seven patients was more than 24 months and four patients, including two patients with lymph node metastases, survived for more than 4 yrs.

In conclusion, carcinoid tumours of the extra hepatic biliary tree are rare and occur in a young age group with a preponderance in females. Preoperative diagnosis is difficult but may be improved with assessment of neuroendocrine markers in suspected cases. Disease free survival is prolonged following surgical excision despite the presence of metastases and these patients should be treated aggressively.

Acknowledgements: The authors would like to thank Kathy M Pogue, Senior Research Technician, Department of Immunology, Royal Victoria Hospital and Eddie Kearney, Theatre Technician, Mater Hospital Trust for their help in obtaining the necessary images.

## References

1. Modlin IM, Sandor A. An analysis of 8305 cases of carcinoid tumors. *Cancer* 1997;**79**(4):813-29.
2. Lauffer JM, Zhang T, Modlin IM. Review article: current status of gastrointestinal carcinoids. *Aliment Pharmacol Ther* 1999;**13**(3):271-87.
3. Belli G, Rotondano G, D'Agostino A, Marano I. Primary extrahepatic bile duct carcinoids. *HPB Surg* 1996;**9**(2):101-5.
4. Davis JW, Mackersie RC, Hoyt DB, Garcia J. Randomized study of algorithms for discontinuing tube thoracostomy drainage. *J Am Coll Surg* 1994;**179**(5):553-7.
5. Pilz E. "Ube Karzinoid des ductus Choledochus". *Zentralbl Chir* 1961;**86**:1588-90. German.
6. Podnos YD, Jimenez JC, Zainabadi K, Ji P, Cooke J, Busuttil RW, et al. Carcinoid tumors of the common bile duct: report of two cases. *Surg Today* 2003;**33**(7):553-5.
7. Volpe CM, Pryor JP, Caty M, Doerr RJ. An adolescent with bile duct carcinoid tumor. *Med Pediatr Oncol*

TABLE I

*Data on 42 Reported Cases of Bile Duct Carcinoids*

| Case | Author/Series | Year | Age | Gender | Symptoms | Site | Metastases | Immunomarkers | Status |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Pilz | 1961 | 55 | f | jaundice,RUQ pain | CBD | PV | | |
| 2 | Little | 1968 | 41 | f | jaundice,RUQ pain | Hilar | | | died PE 3 weeks |
| 3 | Bergdahl | 1976 | 79 | f | incidental finding | CBD | no | | autopsy finding |
| 4 | Judge | 1976 | 19 | m | jaundice,RUQ pain | CBD | LN | | autopsy finding |
| 5 | Gerlock | 1979 | 32 | m | jaundice | CBD | LN | | N/A |
| 6 | Vitaux | 1981 | 30 | m | jaundice | CBD | LN | | NED 4 yrs |
| 7 | Abe | 1983 | 64 | m | RUQ pain | CBD | liver | | died 10 months |
| 8 | Goodman | 1984 | 28 | f | RUQ pain | Cystic Duct | LN | argyrophin | NED 9 months |
| 9 | Jutte | 1986 | 62 | m | back pain | CHD | no | argyrophyn others negative | Ned 24 |
| 10 | Nicolescu | 1986 | 50 | f | RUQ pain | CBD | no | | N/A |
| 11 | Alexander | 1986 | 64 | f | haematemesis | CBD | no | | NED 8 months |
| 12 | Chittal | 1989 | 46 | f | RUQ pain | Cystic Duct | no | CEA,cytokine, | NED 3yrs |
| 13 | Fujita | 1989 | 55 | f | RUQ pain | CBD | no | all negative | NED6m |
| 14 | Bickerstaff | 1989 | 57 | f | jaundice | CBD | no | | NED 6 mos |
| 15 | Brown | 1990 | 35 | f | jaundice | Hilar | no | | alive 7 days |
| 16 | Bumin | 1990 | 38 | f | jaundice | CBD | no | | N/A |
| 17 | Angeles-Angeles | 1991 | 39 | f | jaundice, pruritis, pain | CBD | LN | serotonin,somatostatin | NED 42 months |
| 18 | Barron-Rodriguez | 1991 | 36 | m | jaundice | CBD | liver | | died 4 days,Autopsy |
| 19 | Rugge | 1992 | 64 | f | jaundice | Cystic Duct | no | | NED 12 m |
| 20 | Gembala | 1993 | 28 | m | jaundice | Hilar | liver | | N/A |
| 21 | Mandujano-Vera | 1995 | 53 | f | jaundice | CBD | no | | N/A |
| 22 | Sankary | 1995 | 47 | f | jaundice | Hilar | no | | NED 4 yrs |
| 23 | Hao | 1996 | 47 | m | incidental finding | CBD | | chromogranin,gastrin, serotonin | N/A |
| 24 | Kopelman | 1996 | 44 | m | jaundice | CBD | liver | | N/A |
| 25 | Belli | 1996 | 78 | m | jaundice, pruritis | CBD | N/a | | N/A |
| 26 | Bembenek | 1998 | 12 | f | jaundice | Hilar | | chromogranin, gastrin | |
| 27 | Nahas | 1998 | 61 | f | jaundice | Hilar | n/a | | NED 6m |
| 28 | Hermina | 1999 | 69 | m | RUQ pain | Cystic Duct | LN | | |
| 29 | Perakath | 1999 | 36 | f | jaundice,pain | CHD | LN | | N/A |
| 30 | Ross | 1999 | 65 | f | jaundice | CBD | no | | NED 17 |
| 31 | Chamberlain | 1999 | 37 | f | pruritis | Hilar | no | | NED 18 m |
| 32 | Chamberlain | 1999 | 67 | f | pruritis | Hilar | no | | NED 15 Months |
| 33 | Chan | 2000 | 14 | m | jaundice | Hilar | | chromogranin,synaptophysin, | |
| 34 | Maitra | 2000 | 53 | f | jaundice | CBD | no | | NED 6 yrs |
| 35 | Maitra | 2000 | 61 | f | jaundice, pruritis | Hilar | no | | NED 4 yrs |
| 36 | Juturi | 2000 | 43 | m | jaundice, pruritis | CBD | no | HIAA -ve | NED 3.5yrs |
| 37 | Turrion | 2002 | 51 | f | jaundice, pruritis | Hilar | no | | NED 18 m |
| 38 | Pawlik | 2003 | 59 | m | jaundice | Hilar | LN | | |
| 39 | Podnos | 2003 | 65 | f | cholecystitis | CBD | no | chromogranin, serotonin, | NED 37 m |
| 40 | Podnos | 2003 | 27 | m | jaundice, pruritis | CBD | no | | NED 7.5 years |
| 41 | Volpe | 2003 | 19 | m | jaundice, abdominal pain | CBD | no | chromogranin | NED12 m |
| 42 | Present case | 2003 | 30 | m | jaundice, pruritis | CBD | LN | Normal Neurokinin A, HIAA -ve | NED 18 m |

RUQ: right upper quadrant, CBD: common bile duct, CHD:common hepatic duct, PV: portal vein, LN: Lymph node, CEA: carcinoembryonic antigen, HIAA: hydroxyindole acetic acid, NED: no evidence of disease, N/A: not available,

2003;**40**(2):137-8.

8. Pawlik TM, Shah S, Eckhauser FE. Carcinoid tumor of the biliary tract: treating a rare cause of bile duct obstruction. *Ann Surg* 2003;**69**(2):98-101.
9. Chamberlain RS, Blumgart LH. Carcinoid tumors of the extrahepatic bile duct. A rare cause of malignant biliary obstruction. *Cancer* 1999;**86**(10):1959-65.
10. Angeles-Angeles A, Quintanilla-Martinez L, Larriva-Sahd J. Primary carcinoid of the common bile duct. Immunohistochemical characterization of a case and review of the literature. *Am J Clin Pathol* 1991;**96**(3): 341-4.
11. Badowski A, Sosnicki W, Dumanski Z, Kaszynski H. [Carcinoid tumor of the common bile duct]. *Wiad Lek* 1986;**39**(10):694-9. Polish.
12. Bembenek A, Lotterer E, Machens A, Cario H, Krause U, Holzhausen HJ, et al. Neuroendocrine tumor of the common hepatic duct: a rare cause of extrahepatic

jaundice in adolescence. *Surgery* 1998;**123**(6):712-5.

13. Bergdahl L. Carcinoid tumours of the biliary tract. *Aust N Z J Surg* 1976;**46**(2):136-8.
14. Bader TR, Semelka RC, Chiu VC, Armao DM, Woosley JT. MRI of carcinoid tumors: spectrum of appearances in the gastrointestinal tract and liver. *J Magn Reson Imaging* 2001;**14**(3):261-9.
15. Chan C, Medina-Franco H, Bell W, Lazenby A, Vickers S. Carcinoid tumor of the hepatic duct presenting as a Klatskin tumor in an adolescent and review of world literature. *Hepatogastroenterology* 2000;**47**(32):519-21.
16. Hermina M, Starling J, Warner TF. Carcinoid tumor of the cystic duct. *Pathol Res Pract* 1999;**195**(10):707-9; discussion 710.
17. Juturi JV, Maghfoor I, Doll DC, Evans ML. A case of biliary carcinoid presenting with pancreatitis and obstructive jaundice. *Am J Gastroenterol* 2000;**95**(10):2973-4.
18. Maitra A, Krueger JE, Tascilar M, Offerhaus GJ, Angeles-Angeles A, Klimstra DS, et al. Carcinoid tumors of the extrahepatic bile ducts: a study of seven cases. *Am J Surg Pathol* 2000;**24**(11):1501-10.
19. Perakath B, Chandran BS, Srivastava VM, Nair A, Sitaram V. Carcinoid tumor of common hepatic duct. *Indian J Gastroenterol* 1999;**18**(3):127.
20. Ross AC, Hurley JB, Hay WB, Rusnak CH, Petrunia DM. Carcinoids of the common bile duct: a case report and literature review. *Can J Surg* 1999;**42**(1):59-63.
21. Rugge M, Sonego F, Militello C, Guido M, Ninfo V. Primary carcinoid tumor of the cystic and common bile ducts. *Am J Surg Pathol* 1992;**16**(8):802-7.
22. Turrion VS, Salas C, Alvira LG, Jimenez M, Lucena JL, Ardaiz J. Carcinoid tumour of the common bile duct: an exceptional indication for liver transplantation. *Transplant Proc* 2002;**34**(1):264-5.