

Icteric Intraductal Hepatocellular Carcinoma and Bile Duct Thrombus Masquerading as Hilar Cholangiocarcinoma

Dear Editor,

Obstructive jaundice is a rare presenting clinical feature in patients with hepatocellular carcinoma (HCC). Icteric HCC is otherwise known as icteric-type hepatoma.¹ It is known that intraluminal biliary obstruction may occur by one of 3 mechanisms: haemobilia caused by bleeding from the tumour, migration of tumour debris that has separated from the primary growth, or continuous retrograde tumour growth along the biliary tree. Although, HCC with bile duct thrombus (BDT) was historically associated with a poorer prognosis, some studies have shown that adequate surgical resection can still provide sufficient palliation and occasional cure.^{2,3}

In the past decade, several groups have reported their experience of HCC with BDT and most of these reports described patients with a significantly sized parenchymal lesion.^{4,5} However, a subtype of intraductal hepatocellular carcinoma (IHCC) with BDT without an obvious parenchymal lesion is rarely reported as these predominantly

intraductal lesions are often preoperatively misdiagnosed as cholangiocarcinoma.⁶⁻⁸

In this report, we present a series of 4 patients with icteric IHCC with BDT without apparent parenchymal lesion. We discuss the clinico-pathological characteristics of this unique subtype of IHCC with BDT and describe the surgical approach to these lesions.

Results

Patients' clinical and tumour characteristics and surgical details are summarised in Tables 1 and 2. One patient with a history of previously resected HCC had a preoperative diagnosis of IHCC with BDT. The other 3 patients were diagnosed preoperatively to have hilar cholangiocarcinomas. All 3 patients with primary presentation of disease had elevated mean CA 19-9 at 1356 $\mu\text{mol/L}$. The hepatitis B surface antigen (HBsAg) assay was positive in all 4 cases, and the mean alpha-fetoprotein (AFP) assay was 6.03 UG/L. The mean bilirubin level was 136 $\mu\text{mol/L}$.

Table 1. Characteristics of Presentation, Tumour location, Surgical Intervention and Reconstruction of Patients with Icteric HCC and BDT

Case No.	Age/Gender	Presentation Preoperative Diagnosis	Location of Intraductal Tumour	Preoperative Biliary Drainage	Surgical Intervention	Biliary Reconstruction
1	63 years/male	Recurrent/intraductal HCC	Right main duct and sectorial ducts extending to the confluence, length 5 cm	Nil	Right hemihepatectomy and left main duct margin and tumour thrombectomy	Nil
2	69 years/male	Primary/hilar cholangiocarcinoma	Right ant sectorial to right main duct extending to the left main duct, length 4 cm	Nil	Extended right hepatectomy, caudate lobe resection, radical resection of bile duct	Left main hepatic duct to jejunum
3	67 years/male	Primary/hilar cholangiocarcinoma	Left lateral sectorial to left main to confluence and extending to the right main duct, length 5.5 cm	Nil	Left hemihepatectomy, caudate lobe resection and right and common hepatic duct and radical resection of the bile duct	Right main hepatic duct to jejunum
4	58 years/male	Primary/hilar cholangiocarcinoma	Left main duct and sectorial ducts extending to the hilum and involving the distal right main duct, CBD up to cystic duct confluence, Length 6.5 cm	Right PTBD	Extended left hepatectomy, caudate lobe resection and radical resection of the bile duct, right hepatic duct and tumour thrombectomy	Right sectorial ducts cloacalised and anastomosed to jejunal limb

BDT: Bile duct thrombus; CBD: Common bile duct; HCC: Hepatocellular carcinoma; PTBD: Percutaneous transhepatic biliary drainage

Table 2. Clinical and Biochemical Profile of Patients with Intraductal Hepatocellular Carcinoma

Case No.	Chronic Hepatitis	Cirrhosis (Childs Status)	Comorbidities	Albumin	Bilirubin	ALP	ALT	AST	GGT	AFP	CA 19-9	CEA
1	B	Nil	Hypertension	34	153	162	89	62	362	1.9	Nil	Nil
2	B	A	Hypertension, diabetes mellitus	34	141	258	203	145	229	10.7	467	2.8
3	B/Chronic alcoholism	B	Nil	33	201	330	154	110	1091	5.3	2213	2.2
4	B	B	Nil	36	49	231	79	73	413	6.2	1388	Nil

AFP: Alpha fetoprotein; ALP: Alkaline phosphatase; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; CA 19-9: Cancer antigen 19-9; CEA: Carcinoembryonic antigen; GGT: Gamma-glutamyl transpeptidase

All patients were operated on within 1 week of diagnosis. One patient underwent preoperative percutaneous drainage at another institution for treatment of cholangitis. The surgical procedure was determined based on the preoperative determination of the location of the primary tumour and the tumour/tumour thrombus extension in the biliary system, the precise operative exploration results, or both. All 4 patients had Satoh type II BDT (Fig. 1).⁵

The patient with the preoperatively diagnosed recurrent IHCC underwent a hemihepatectomy with removal of the ipsilateral bile duct and tumour thrombectomy via the transected end of the bile duct. On histological examination, there was a small 2 mm focus of parenchymal tumour close to the main bile duct, the thrombus which extended distally had no significant attachments to the lumen of the common hepatic duct (CHD) (Figs. 2 and 3).

In the other 3 patients with preoperative diagnosis of hilar cholangiocarcinoma, major hepatic resection of the dominant side of the tumour, caudate lobectomy, and radical

resection of the bile duct was performed. Histological examination showed that the IHCC were found to invade the main bile duct and extend 1 cm to 2 cm radially into the hepatic parenchyma in all 3 cases. The BDT extended distally into the CHD, but did not show significant thrombus attachments to the CHD and consisted mainly of inspissated bile. Notably, all 3 patients had evidence of microvascular invasion and 2 had associated portal vein invasion (Table 3).

The patients were all discharged within 2 weeks of hospitalisation and had no major complications necessitating further procedures. Two patients developed recurrent tumours at 7 and 24 months and passed away at 9 and 50 months, respectively. Two patients were disease-free at 16 and 29 months to date (Table 4).

Discussion

Jaundice in HCC usually occurs in advanced liver cirrhosis, caused by tumour mass effect compressing

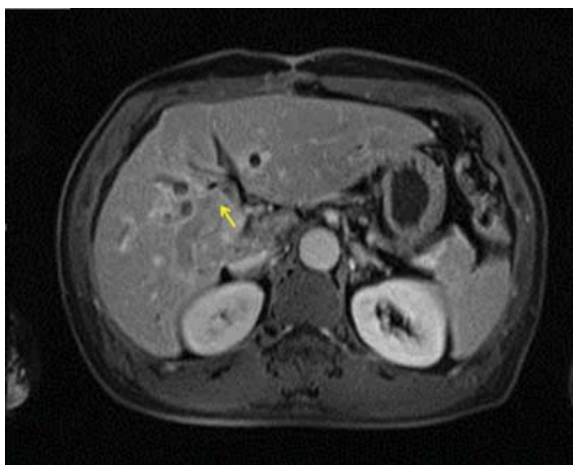


Fig. 1. A CT scan of a patient with intrahepatic bile duct thrombus. Arrow points to the thrombus.

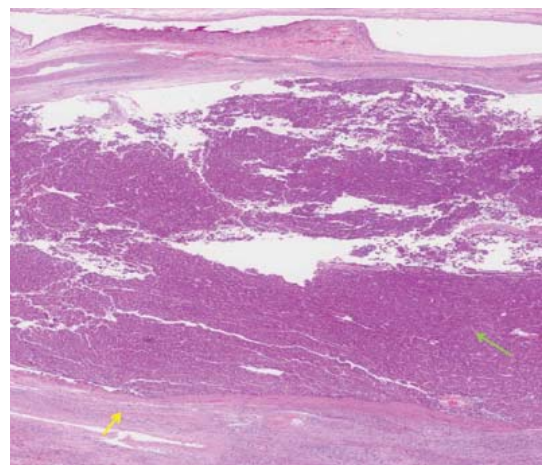


Fig. 2. Histological slide of intrahepatic bile duct thrombus. Long arrow points to the tumour thrombus and the short arrow points to the bile duct wall.

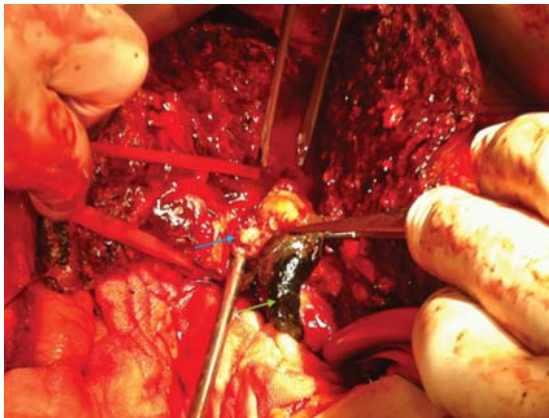


Fig. 3. Intraoperative picture of intrahepatic bile duct thrombus. Upper arrow points to the tumour thrombus, lower arrow points to the inspissated bile thrombus that is removed easily.

on bile ducts or massive tumour infiltration of the liver parenchyma.^{9,10} Jaundice caused by BDT is a rare obstructive variant, being identified in only 1% to 13% of patients treated operatively.^{3,11,12} Satoh et al classified the subtypes of HCC with BDT according to the level of BDT.⁵ However, IHCC with BDT with no apparent parenchymal lesion was not well described within the larger series.^{4,6} In this report, we point out the important pathological differences which significantly impact the surgical approach.

The low rate of surgical resection of patients with HCC and BDT is due to liver impairment secondary to liver cirrhosis exacerbated by obstructive jaundice.¹³ Thus, an attractive treatment option for HCC is the removal of

the bile duct thrombus without en bloc resection of the involved bile duct and liver parenchyma, although some authors hypothesised that tumour thrombectomy through a choledochotomy might cause peritoneal dissemination and local recurrence at the site of choledochotomy due to intraoperative implantation.¹⁴ Satoh et al and Shiomi et al showed that there were no significant differences in the survival of patients who underwent thrombectomy of the BDT compared with those who underwent bile duct resection, provided that there was no invasion of the bile duct.^{4,5} Narita et al also reported that bile duct tumour thrombi were only attached to the mucosa of the bile duct by a thin stalk without invasion into the submucosa.¹⁵ This leads to the suggestion of curative tumour thrombectomy without a need for extended liver resection as a viable option of treatment for HCC with BDT.

However, in 3 of our cases with IHCC and BDT, the pathological specimens showed that the main bile ducts at the epicentre of the tumour were extensively involved with surrounding parenchymal involvement such that resection of the bile ducts and its associated liver segments were necessary to remove the tumour en bloc instead of a simple tumour thrombectomy. This was in contradistinction to the pathological findings from all the reported series of HCC with BDT that main bile duct invasion was not seen in the reported cases.^{4,5,8} This finding is significant as it mandates surgical resection of the hepatic parenchyma surrounding the intraductal HCC in this subtype of IHCC.

In our cases, when the main tumour lesion was resected, the residual BDT which extends distally into the common

Table 3. Pathological Characteristics of the Intraductal Hepatocellular Carcinoma and Bile Duct Thrombus

Case No.	Edmonson Grade	Tumour Capsule/ Size of Intraductal Tumour	Margins (mm)	Intrahepatic Main Bile Duct Invasion	Bile Duct Thrombus	Portal Vein Invasion	Lymph Node Involvement	Micro Vascular Invasion
1	Moderate	NA/ 2 mm, focal involvement of the parenchyma	20	No	Extending distally into the CHD and consists of inspissated bile only	No	NA	No
2	High	Incomplete/ invading radially into the bile ducts and 1 cm into the parenchyma	15	Yes	Extending distally into the CHD and mainly inspissated bile	No	No	Yes
3	Moderate	Incomplete/ invading radially into the bile ducts and 2 cm into the parenchyma	1	Yes	Extending distally into the CHD and mainly inspissated bile	Yes	No	Yes
4	High	Incomplete/ invading radially into the bile ducts and 2 cm into the parenchyma	10	Yes	Extending distally into the CHD and mainly inspissated bile	Yes	No	Yes

CHD: Common hepatic duct; NA: Not applicable

Table 4. Postoperative Outcomes and Long Term Follow-up Results

Case No.	Complications	DFS/Months	Recurrence	Adjuvant Therapy	OS/Months
1	Nil/discharged POD 10	16	Nil	Nil	16
2	Nil/discharged POD 10	7	Recurrent at Segment 4	Nil	9
3	Nil/discharged POD 9	24	Recurrent at Segment 6	TACE X1 cycle	50
4	Nil/discharged POD 8	29	Nil	Nil	29

DFS: Disease-free survival; OS: Overall survival; POD: Postoperative day; TACE: Transarterial chemoembolisation

hepatic duct consisted mainly of inspissated bile and were easily removed via thrombectomy with no attachment to the bile duct. This suggests that the observations of the previous studies held true for thrombi which were extending far away from the epicentre of the tumour.^{4,5,8} For certainty of the oncologic clearance, resection of the parenchyma around the epicentre of the tumour thrombus, usually in the main bile ducts, is recommended for IHCC based on our experience.

Conclusion

Icteric IHCC with BDT are a rare subtype of HCC and are associated with main bile duct invasion and parenchyma involvement around the epicentre of the IHCC. We advocate parenchyma resection around the IHCC in the main duct. The distally extending BDT are often not attached to the bile ducts and can be safely removed via thrombectomy.

REFERENCES

- Lin TY, Chen KM, Chen YR, Lin WS, Wang TH, Sung JL. Icteric type hepatoma. *Med Chir Dig* 1975;4:267-70.
- Tantawi B, Cherqui D, Tran van Nhieu J, Kracht M, Fagniez PL. Surgery for biliary obstruction by tumor thrombus in primary liver cancer. *Br J Surg* 1996;83:1522-5.
- Chen MF, Jan YY, Jeng LB, Hwang TL, Wang CS, Chen SC. Obstructive jaundice secondary to ruptured hepatocellular carcinoma into the common bile duct. Surgical experiences of 20 cases. *Cancer* 1994;73:1335-40.
- Shiomi M, Kamiya J, Nagino M, Uesaka K, Sano T, Hayakawa N, et al. Hepatocellular carcinoma with biliary tumor thrombi: aggressive operative approach after appropriate preoperative management. *Surgery* 2001;129:692-8.
- Satoh S, Ikai I, Honda G, Okabe H, Takeyama O, Yamamoto Y, et al. Clinicopathologic evaluation of hepatocellular carcinoma with bile duct thrombi. *Surgery* 2000;128:779-83.
- Ise N, Andoh H, Sato T, Yasui O, Kurokawa T, Kotanagi H. Three cases of small hepatocellular carcinoma presenting as obstructive jaundice. *HPB (Oxford)* 2004;6:21-4.
- Ramakrishna B, Shah GJ, Vyas F. Intraductal Hepatocellular Carcinoma without Parenchymal Tumor: A Case Report. *J Gastrointest Cancer* 2012;43 Suppl 1:S77-9.
- Peng SY, Wang JW, Liu YB, Cai XJ, Deng GL, Xu B, et al. Surgical intervention for obstructive jaundice due to biliary tumor thrombus in hepatocellular carcinoma. *World J Surg* 2004;28: 43-6.
- Nakashima T, Okuda K, Kojiro M, Jimi A, Yamaguchi R, Sakamoto K, et al. Pathology of hepatocellular carcinoma in Japan: 232 consecutive cases autopsied in ten years. *Cancer* 1983;51:863-77.
- Lee NW, Wong KP, Siu KF, Wong J. Cholangiography in hepatocellular carcinoma with obstructive jaundice. *Clin Radiol* 1984;35:119-23.
- Ueda M, Takeuchi T, Takayasu T, Takahashi K, Okamoto S, Tanaka A, et al. Classification and surgical treatment of hepatocellular carcinoma (HCC) with bile duct thrombi. *Hepatogastroenterology* 1994;41:349-54.
- Ikeda Y, Matsumata T, Adachi E, Hayashi H, Takenaka K, Sugimachi K. Hepatocellular carcinoma of the intrabiliary growth type. *Int Surg* 1997;82:76-8.
- Wu CS, Wu SS, Chen PC, Chiu CT, Lin SM, Jan YY, et al. Cholangiography of icteric type hepatoma. *Am J Gastroenterology* 1994;89:774-7.
- Mok KT, Chang HT, Liu SI, Jou NW, Tsai CC, Wang BW. Surgical treatment of hepatocellular carcinoma with biliary tumour thrombi. *Int Surg* 1996;81:284-8.
- Narita R, Oto T, Mimura Y, Ono M, Abe S, Tabaru A, et al. Biliary obstruction caused by intrabiliary transplantation from hepatocellular carcinoma. *J Gastroenterol* 2002;37:55-8.

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