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Management of Cholangiocarcinomas in Developing Countries. : Report of Seven Cases and Review of Literature.

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Background: ***Cholangiocarcinomas are primary malignant tumours developing from the epithelia of the biliary ducts from the liver to the end of the bile duct in the duodenum. The objective of this review was to share our experience of seven well documented with this condition out of eleven observations treated at the Lusaka University Teaching Hospital (UTH) and point out the impact of palliative surgery played to provide comfortable quality survival.***

Methods: ***This was a ten-year retrospective study all patients operated on at the Lusaka University Teaching Hospital with confirmed diagnostic of cholangiocarcinoma. Seven well documented cases out of eleven treated were considered for this study.***

Results: ***Of the seven patients diagnosed with cholangiocarcinoma, four were males and three were females with ages ranging from 57 to 68 years and mean age of 64 years. At the time of admission, painless obstructive jaundice, with loss of appetite and loss of weight were recorded in 5 of the 7 patients followed by chronic right upper quadrant pain (28.56%). Abdomen Ultrasound and CT Scan were performed only in two patients (28.56%) and the per trans hepatic cholangiogram in one patient(14.48%). Not any histological diagnosis was made pre or intra operatively. The findings and management outcomes are described.***

Conclusion: ***Despite the small number of these tumours (very rare worldwide) but by reviewing literature data, authors noted the severity of the condition related to long standing jaundice and co-morbidities, confirmed the challenge in diagnosis and therapeutic decision making . They encourage reasonable tumour resection and bile diversion as able to procure satisfactory survival as they had many twelve-month survivals after palliative surgery without free margins as expected in world literature. However they continue appealing for more modern medical imaging and histological diagnostic tools in their surgical facilities.***

Key words: Cholangiocarcinoma, Bile ducts, Gall bladder, Bile obstruction, biliary convergence, Surgery.

Introduction

Cholangiocarcinomas are malignant tumours of mutated epithelial cells of the biliary ducts from the liver to the duodenum[1]. These cancers of the bile ducts are rare: 1-2 cases/100.000 inhabitants in the Western world but seem increasing in some circumstances as stated by Landis et al[2], prevailing in people of 50 to 70 years old[3]. They always present serious diagnostic and treatment challenge since they usually grow slowly and spread gradually and are diagnosed in advanced stages[2, 4] making the prognosis poor worldwide with a 5-year relative survival estimated for intrahepatic bile duct cancer: 15% (localized), 6% (regional), 2% (distant) and for extrahepatic bile duct cancer: 50% (localized), 24% (regional), 2% (distant) as stated by American cancer society[5]. The usual chronic shortage of required management tools in developing countries enhances this challenge in our settings. The objective of the study was to analyze a ten-year experience on bile duct cancer at the Lusaka with regard to the management of these tumours and a 12-month postoperative follow-up.

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Patients and Methods

This was a ten-year retrospective study from 1/1/2001 to 1/11/2010 at the Lusaka University Teaching Hospital (UTH) including all patients undergoing surgery for cholangiocarcinoma. Authors served also as participant observers. The Lusaka UTH is the surgical catchment of Zambia and the tertiary referral of the country for all major in general and biliary tree cancer in particular. A total of eleven bile duct cancers were retrieved during the study period but only seven with well documented record with regard to targeted variables were considered with this study taking in account a twelve-month postoperative follow-up.

The study used a structured questionnaire including age, sex, ABO group, co-morbidities, risk factors, main complaints at the time of admission, clinical examinations findings, performed investigations and findings, surgical techniques as well as problems encountered in decision making, histological diagnosis and the twelve month-follow up with regard to complication and mortality. Despite the small number of patients, after data collection, variables were categorized among independent and dependent, compiled and presented on tables and diagrams.

Case Reports

The findings in the seven cases are summarized in the tables below.

Table 1. Case 1.

Features / complaints	**MB...NG.; F/62Y; DOA: 15/02/01; ABO group: A+**
Symptoms	Right upper quadrant pain; Loss appetite; Asthenia; Weight loss
Co-morbidities	High Blood pressure; Diabetes milletus/2; ASA:2
Risk factors	Cholecystitis; Gallstone
Signs	Right upper quadrant tenderness; Murphy test +; liver enlargement, High blood pressure
Laboratory tests	Hb/10,5g/dL; Bilrubin: 20µmol/L; ALP:40iu/L; Fast BS: 18mmol/L; HBSAg: negative
Medical Imaging	Plain Xrays: Right lung basal infiltration, Raised rightt diaphragm; Enlarged liver
Per operative findings and treatment	27/2/01: Right Gall bladder tumour evading liver, Perihepatic lymph nodes: Extended cholecystectomy to 5th , 6th liver segmentectomy+ clearance+ intraoperative cholangiographie through T tube
Outcome	Clavien 2 complications. Discharge on 11/3/01; last review 12months later; WHO score 2

KEY: Hb: Hemoglobin, BS: Blood sugar, ALP: Alkaline phosphatise, HBSAg: Hepatitis B serum Antigen. Ultra sound. PUD: Peptic ulcer disease. BP: Blood pressure

Table 2. Case 2

Particulars and complaints	**LUK.DAN ; M/57Y ; DOA 05/09/02. ABO group: B+**
Symptoms	Painless jaundice; Loss appetite; Asthenia; Weight loss
Co-morbidities	Drinker 20 years; Smoker 15 years; ASA: 3
Risk factors	Hepatitis B; Liver cirrhosis
Signs	Deep jaundice; Enlarged liver; Right hypochodrium mass; Murphy test+
Laboratory tests	Hb/9,5g/dL. Bilrubin: 600µmol/L ALP:70iu/L; HBSAg: positive
Medical Imaging done	Plain Xrays/ non specific infiltration of lungs, US: enlarged liver, dilated common bile ducts
Per operative findings and treatment	19/10/02: Exploratory laparatomy; Cholecystectomy+ clearance+ Ttube + Intra-operative cholangiogram; Intrahepatic peripheral and peri hepaticpedicle biopy: cholangiocarcinoma
Outcome	Clavien 2 Complications; Discharged on 11th November 2002; Last new 2nd month after discharge; WHO score 3; Death 3/12 postoperatively

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Table 3. Case 3.

Particulars and complaints	**CHI...PAT; F/64Y; DOA 17/07/04. ABO group: A+**
Symptoms	Puritis before Painless jaundice; Asthenia; Loss of appetite; Weight loss
Co-morbidities	Diabetes mellitus type 2; HBP ; Atenolol Alcohol (occasionally.); ASA: 3
Risk factors	Gall bladder stones (previous cholecystectomy)
Signs	Deep jaundice; Enlarged liver; Murphy test negative; BP: 160/90+
Laboratory tests	Hb/10,5g/dL; Bilrubin: 80µmol/L; ALP:90iu/L; FastBS 12mmol/L;
Medical Imaging done	US: Very dilated intra hepatic ducts. Transhepaticcholangio+++: dilatation of left and right intra hepatic ducts, not visualization beyond
Per operative findings and treatment	17/08/04: Thoracolaparotomy: Klatskin tumour; Hepaticojejunostomy (Y-loop end to side + biopsies)
Outcome	Clavien 2 Com-plications: bile leak+sepsis. Discharged on8 th//9/04 Last new 12 month after discharge: WHO score 3 ; Alive 12th month postoperatively.

Table 4.Case 4.

Particulars and complaints	**NK..CHA ; M/66Y ; DOA 11/06/05. ABO group: B+**
Symptoms	Painless jaundice; Puritis before; Loss of appetite; Asthenia; Weight loss
Co-morbidities	High blood pressure 15 years; Alcohol occasionally; ASA2
Risk factors	PUD on triple therapy for 6 years
Signs	Deep jaundice; Enlarged liver; Distended gall bladder, Murphy test positive; BP: 150/95+ Pulse rate 110
Laboratory tests	Hb/11g/dL. Bilrubin: 95µmol/L ALP:92iu/L; Blood culture: Kebsiella; AgHBS: negative
Imaging done	US: enlarged liver, acalculous gall bladder., Dilated bile duct from suprapancreatic area segment: Transhepatic cholangiogram informative+++:
Per operative findings and treatment	17/07/05: Exploratory laparotomy; Tumour excision +Choledoco-jejunostomy (Y loop end to side + biopsies); 4 units blood; Abdominal drain
Outcome	Clavien 1 Complications: Discharged on 3/8/05 Last new 12 month after discharge: WHO score 2 ;

Table 5. Case 5.

Particulars and complaints	**SE MUN ; M/65Y; DOA 27/07/07. ABO group: B+**
Symptoms	Painless jaundice; Puritis before; Asthenia; Loss of appetite; Weight loss
Co-morbidities	HBP for 8 years Alcohol (occasionally.) ASA3
Risk factors	Ulcerative colitis 6 years
Signs	Deep jaundice; Enlarged liver; Distended gall bladder, Murphy test positive; BP: 140/95+
Laboratory tests	Hb/10g/dL. Bilrubin: 90µmol/;L ALP:96iu/L; AgHBS: negative;
Medical Imaging done	US: enlarged, hetergenous liver, acalculous gall bladder; dilated suprapancreatic and intrahepatic ducts. CT Scan.informative+++
Per operative findings and treatment	15/8/2007: Exploratory laparotomy; findings: retropanceratic bile duct mass; Cholecysto-jejunostomy (Y loop end to side + biopsies); 4 units blood; Abdominal drain; biopsy
Outcome	Clavien 1 Complications: Discharged on 25TH August 2007 Last new 12 month after discharge:WHO score 3

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Table 6. Case 6 .

Particulars and complaints	ND..SHI ; F/65Y ; DOA 25/11/09 ; ABO group: A+
Symptoms	Right hypochondrium pain; Asthenia; Loss of appetite
Co-morbidities	High Blood Pressure; Duodenal PUD; ASA: 2
Risk factors	Right hypochondrium chronic pain: cholecystitis, gallstone
Signs	Right hypo-chondrium tenderness, Murphy test positive; Right upper quadrant mass, Raised blood pressure
Laboratory tests	Hb/10,5g/dL. Bilrubin: N ALP N Fast BS: 8mmol/L;
Imaging done	Chest Xrays + plain abdomen Normal
Per operative findings and treatment	27/2/01:: Exploratory laparotomy: Tumoral gall bladder with stones. Cholecystectomy. Intraoperative cholangiogram. Histology: Adenocarcinoma of Gall Bladder
Outcome	Clavien 1 complications.; Discharge after 1 week; Last review WHO score 1

Table 7. Case 7.

Particulars and complaints	**BA. FU; M/68Y; DOA: 22/4/10 /04/10. ABO group: O+**
Symptoms	Painless Jaundice 2/12;Puritis before; Asthenia Loss of appetite; Weight loss
Co-morbidities	HBP, Alcohol ASA3
Risk factors	Ulcerative colitis 6 years
Signs	Deep jaundice; Enlarged liver; Distended gall bladder, Murphy test positive
Laboratory tests	Hb/9g/ dL. Bilrubin: 100µmol/L ; ALP:98iu/L; AgHBS: negative.
Imaging done	US: enlarged hetergenous liver, acalculous gall bladder; dilated supra pancreatic and intrahepatic ducts. Abdomen CT Scan.informative+++
Per operative findings and treatment	17TH May 2010: Exploratory lap; findings; Retro pancreatic bile duct mass; Cholecysto-jejunostomy (Y loop end to side + biopsies); 4 units blood; Abdominal drain; biopsy
Outcome	Clavien 1 Complications: Discharged after 10 days. Last new 3 month after discharge:WHO score 3. Death 5 months post discharge

There were seven patients: four males (57.1%) and three females (42.9) with ages ranging from 57 to 68 years and mean age of 63.95 years. Males to Females ratio was of 4/3: 1.33. The patients' ABO groups ranged as follows: 3 A+ (42.9%), 3 B+ (42.9%) and 1 O+ (14.3%). At the time of the admission the prominent symptoms were: painless obstructive jaundice, with loss of appetite with or without pruritis in five patients (71.4%), followed by chronic right upper quadrant pain (28.6%).

All seven patients have co-morbidities (100%) with ASA classified at ASA3 for four patients (57.1%), ASA2 for three patients (42.9%); high blood pressure in six patients (85.71%); alcohol abuse in three patients (42.9%); diabetes mellitus in two (28.6%) and tobacco abuse in one (14.3%)

At least one risk factor of developing a cholangiocarcinoma was found in each patient (100%); history of gall stone or cholecystitis or cholecystectomy in three patients (42.86%); peptic ulcer disease in two (28.86%); liver cirrhosis in one (14.28%), hepatitis B in one (14.28%) and ulcerative colitis in one (14.3%)

The main physical signs were included deep jaundice (71.4%), enlarged liver (85.71%), right upper quadrant tenderness (42.9%), right upper quadrant mass (42.9%), high blood pressure at

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the time of admission (85.7%). Liver function tests confirmed the obstructive (71.4%) with raised conjugated bilirubin and alkaline phoshatase. Six patients (85.7%) had an haemoglobin rate lower than the normal. Only in three cases (42.9%) out of seven the real location of the tumour had been estimated by pre-operative medical imaging: transhepatic cholangiogram (third observation), Ultrasonography and CT Scan (fifth and 7th observations). Almost for all the seven cases (100%) the precise location was made during the operation with or without intraoperative cholangiogram that served also in checking the quality of the repair.

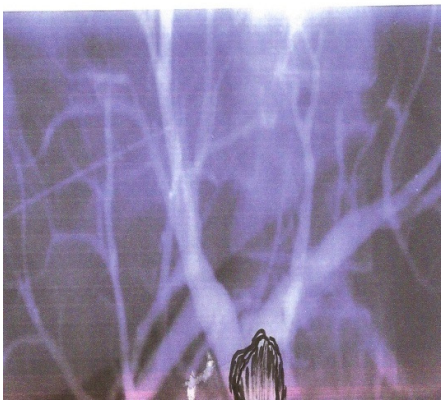

Figure 1. Transhepatic cholangiogram: hilar tumour without extension

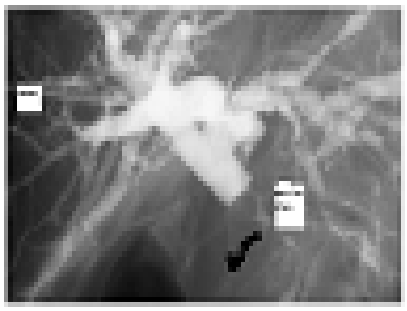

Figure 2. Transhepatic cholangigram: infra hilar obstruction

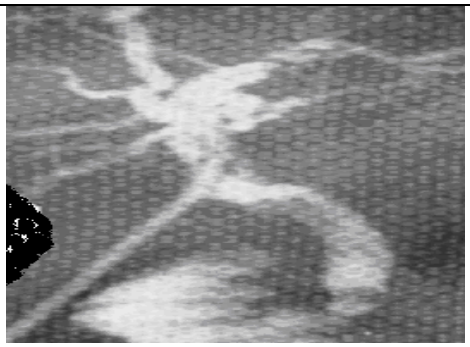

Figure 3 . Intra-operative cholangiogram: Slightly dilated bile duct. Absence of bile leak

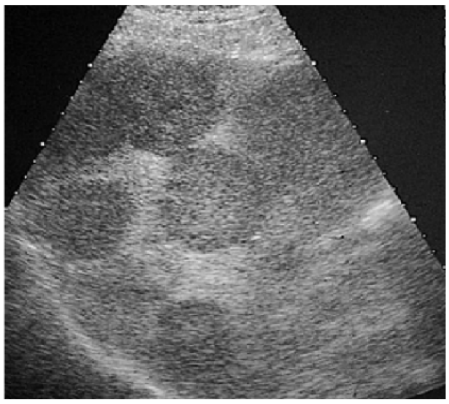

Figure 4. US: Low density liver metastases

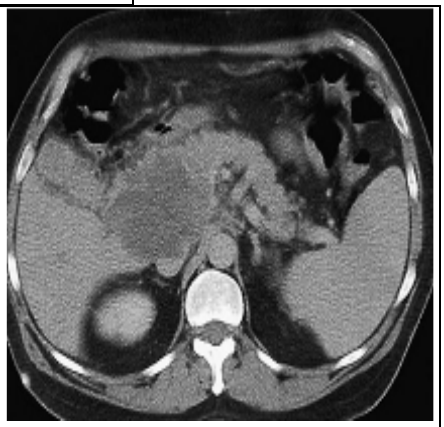

Figure 5. CTscan Tumour Head of Pancreas

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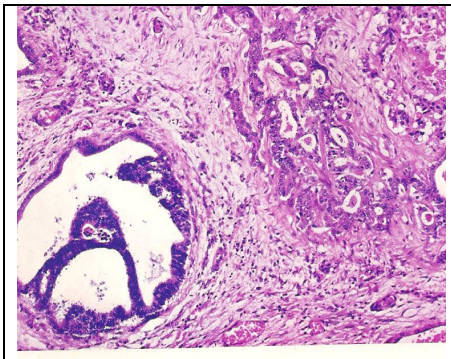

Figure 6. Well differentiated Cholangiocarcinoma (gall bladder) Observation 1

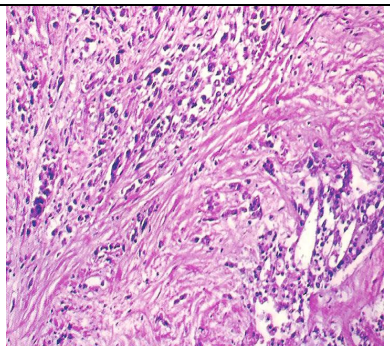

Figure 7. Poorly differentiated cholangiocarcinoma Intrahepatic duct bile . Observation 2

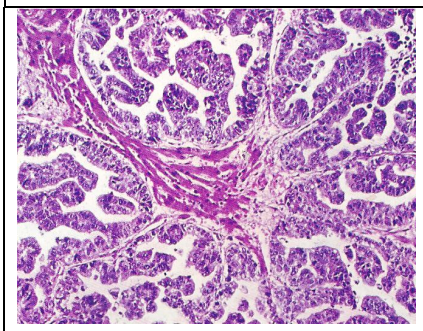

Figure 8. Cholangiocarcinoma: papillar type

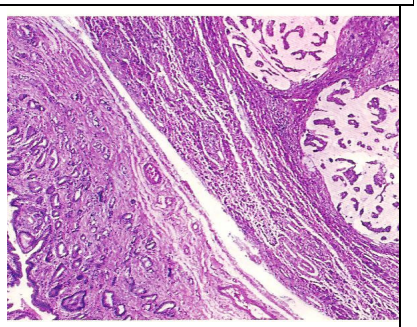

Figure 9. Bile duct carcinoma, mucine type

The intraoperative findings, procedures of treatment and outcomes are summarized in Table 8

Apart from one from the gall bladder tumour discovered on the piece of cholecystecomy done for cholecystitis, the six other cases were considered as advanced tumours with macroscopically distant deposit and performed surgery was assumed palliative. Palliative surgery and 12-month follow-up for the various tumours stood as follows: four patients were still alive on the 12th month review (longer survival than that from literature): one after an extended cholecystectomy for gall bladder cancer, a second after post cholecystectomy for gallbladder stone and tumour, a third after convergence tumour excision and hepaticojenostomy, a fourth after partial supra pancreatic bile tumour excision and choledoco-jejunostomy for an infra hilar and pre pancreatic biliary tumour and the fift after a cholecysto jejunostomy for retro-pancreatic bile duct tumour.

The death occurred in two other cases: three months after an exploratory laparotomy with biopsy of bilateral intrahepatic cholangiocarcinoma and the last after cholecysto-jejunostomy for retropancretic bile duct malignant tumour

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Table 8. Intraoperative Findings, Techniques, Early and Follow-up)utcomes

Case Nos	Intraoperative Finding	Technique	Intrahospital Complications	Discharge	12-month follow-up Complications
1	Gall bladder tumour Evading adjacent liver	Extendended cholecystectomy + 5th and 6th liver segmentectomy + intraoperative cholangiogram (Thoraco-abdominal approach)	Clavien 2	2 weeks post operatively	Alive on 12th month postoperative review WHO score 2
2	Hepatic mass + Lymphe nodes enlargments	Exploratory laparotomy + biopsy+ intraoperative cholangiogram	Clavien 2	3 weeks post operatively	WHO score 3 Deceased on 3rd month post operatively
3	Biliary congergence tumour	Convergence and tumor excision + hepatico jejunostomy: Y-loop end to side anastomosis+ biopsy +intraoperative cholangiogram (Thoraco-abdominal approach)	Clavien 2	3weeks post operatively	WHO Score 3 Alive on 12th month post operative review
4	Infrahilar bile duct tumour	Partial bile and tumour excision+ choledoco-jejunostomy (Y end to side anastomosis) + biopsies.	Clavien 1	3 weeks post operatively	WHO score 2 Alive on 12th month post operative review
5	Retropancreatic tumour, distended gall bladder	Cholecysto-jejunostomy (Omega loop side to side), biopsies	Clavien 1	10 days post operatively	WHO score 3 Alive on 12th month post operative review
6	Tumoral gall bladder with stone	Anterograde cholecystectomy Intraoperative cholangiogram	Clavien 1	7 days post operatively	Alert on 12th month post operative review
7	Retropancreatic tumour, distended gall bladder	Cholecysto-jejunostomy (Omega loop side to side), biopsies	Clavien 1	7 days post operatively	Deceased before the 6th month post operative review

All our cases were confirmed postoperatively by histological reports as shown in Figures 6-9.

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Discussion

Topographical Groups

Cholangiocarcinoma is a primary tumour arising from the biliary duct and not a metastatic deposit of another cancer or regional tumour evading or compressing biliary duct. Launois B et al[6] and Balladur et al[7] describe these tumours as extrahépatic tumours or extrabiliary ducts cancers and consider separately gallbladder cancers. As these tumours etymologically arise from an epithelial surface of duct (angio) containing bile (chole) we are of the opinion of calling all these tumors cholangiocarcinoma wherever biliary trees are found: in the liver (liver ducts) and in the gallbladder (cystic duct). Cholangiocarcinomas then represent a second group of primary biliary cancers beside the hepatocellular carcinoma arising from liver cells.

Based on the location, five types are described[4, 8]. These include:

1. Intra-hepatic peripheral cholangiocarcinoma: it may be uni or bilateral located in liver parenchyma but not involving the hilus;
2. Cholangiocarcinoma of the hilus (also called Klastkin tumour or tumour of the proximal third of the extra-hepatic biliary duct, most frequent location cholangiocarcinomas);
3. Middle third extra biliairy duct cholangiocarcinoma is a tumour of the segment of the bile duct between the cystic duct junction and the superior border of the pancreas and
4. Retro- or intra-pancreatic bile duct cholangiocarcinoma arises from the retropancreatic portion of the bile duct and its clinical diagnosis with the cancer of the pancreas is not easy and the cholangiocarcinoma of gall bladder.

With regard to hilar or Klatskin tumours (proximal third), Bismuth[9] and Bismuth et al[10] have described 4 types :

1. Main convergence free,
2. Main convergence interrupted ,
3. Main convergence interrupted + interruption of one secondary convergence ;
4. Interrupted major convergence and two secondary convergences

Another classification, MSKCC, the Type I is involvement of the convergence with or without unilateral extension

Our report is composed of one peripheral intrahepatic case (Case 2); one hilar case (a cholangiocarcinoma type MSKCC 1 without extension in case 3; one patient with an infra-hilar and supra pancreatic tumour in case 4); two retropancreatic cholangiocarcinomas (cases 5 and 7) and two gall bladder cholangiocarcinomas (Cases 1 and 6).

Frequency and Prognosis

In our study, the 7 documented cases were seen during a period of 10 years out of 684 digestive cancers diagnosed during the same period throughout all five units of visceral surgery. This gives a rate of less than one case per year and less than 1% digestive cancers. There were 4 males and 3 females. Four only were reviewed after one year postoperatively.

In worldwide literature, cholangiocarcinoma seems also a rare condition representing 1% of digestive system cancers and most prevalent in people ages 50 to 70, as observed by Balladur et al[7], Anderson et all[4] and Kim et al[8]. However, Patel[11] noted that mortality from biliary tract malignancy was rising last decades and considered the condition incurable and rapidly lethal

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unless both primary and possible metastases can fully excised. All these authors currently, the main objective is to obtain a margin negative resection in selected patient for expecting a survival of more than 12 months. Our survival of more than 12 months without margins free or after simple bile diversion encourage for palliative surgery

Pathogenesis and Risk Factors

As for other malignant tumours, aetiology of biliary duct cancers is unknown. However, factors able to facilitate the development are known as well as the major co-morbidities. Gallstones were found in three of our patients (Cases 1, 3 and 6). There was also history of peptic ulcer disease in two patients (Cases 4 and 6) and of ulcerative colitis in two others (cases 5 and 7). One patient had liver cirrhosis (Case 2). As co-morbidities we found in our patients mainly: high BP, diabetes mellitus; chronic alcoholism and smoking.

The most cited factors by Balladur et al[7], Anderson et all[4] and Kim et al[8] were sclerosing cholangitis, bowel chronic inflammatory disease, biliary ducts papillomatosis, Caroli's disease, biliary ducts congenital cysts, cholecystolithiasis and cirrhosis. Leone et al[12] have advocated the role an epidermal growth factor receptor might place. Kim et al[8] have emphasized on the place of immune suppressive networks.

Macroscopically cholangiocarcinoma appears as a nodular or sclerosing lesion and rarely as a papillary tumour. The histological type is usually a well differentiated adenocarcinoma (Balladur[7], Anderson et al[4] and Mayo Foundation[3]). More of our cases were nodular and the histology type well differentiated. We had also some poorly differentiated cases.

Clinical presentation Clinical presentation Clinical presentation depends on the location and the stage of the tumour. Asymptomatic type may be found in liver and in the gall bladder. The diagnosis will be in this case a result of histology of liver biopsy done for another reason or on a specimen of cholecystectomy performed e.g. for cholecystitis.

A gall blabber cancer is generally suspected before complaint of long standing right hypochondrium pain in an old patient (mainly a woman). The clinical diagnosis is based on right hypochondrium mass indistinctive from the liver. The jaundice that may occur in advanced gall bladder cancer is secondary to either extra-hepatic biliary duct (tumour or adenopathies) or to the liver evasion by the tumour. Ultrasonography followed or not by CT scan may confirm clinical impression [Balladur P (7); Anderson CD et al (4), Slattery JM (13), and Mayo Foundation (3). The preoperative histology may be obtained on ultrasound or CTscan guided percutanous biopsy[Tomkins RK (14) and Mayo Foundation(3)]. In our case n01, the lack of above mentioned diagnostic methods, we could only rely on clinical experience with some indirect signs from chest and abdominal X-rays. Being the lack of frozen section, the histology result was known one month after operation. The case N06 was likely a good case discovered as cholecystitis on stone without liver evasion.

Peripheral intra-hepatic symptomatic cholangiocarcinoma is usually diagnosed later[Tomkins RK (13) and Mayo Foundation(3)]. In the beginning, symptoms and clinical signs are those of the hepatocellular carcinoma and based on enlarged liver. This hepatomegaly is of variable size, nodular, hard, tender with ascitis of rapid growth. Sooner than in hepatocellular carcinoma occurs obstructive cholestasis The jaundice may follow obstruction of intrahepatic ducts or compression of extra-hepatic ducts by peropedicular lymphadenopathies as in our case n02. Biological and morphological investigations are necessary to confirm the diagnosis. For the same tumour volume, the obstructive cholestasis is higher in choloangiocarcinoma than in hepatocellular carcinoma (total Bilirubin with predominant of conjugated Bilirubin; Alkaline phosphatases). The AFP in contrary is higher in hepato-cellular carcinoma than in cholangiocarcinoma. The embryonic carcino antigen (ECA) is less specific than the AFP. The

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morphological investigations are very useful to analyse the impact of tumour on the liver, the biliary and portal ducts. They are done mainly by ultrasound, CT Scan and IRM

In our observation N02, the diagnosis was done on liver and pedicle lymphatic biopsies performed during an exploratory laparotomy carried out for obstructive jaundice mainly caused by per pedicle lymphadenopaties. The only pre-operative morphphological investigations available were chest and plain abdominal X-rays and ultrasound. This latter showing dilated bile duct justified the laparotomy that allowed performing liver biopsies of nodular hepatic lesions.

Extra-hepatic choloangiocarcinoma, from the hilus to the duodenum, presents a similar clinical feature of a painless, gradually increasing and apyretic obstructive jaundice. It is generally preceded one or two months before by a diffuse pruritis. It is accompanied with alteration of patient's general condition: loss of appetite and loss of weight. During the evolution, biliary sepsis (angiocholitis) may add to the picture abdomen pain, fever and shillings. Physical examination notes scratching lesions and may confirm Courvoisier's law if the tumour is beyond the cystic duct junction.

Biological findings are those of the surgical jaundice (bile retention): increase of alkaline phosphatases, gamma GT, bilirubin (conjugated bilirubin). Markers dosages (like ECA and AFP) are often negative.

Ultrasounds, CT scan and IRM confirm the existence of neoplasic obstructive jaundice as noted by Balladur P et al (7), Anderson CD et al (4),Slaterry JM (13) and Mayo Foundation (3): enlarged liver, dilatation of extra and intra-hepatic ducts. These three investigations may indicate the nature of the obstruction and possible hepatic metastatic or primary tumours. However better description of the biliary tree lesions are given by biliary ducts contrast study carried out during the jaundice by two special investigations: the percutaneous transhepatic cholangiogram (PCTHC) and the endoscopic retrograde pancreato-cholangiogram (ERPC). The PCTHC shows the upper site of the obstacle and the ERPC its lower configuration.

In our study, the ERPC could not be performed. Only the PCTHC was done in observations n0 3 and 4 and allowed to diagnose a Katskin tumour and an infra hilar and supra pancreatic mass. In observation n03, because the hilus was obstructed right and left catheterisation was necessary. To minimise its complication, it was performed the day of the operation, preoperatively. We must mention also the role plaid by intra-operative cholangiogram in our study. Coelio-mesenteric angiogram, endoscopic ultrasound, Doppler, IRM, SPEC were not available at the time of the study as well as the frozen sections during surgery. In the liver, it is necessary to rule out benign conditions like biliary adenoma, biliary cystadenoma, parenchyma harmatomas and connectine liver tumours. A biliary adenoma or benign cholangioma is rare and almost always benign and might be taken as a liver metastase. It is generally of small size. A biliary cystadenoma is also very rare. It is big size and grows slowly and frequently multiloculated on ultrasound and CT scan. The surgical treatment is advocated because it is hardly distinguishable with a cystadenocarcinoma. A parenchyma hamartoma is also a rare condition but big size, multicystic and lobulated in children or in young adult. The treatment is usually surgical excision. Connective liver masses may also be observed as hemangio-endothelioma, generalized lymphagiomatosis, lipoma, angiolipoma as observed at the CHRU Pontchaillon.

Principles of Treatment

More than half of our references are reporting various therapeutic methods dedicated to the treatment of cholangiocarcinoma. Evander A et al[15] evaluated the results from aggressive surgery. Imai K et al[16] compared surgery of intrahepatic cholangiocrcinomas. Kaiser et al[17] compared liver resection to transplantation in klastin tumor. The treatment in fact remains essentially surgical like in our cases. Other methods mentioned in literature include radiation

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therapy, experimental therapy and photodynamic therapy[3, 4, 7, 18]. The treatment varies with the location and the size of the tumor and how it grows and spreads.

Radiation therapy uses of high-energy X-rays to kill cancer cells and shrink tumors as neo-adjuvant (before surgery) or adjuvant (after surgery) using either **e**xternal-Beam Radiation Therapy (tele-radiotherapy) or **i**nternal Radiation Therapy (brachytherapy or curietherapy) using radioisotopes put into the area where the cancer cells are found through thin plastic tubes: brachy-radiotherapy). At the moment, there is no formal proof of radiotherapy effectiveness in increasing the survival duration or avoiding recurrences as noted by Buskirk et all[19], Grove et al[20], Balladur[7], Anderson et al[4], and Mayo clinic Foundation[3].

Experimental Therapy has been cited by many authors[4, 21, 22, 23]. Many types of drugs are being studied in clinical trials chemotherapy of cholangiocarcinoma, including e.g. docetaxed and topotecan and biological therapy or increase of immune system therapy. Photodynamic Therapy[4] is still another type experimental therapy using a specific type of light and photosensitizing agent to kill cancer cells. Cholangiocarcinoma sensitivity to chemotherapie is very low. However, combination of 5-FU and cisplatine has revealed useful in some cases. The combination between radiotherapy-chemotherapy need some prospective study.

Surgery offers the best mode of treatment[3, 4]. Unfortunately the majority of patients present with an unresecable tumour. So many options exist.

If the cancer is small and has not spread beyond the bile duct, the whole bile duct and the tumour are excised a new duct is made by connecting the duct openings to the intestine. Lymph nodes also are cleared and examined under the microscope (frozen sections). A cholangiocarcinoma of the gall bladder needs extended cholecystectomy (including peri pedicular lymph nodes clearance with appropriate liver segmentectomy if hepatic involvement as in our case 1. An isolated peripheral intrahepatic tumour without spread out the liver justifies a right or a left hepatectomy with lymph nodes clearance.

Many surgical procedures have been described for proximal third carcinoma [6, 10, 24,25]. An isolated middle third extrahepatic cholangiocarcinoma like in our case 4 and tumour excision and pedicular clearance with choledocojejunostomy. Rarely a retropancreatic tumour will lead to a cephalic duodenopancreatectomy with lymphe nodes clearance followed by the connection of the bile duct, stomach and pancreatic duct to a Y jejunum loop (Whipple-like procedure) . Total hepatectomy and graft is an option for tumours confined in the liver and cannot be removed right or left hepatectomy (without distant metastases), as noted by Balladur et al[7].

If the cancer has spread and cannot completely be removed and patient able to undergo surgery, palliative surgery is performed to relieve bile retention symptoms. This is done in some hilar tumours with free segment of right and left hepatic ducts and all infrahilar advanced cholangiocarcinomas. In our case 3, it was performed a bilateral hepatico-jejunostomy for type MCCK hilar tumour and in our case 5 a simple cholecystojejustomy was carried out for advanced retropancreatic tumour with liver metastases. In some advanced bile duct tumours with free hilum: some authors had performed as palliative surgery a direct liver-intestine diversion called hepatojejunostomy or hepato-entorostomy intrahepatic cholangio-jejunostomy or intrahepatic cholangio-enterostomy[9. 27, 28]. There exist in these operated cases for palliative surgery, some indications of use tubes left in situ or coming outside the body and very uncomfortable (transtumoral drainage or intubation). If stents are available and mainly if the patients are weak with no hope to cure them, percutaneous transhepatic cholangiography (PTC) and endoscopic

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retrograde cholangiopancreatography (ERCP) can be used to place plastic or metal stents, which help to relieve obstructions. The simple drainage of bile might be undertaken as to prepare the operation or as a palliative treatment while nothing else can be done for all advanced hilar or infra liver obstruction. A preoperative drainage as noted by Mc Pherson et al[29] and Terblanche et al[30] may also be helpful.

Conclusion

Cholangiocarcinoma presents a real diagnostic and treatment challenge worldwide. These difficulties become crucial in developing countries where the chronic shortage of managerial tools does not allow an accurate diagnostic preoperatively for planning for a complex therapeutic procedure consisting on margins free resection of tumour and bile duct with appropriate bile diversion.

However surgeon's clinical and therapeutic experience play a real role in offering some hope to these patients: with correctly performed surgical procedures for bile diversion, since other therapeutic means are still to consider as clinical trials. Five 12-month survivals reported in study (more than expected in worldwide literature) by reasonable resection with bile diversion without free margins are encouraging in this way. Authors still appeal for more modern medical imaging and histological tools in their settings.

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