

HILAR CHOLANGIOCARCINOMA - KLATSKIN'S TUMOUR

Review of the literature and report of first successfully resected case in Malta

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INTRODUCTION

Hepatic duct confluence sclerosing cholangiocarcinoma (Klatskin's Tumour) is described as a small tumour in an inaccessible position, high up in the hilum of the liver. In the past the position of the tumour made it difficult to diagnose at operation, but nowadays with intelligent use of ultrasonography, percutaneous transhepatic cholangiography and digital subtraction angiography, pre-operative identification and localisation of this tumour is possible in a high percentage of cases. In this article the first case successfully treated by curative resection in Malta is presented after reviewing in detail the present international state of surgery for these tumours.

LITERATURE REVIEW

According to Renshaw, (1) Durand-Fardel reported the first case of primary carcinoma of the common bile duct in 1840 and in 1878, Sceupel described the first case of carcinoma of the hepatic duct, but it was not until 1957 before the first case of adenocarcinoma at the bifurcation of the hepatic ducts was described by Alheimer.(2) By publishing an extensive review of the distinctive manifestations of this tumour in 1965, however, it was Gerald Klatskin's name that remained associated with the condition. (3)

The reported autopsy incidence of extrahepatic bile duct carcinoma, excluding carcinoma of the gallblad-

der and the ampulla of Vater, varies between 0.01% and 0.45%, (4,5) with Klatskin's tumour making up 43% of these tumours. There is evidence that at least in the United States of America, the incidence of bile duct carcinoma is increasing, (6) although this increase is almost certainly apparent because of the advent of new diagnostic methods applicable to obstructive jaundice with which one is achieving a much higher pickup rate. Sako et al, (4) quote that out of 433 cases of cholangiocarcinoma, 264 were men and 169 were women with a ratio of 3:2. In his original review of 13 cases of hilar cholangiocarcinoma, Klatskin, (3) reported a male to female ratio of 9:4 and more recently in a series of 31 cases, Beazley et al (7) noted a similar ratio of 2:1. In fact in most series, cholangiocarcinoma in general and hilar cholangiocarcinoma in particular, manifest a distinct male predominance. This is in marked contrast with carcinoma of the gallbladder which occurs up to 4 times more frequently in women.(4) This difference is due to the fact

that unlike carcinoma of the gallbladder, cholangiocarcinoma is not directly related to the presence of gallstones. Plausible causative factors include the carcinogenic action of cholic acid, evolution from benign glandular papilloma, Giardia Lamblia infestations and Sarcoidosis.(4)

Jaundice is undoubtedly the commonest presenting feature as biliary obstruction is inevitable with these tumours (fig.3). In those cases presenting with right subcostal pain, anorexia or fever, (3,7,8) jaundice invariably appears within the first 8 weeks from the onset of symptoms. Hepatomegaly (3,7) and laboratory findings of biliary obstruction with secondary liver damage though invariably present contribute very little to the diagnosis.

Due to the position of the tumour, the diagnosis of hilar cholangiocarcinoma is frequently not made in patients submitted to laparotomy. Seventy five per cent of Klatskin's original series, had undergone an

Fig 1. Distribution of cholangiocarcinoma by sex

Study	No of cases	Males	Females	Ratio Males : Females
Sako et al*	433	264	169	3 : 2
Klatskin	13	9	4	9 : 4
Tompkins et al	96	-	-	3 : 2
Beazley et al	31	20	11	2 : 1

Study of Cholangiocarcinoma in general excluding Carcinoma of gall bladder and the Ampulla of Vater

Fig 2. Age distribution and means in various studies reviewing Klatskin tumour.

Study	Age range	Mean
Klatskin	29 - 88 yrs	58.2 yrs
Launois et al	41 - 81 yrs	62.2 yrs
Beazley et al	33 - 71 yrs	54.5 yrs

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Fig 3. Predominant presenting symptoms and signs

	Jaundice	Pain	Nausea	Diarhoea	Hepatomegaly
Klatskin	92%	46%	38%	38%	77%
Launois et al	100%	48%	-	-	-
Beazley et al	100%	16%	22%	13%	66%

inconclusive laparotomy. In recent years the practice of performing an exploratory laparotomy in obstructive jaundice has been almost universally abandoned because of the availability of sophisticated pre-operative investigative procedures which allow accurate diagnosis and more appropriate surgical planning. Beazley reports a 100% pre-operative diagnostic accuracy with an ordered use of ultrasonography, percutaneous transhepatic cholangiography (PTC) and endoscopic retrograde cholangiopancreatography (ERCP).

The tumour takes 3 pathological forms: a papillary lesion within the duct lumen, a nodular mass involving a portion of the duct, or a diffuse sclerotic lesion with duct wall thickening over an extensive area, indistinguishable from sclerosing cholangitis.(3)

The majority of these tumours are well differentiated adenocarcinomas, small in size, fibrotic in character and have a tendency to remain sharply localised giving few and small sized metastases. Though present these invasive lesions do not appear to play a significant role in fatality from the disease, the tumour kills by virtue of its inaccessible position which causes complete biliary obstruction with rapid and progressive hepatic failure.

TREATMENT OPTIONS

The place of resection for attempted cure of hilar cholangiocarcinoma is strongly debated, as are resectability and mortality rates. Resectability is mainly determined by the availability of expertise in major hepatobiliary surgery and by the presence of vascular involvement. Compression or invasion of the main trunk of the portal vein, or involvement of the portal vein in one lobe and of the contralateral arterial supply, are definite indications of irresectability.(9) On the other hand, as demonstrated by Beazley et al,(7) involvement of both the hepatic artery and portal vein on one side, may be compatible with resection, as the lobe, tumour, portal vein and hepatic artery on that side may be removed en bloc. Pre-operative arteriography and venoportography, which have been favoured in some

centres, (10, 11) while useful in planning treatment, cannot always predict vascular invasion. In fact, out of 13 cases operated by Blumgart with preoperative investigations indicative of resectability, only 8 were in fact resectable at operation.(5) This experience is shared by other specialist hepatobiliary centres where the majority of these tumours are deemed irresectable at operation. (6,7,8).

Surgical procedures for these tumours are either palliative or potentially curative. Palliative procedures include:

1. Segment III hepaticojejunostomy
2. Roux-en-Y hepaticojejunostomy
3. U-tube hepaticojejunostomy
4. Transtumoral stenting using "T-" or "U-" tubes.

The potentially curative procedures include:

1. Excision of common hepatic duct tumour with or without hepatic segmentectomy IV with Roux-en-Y hepaticojejunostomy or
2. Excision of common hepatic duct tumour with hepatic lobectomy if ipsilateral portal vein or hepatic artery are invaded.(5)

These curative procedures are in general performed only in specialist hepatobiliary centres. The overall mortality for palliative and radical surgical treatment ranges from 11 to as high as 53%. However, comparing palliative procedures with radical surgery, one notes that while radical surgery has a mortality ranging from 11% to 23%, palliative treatment is associated with higher mortality rates of the order of 24% to 53% (fig.4). Furthermore according to Pitt et Al, (12) in biliary tract surgery a 44% mortality is to be expected in the presence of malignant obstruction, albumin below 30g/100ml, haematocrit of less than 30%, a total bilirubin level higher than 10mg/100ml and raised alkaline phosphatase. Yet, despite the fact that almost all these patients have these risk factors, increasing world-wide experience with major hepatobiliary surgery of this nature, is achieving progressively lower mortality rates. Preoperative percutaneous transhepatic decompression, which relieves the jaundice and improves hepatic

function prior to surgery, has been employed and advocated by several authors. (13-17)

Although theoretically very attractive, septic complications of this form of drainage have been found to contribute to increased postoperative morbidity and mortality. Blumgart actually abandoned a long term trial of preoperative biliary drainage because of serious septic complications which were adversely affecting the survival rates of patients subsequently undergoing resection. Mean survival times vary between 5.5 and 7.6 months for palliative treatment and 17.3 and 18.4 months for radical resection. Forty five per cent of Launois (8) series were still alive at the time of writing their review, with survival times ranging from 5.5 to 17.3 months. A similar percentage of 40% was reported by Beazley et al.(7) with a range of 10 to 57 months. While survival times are useful to compare the effectiveness of a procedure, the quality of survival is of importance when considering the benefits to the patient of undergoing such a procedure. The quality of survival was assessed by Beazley et al,(7) by interviewing the patients or a relative in the case of a non-survivor, and then categorising the patients into one of the following 3 groups:

- a. WELL: patients who were free of any signs of their disease, maintaining weight and active or working.
- b. FAIR: patients who occasionally had signs of cholangitis, decreased appetite and mild weight loss but were active and still managing selfcare.
- c. UNWELL: patients who were essentially bedridden by recurrent jaundice, infections or with significant weight loss and unable to care for themselves or were hospitalised.

This study showed that patients after radical resection were considered well 88% of the time as compared to those following palliative procedures, who were considered well for only 7% of the time. The latter group were in fact unwell for 40% of the time. In post resection patients the usual causes of death are tumour recurrence (7) and ascending cholangitis (4).

CASE REPORT

In the light of the international experience in the surgery of hepatic duct confluence cholangiocarcinoma presented above, the first case to be treated by aggressive curative surgery in Malta will now be reviewed.

The patient was a 71 year old Maltese male and returned migrant, who smoked 60 cigarettes a day till 17 years previously. He presented with a 2 month history of pruritus and 2 weeks of deepening jaundice, in May 1987. He had noted marked anorexia and significant weight loss and episodes of right upper quadrant pain. On examination he was deeply jaundiced, with right subcostal tenderness and he had a smooth, moderately enlarged liver. The laboratory findings were those of cholestatic jaundice with secondary hepatic parenchymal dysfunction, and severe hypoalbuminaemia was evidenced by a level of serum albumin of 21mg/dl.

Ultrasound examination of the biliary tree, revealed no gallstones and no dilated ducts, but on CT scan, dilated, intrahepatic ducts were noted in the absence of visible common bile duct dilatation. These findings corresponded to proximal intra or extrahepatic obstruction of the biliary tree. A percutaneous transhepatic cholangiogram was performed and this confirmed a hilar cholangiocarcinoma of the Klatskin's type involving both hepatic ducts and apparently occluding their proximal first order bifurcation (plate 1).



At this stage vascular involvement of the hepatic arteries and portal vein was excluded by means of selective coeliac axis angiography and venous phase venoportography. The right hepatic artery and the portal vein were compressed but not obviously infiltrated by tumour. Attempts were made preoperatively with plasma and albumin transfusions to raise the serum albumin above 17mg/dl (a level reached during the investigative period), which was far too low for a successful outcome from radical surgery to be likely but no significant improvement could be obtained and surgery was undertaken in the presence of severe hypoalbuminaemia. Similarly, the patient's clotting abnormalities were not correctable despite high doses of Vitamin K1 during the preoperative hospital stay. Appropriate amounts of fresh frozen plasma

and platelet concentrates were made available to reduce bleeding tendencies during surgery.

OPERATION AND OPERATIVE TECHNIQUE

The operation was performed by the senior author on 30th June 1987 and consisted of resection of hepatic segment IV for exposure of the tumour and radical resection of the tumour with a second order quadruple hepatic duct Roux-en-Y hepaticojejunostomy. The extent of surgery could only be decided on the table as angiography does not completely exclude vascular invasion.

The peritoneal cavity was approached employing a roof-top incision, Couinaud hepatic segment IV was identified (fig.5a). Transverse transection of the parenchyma was followed by the opening of the anterior part of the main scissura (fig.5b), and then the umbilical fissure was opened. All portal pedicles entering the posterior part of the quadrate lobe were ligated and the hepatic segment removed. This exposed the tumour at the hepatic duct confluence up to the second order bifurcations. The gallbladder was then removed and the common bile duct transected (fig.5c). The CBD was then used to retract and dissect the tumour off the portal vein. At this level the tumour was densely adherent to the vein and dissection was very difficult. Once the tumour was freed from the portal vein and hepatic arteries, the second order hepatic ducts were divided (fig.5d). A Roux-en-Y jejunal loop was brought up and the pedicles of the four intrahepatic ducts anastomosed to the loop (fig.6).

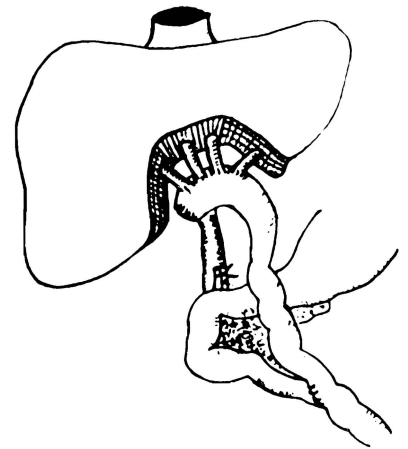


Fig 6 Schematic representation of the reconstruction following tumour resection.

The operation lasted a total of 5.5 hours with a blood loss of around 3000ml. Postoperatively the patient was transferred to the ITU where his condition remained stable, though repeated plasma and factor IX transfusions were needed in an attempt to correct the severe hypoalbuminaemia and his bleeding tendency which persisted for 48 hours post-op. On the 5th day post-op the patient was transferred back to the general surgical ward.

Pathologically the tumour appeared greenish brown and was of the sclerosing variety. Microscopically the tumour was formed of atypical ductal formations some of which were compressed by the surrounding fibrocollagenous tissues. The pathologist confirmed classical sclerosing confluence cholangiocarcinoma of Klatskin's type.

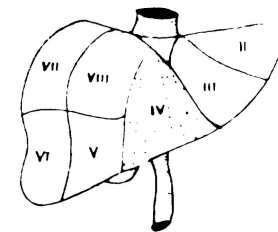


fig.5a

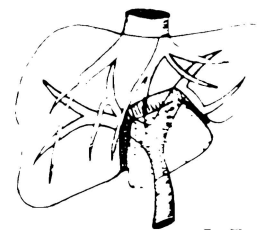


fig.5b

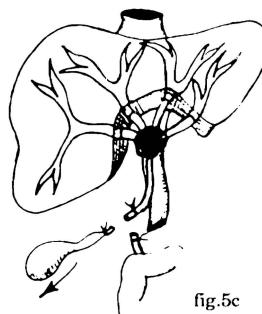


fig.5c

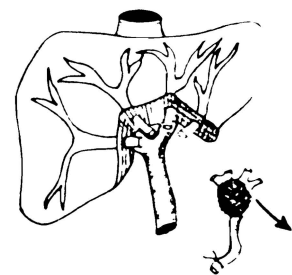
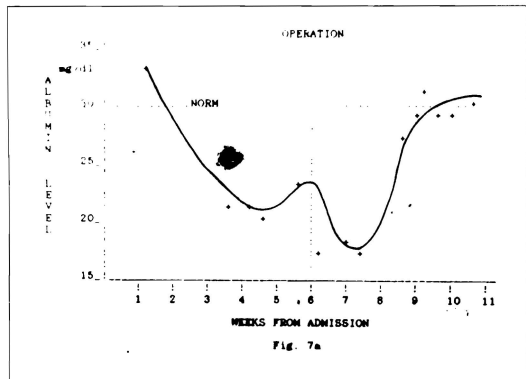


fig.5d

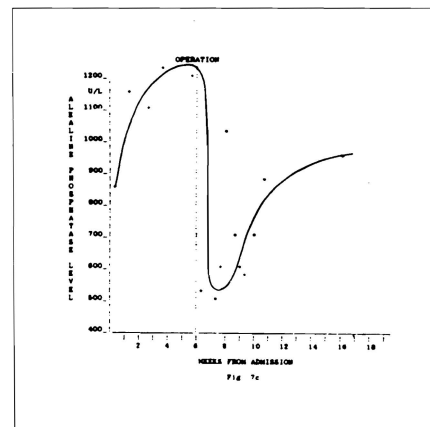
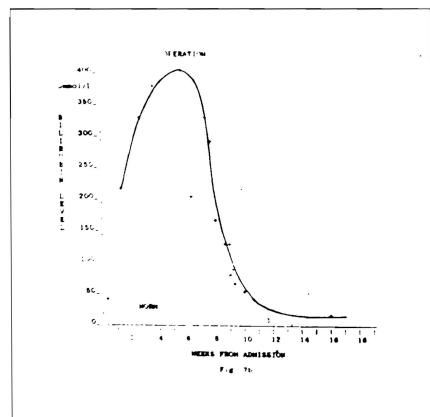
four steps showing the operative technique. Fig 5A hepatic segments with segment IV shaded; Fig 5B, excision of segment IV; Fig 5C exposure of tumour with ligation and transection of the common bile duct and cystic duct, Fig 5D tumour dissected and excised leaving for second order hepatic duct pedicles.

RESULT

During the subsequent postoperative period repeated plasma transfusions were given and by the end of the first week, the albumin level started to rise (fig.7a). By the



2nd week the albumin level had reached normal values. The bilirubin level started to fall during the first few days postoperatively and reached normal levels by the 6th week (fig.7b). The alkaline phosphatase showed a sharp drop during the first week post-op, falling from 1200 units pre-operatively to 500 units after the first few days, but subsequently it continued to fluctuate for many months, though the general trend was downwards (fig.7c).



There were no postoperative complications and the patient was discharged with a normal albumin level and in good health 40 days postoperatively.

Since discharge he has been followed up regularly with the last visit he was enjoying good health, had markedly improved appetite and was somewhat overweight. His albumin and bilirubin levels were normal, though his alkaline phosphatase continued to fluctuate for 15 months. He has no signs of recurrent disease and is maintaining a normal, very active life 853 days (28 months) after operation, fitting comfortably into Beazley's WELL category. A CT scan performed 15 months after surgery confirmed absence of local recurrence or metastases.

CONCLUSION

An aggressive surgical approach aiming at tumour resection rather than palliative bypass surgery is likely to achieve excellent disease free survival which has now already extended to 28 months in this first case to be performed successfully in Malta. A high mortality and morbidity are to be expected as evidenced by international experience from major hepatobiliary centres, but untreated these patients die of progressive hepatic failure in a matter of weeks.

ACKNOWLEDGEMENTS

Sincere thanks go to Dr. J. Cacciattolo to Dr. N. Azzopardi to Professor M. Camilleri to Dr. J. Zarb-Adami and the ITU team to Dr. Bernard Coleiro who were also involved in the patient's care.

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Fig 4. Mortality rates of palliative and radical procedures

Percutaneous palliative drainage		30 Day Mortality (%)	
Dooley et al (1981)		30	
Burcharth et al (1981)		30	
Mueller et al (1982)		33	
Lorelius et al (1982)		52	
Endoscopic palliative drainage		30 Day Mortality (%)	
Cotton (1982)		20	
Hagemuller et al (1982)		53	
Tytgat et al (1983)		24	
Radical resection		30 Day Mortality (%)	
	Local Resection	Major Liver Res.	Overall
Launois et al (1979)	25	14	18
Tompkins et al (1981)	--	--	23
Blumgart (1984)	0	16	11

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