

New development of biliary surgery in China

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CHARACTERISTICS OF BILIARY CALCULOUS DISEASES IN CHINA: THE CHANGING SCOPE

Diseases of the biliary tract in China is complicated with the prevalence of primary infection of the bile duct system. In the middle of the 20th century, biliary infection, biliary parasitic infestation, and biliary stones made up the three chief components of biliary diseases in China. As to the calculous diseases of the biliary tract, the relative incidence of primary bile duct stones accounted for 50% of the total cases. Therefore, calculous disease accounted for 60.1% among 228 surgical cases in the Chongqing Southwest Hospital, and 60 of the 80 common bile duct stones were primary bile duct origin (including primary intrahepatic duct stones)^[1,2].

Among 2390 autopsies in Chongqing area, 50 cases were found to harbor stones in the biliary tract, and intrahepatic stones accounted for 38% of the cases^[3]. Furthermore, among 2398 cases of biliary calculous disease reported in the Chinese Journal of Surgery and analyzed by Huang Chia-Su, 36% were with gal lbladder stone, 14.3% with secondary bile duct stones and 49.3% with primary bile duct stones (including intrahepatic stones)^[4]. These findings witnessed the importance of primary bile duct stones, especially the intrahepatic stones, in the surgical treatment for biliary calculous diseases in China.

In the years of 1983-1985, we conducted the first nationwide survey under the sponsorship of the Chinese Surgical Association, totally 11342 surgical cases of gallstones were collected and analysed^[5]. The results showed that 52.8% were gallbladder stones, while 20.1% were primary bile duct stones

and 16.1% intrahepatic stones. The second survey was conducted in 1992, 10 years after the first survey, the results showed a further increase of relative incidence of gallbladder stones (79.9%) with the decrease of relative incidence of primary bile duct and intrahepatic stones (6.1% and 4.7% respectively). This trend of changes was mostly marked in the metropolitan cities^[6].

This change of the spectrum of gall stone disease in China was explained by: the improvements of people's living standard and sanitary conditions; and the widespread use of ultrasound for diagnosis and screening purpose.

Revisit of clinicopathology and surgical treatment of intrahepatic lithiasis

In general, there is a trend of decline in prevalence of intrahepatic stones accompanied with the decrease of new patient number. However, it is not a disappearing disease in China. Intrahepatic lithiasis complicated with biliary obstruction and hepato-biliary infection is still the most frequent cause responsible for the death from benign biliary diseases.

Intrahepatic stone is a common disease in East Asian countries. The prevalence is 4.1% in Japan. In 1986, Nakayama reported a prevalence of 53.5% in Taiwan, which is obviously deviant because of the limitation of data source. Recently, Su *et al* reported a retrospective review of 17182 cases with biliary calculous surgery performed over the years from 1971 to 1990 in 28 Chinese hospitals in Taiwan and found the prevalence of 20.3% for intrahepatic stones which was higher than 16.1% in mainland China^[7-9].

The classical clinical picture of intrahepatic stones is often a debilitated patient with wide spread intrahepatic stones, and has received a number of operations. Patients usually come to the hospital for treatment of severe complications. Surgery was often limited to control biliary infection. Therefore, in the analysis of 4197 cases of intrahepatic lithiasis collected from 71 hospitals in 1988, 90% of them showed hypoproteinemia, one third showed marked anemia, 37% had previous operations, more than 30% complicated with postoperative residual stones and serious morbidity complicated the postoperative course in 13% of the cases^[10].

Scanning electronic microscopic observations of the microvasculature of resected liver specimens that

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harbored intrahepatic stones revealed that there were marked changes of portal venules i.e. distorsion, narrowing and obliteration of the lumen together with extensive fibrosis and disappearance of liver parenchymal tissue. These changes were strictly segmental, confined to that segment where intrahepatic stones located and causing mechanical obstruction. Furthermore, these changes leading to the atrophy of liver parenchyma were irreversible in the late stage of disease^[11]. However, in the recent 10-20 years, owing to the wide spread use of antibiotics in the treatment of biliary infections and the improvement and accessibility of modern imaging facilities (BUS, CT scan, etc.), intrahepatic stones at its earlier stage with minimal infectious complications or clinical symptoms can be diagnosed with certainty. In the early stage, intrahepatic stone was often found to be a very localized lesion, strictly confined to one segment or two subsegments (most frequently the II and VI segment of Couinaud's classification), while the remaining portion of the liver was found to be normal grossly^[12].

Since hepatic lobectomy for the treatment of intrahepatic stones was advocated by Huang in 1958^[13], liver resection has become widely accepted as a routine for management of intrahepatic stones, especially those in the left lateral segment of the liver^[14-19]. In a survey of 4197 surgical cases of intrahepatic stones^[10], lobectomy or segmentectomy was used in 728 cases (17.3%). However, in those hepato-biliary surgical centers, adoption of liver resection for the treatment of intrahepatic stones was around 50% of the total operations, this was also true in the reports from hospitals in Taiwan and Hong Kong^[9,18]. But, if those data were subjected to detailed analysis, one would find that more than 85% of the liver resections were done on the left side of the liver. This is in disaccordance with the distribution of stone inside the liver, in which right side of the liver is not excepted. The main reason of the less use of right liver resection in intrahepatic stones is technical. A complete removal of intrahepatic stones requires a regular lobectomy or segmentectomy, it differs from those irregular resections commonly practised in the treatment of liver cancer^[12].

In 1994, the author advocated the use of systemic regular segmentectomy or subsegmentectomy in the treatment localized intrahepatic stones especially in right side of the liver. The operations were technically feasible and theoretically correct.

The results of surgical treatment of intrahepatic stones has been much improved in the past decades. However, the aim of complete cure still awaits solution of some serious problems such as residual

stones, recurrence and progressive liver damages. The types of surgical operations have been variable, but they can be categorized into three main types: liver resection, hepaticojejunostomy and cholelithotomy. Clinically they were often used in combination. We have evaluated the long-term results of surgical treatment of 959 cases of intrahepatic stones in a period of 40 years in the Southwest Hospital, Chongqing, according to three different periods (1963-1975, 1975-1981, 1983-1992). Satisfactory results were obtained in 73.9%, 80.1%, and 87.1% respectively^[6]. Therefore, results appeared to be improving, but, only half of the patients could obtain a complete relief from symptoms.

Among the surgical modalities, resection was found to give the best outcome, as demonstrated by a 91.16% success rate among 439 cases. This result has been proved by many other reports in China. Liver resection usually combined with hepaticojejunostomy to solve the problem of bile stasis, however, our clinical experience tended to favor resection alone for localized intrahepatic stones which might be more suitable for those earlier cases, since it might give better long-term benefit than combined hepaticojejunostomy.

THE PROBLEMS OF HEPATIC DUCT STRICTURES

Strictures of the large hepatic ducts as the results of inflammation and cicatrization was responsible for more than 80% of the surgical failures of intrahepatic stone operations^[20,21]. However, stricture of the hepatic duct is a common complication of intrahepatic stones, it was seen in 25% to 65% of surgical intrahepatic stone cases. In a review of 3938 cases of intrahepatic stones, stricture of the hepatic duct occurred in 6.96% to 41.94%, being 24.28% on an average^[4,10,20]. The strictured segment of hepatic duct was usually circumscribed and accompanied with destruction of elastic fibers, ductal and periductal fibrosis. Stricture of the hepatic duct was found more frequently in repeated bile duct operations.

As to the treatment of accompanied hepatic duct strictures, a series of novel operative procedures have been developed by the author^[18,21,22]. The basic surgical principles of these procedures include wide incision of the strictured site, excision of the stenotic valve and approximation of posterior bile duct wall to create a wide hepaticojejunostomy stoma by using the incised stricture segment as its posterior wall and the Roux-en-Y limb anteriorly. Such operation may be combined with hepatic resection to ensure complete removal of the lesion. It was called combined procedure.

Plastic operation on hepatic duct strictures

made a better result on surgical treatment of intrahepatic stone. Therefore, in 107 cases of intrahepatic lithiasis complicated with hepatic stricture, good result was obtained in 87.9% of the cases. In some cases, the combination of wide hilar incision and partial liver resection enables larger exposure of the bile duct over hepatic hilum. This wide incision may especially benefit the cases with widespread intrahepatic stones and markedly dilated intrahepatic bile ducts, and good results, whether evaluated on short-term or long-term base, can be anticipated^[23,24].

CARCINOMA OF THE BILIARY TRACT

Primary carcinoma of the gallbladder and the bile duct appeared to be more frequently seen in recent years. However, it is not certain whether there was an actual increase in case instances or only more of these patients were diagnosed correctly as a result of more availability of modern imaging facilities. In a nationwide survey of surgical cases of biliary tract cancer in 1989, 1098 cases were analysed^[25]. Extrahepatic bile duct cancer was found in 75.2% of the total cases, and gallbladder cancer accounted for 24.4%, with preponderance of bile duct cancer. While Shi from the Xi'an Medical University Hospital reported^[26] a retrospective analysis of 830 cases covering the past 40 years in the 7th National Biliary Surgical Conference held in Xi'an in 1997 that carcinoma of the gallbladder occurred in 72.4%, in comparison with 27.6% of extrahepatic bile duct carcinoma. This discrepancy reflected the variations of the disease prevalence in different portions of China.

CARCINOMA OF GALLBLADDER

Carcinoma of gallbladder accounted for about 1%-2% of cholecystectomies as revealed through analysis of 31 series totally of 2300 cases reported in the 7th National Biliary Surgical Conference, 1997. Other clinical characteristics of gallbladder cancer in China were: the female to male ratio 2:1, the average age was 57 years, and 60% of the patients complicated with gallstone. Zou in a second gallbladder cancer survey in 1999^[27], analysed 3776 cases, the prevalence of carcinoma of gallbladder was 0.4%-3.8% of gallbladder operations, averaging 1.96%. This result corresponds well with that obtained in 1997.

The prognosis of surgical treatment of carcinoma of gallbladder is still grave except in those lesions confined to Nevin I, II grade. According to Zou's report that the 3 and 5-year survival rate of Nevin IV, V grade tumors in 211 patients treated by radical cholecystectomy was 2.8% and 0% respectively, while among 189 patients treated with extended radical resection was

5% and 1.3% respectively. The main problem in the treatment of gallbladder cancer was the lack of early diagnosis, for most of the patients, even at the present, were still admitted to the hospitals with clinical triads (abdominal pain, abdominal mass and jaundice). Cholecystectomy for carcinoma of gallbladder in situ and in those patients with malignant changes of adenoma of the gallbladder carried an excellent result for long-term survival.

Both clinical and pathological observations support the concept of gall adenoma-carcinoma sequence, but how many primary gallbladder carcinoma came from adenoma is still unclear. Adenoma of gallbladder is often diagnosed as "gallbladder polyps" by ultrasoundists. In a survey of 341 cases of gallbladder polyp in 1989 by the author, cholesterol polyp accounted for 57.7%, inflammatory polyp 12.0%, adenoma 17%, myoadenoma 1.7%, hyperplasia 5.5%, and carcinoma 5.8%. In a series of 235 cases of gallbladder carcinoma, 23 was proved to be of malignant change of adenoma, accounting for 10% of the total cases of gallbladder carcinoma.

BILE DUCT CARCINOMA

Clinically, prevalence of carcinoma of the bile duct was found to be increased in recent years. In a review of cancer of the biliary tract, we are of the opinion that the entire bile duct system, for simplicity, may be divided into three parts, that is the intrahepatic bile duct, the hilar bile duct, and the extrahepatic bile duct. Hilar bile duct is the most common site of extrahepatic bile duct carcinoma (exclude the ampullary cancer), it covered 58%-75% of the total cases. The diagnosis of hilar bile duct cancer was difficult and the resectability rate was low, about 10% of the surgical cases. However, marked improvement was noted both in the preoperative diagnosis and the surgical treatment since the middle of the 80s due to the accessibility of modern imaging facilities, the earlier diagnosis, the better selection of operative patients, and the improvement in surgical technique. The resectability rate, at present, of hilar bile duct carcinoma has been increased to about 50% with a mortality rate below 5%. From 1986 to 1990, Huang ZQ from The General Hospital of PLA, Beijing reported a series of 50 cases of hilar bile duct carcinoma in which resection was completed in 31, with a resectability rate of 62% and no postoperative 30-day mortality^[28,29]. In the Fifth National Biliary Surgical Conference held in Guangzhou, 1991, 139 resections of hilar bile duct carcinoma were reported with a mortality rate of 0%-22%, being 5% on average. Furthermore,

recent reports from the Beijing Surgical Week, 1999, that in a period of 12 years (1987-01/1999-01), the General Hospital of PLA, Beijing, treated 157 cases of hilar bile duct carcinoma, 106 cases completed the resection, with a resectability rate of 67.5%. Among those resections, 59 (37.6%) were considered to be radical (no macro-or microscopic tumor residuals in the resected margins)^[30]. Another report from the Southwest Hospital, Chongqing, showed that from 1978 to 1997 totally 181 cases of hilar bile duct carcinoma were treated, in which 97 were resected, the resection rate being raised to 66.3% in the second period after 1991, and the radical resection rate was also increased from 18% to 38% after the year 1991.

Carcinoma of the hepatic duct bifurcation often known as Klatskin tumor, was considered to be a slowly growing malignancy and might be with a better prognosis. However, from recent experience, this conclusion has been challenged. The long-term result of surgical resection of hilar bile duct carcinoma has been far from satisfactory. The 5-year survival rate of the radical resection group was from 13.2% to 17%^[30,31]. Patients often died of local recurrence and hepatobiliary failure. Therefore, researches on the mode of recurrence in hilar bile duct carcinoma was undertaken by the author and his collaborators.

Coordinated clinical and pathological studies showed that metastasis of hilar bile duct cancer occurred rather early in the clinical cases. Therefore, in 32 cases of resections, metastasis was evidenced in 26(83.9%) of the cases, but the mode of spread was particular, such as nerve invasion in 57.7%, direct liver invasion in 42.3%, soft tissue infiltration in 42.3%, liver metastasis in 7.7%, and lymph node metastasis was only found in one case (1.8%). Histologically, 21 (65.6%) of the 32 resected specimens were well differentiated adenocarcinoma, 6 papillary adenocarcinomas, 3 were of low differentiation, and 2 carcinoma simplex^[29].

In 40 resected cholangiocarcinoma specimens, perineural space infiltration index (PNI) by cancer cells in relation to the median survival time was investigated, the result showed a reverse correlation (Table 1).

Table 1 Neural infiltration index and median survival time

Differentiation of tumor cells	PNI [*]	Median survival time (m)
Papillary	0.31±0.12	32
High diff.	0.39±0.18	13.5
Moderate diff.	0.74±0.39	10.8
Low diff.	0.85±0.41	7.2

*PNI>7.0=severe nerve infiltration.

In 78 surgical cholangiocarcinoma resection specimens (collected between 1989-1996), the significance of neural cell adhesion molecule (ECAM) in relation to clinicopathological findings was investigated, 68 of the 78 specimens showed nerve infiltration, blood vessels infiltration in 72, and lymphatic infiltration was present in 68. In 68 cases with neural infiltration, NCAM expression was found positive in 51 cases. Furthermore, a reverse relationship was found between the positive NCAM expression and the degree of tumor cell differentiation (Table 2).

Table 2 Expression of NCAM and tumor differentiation

Cell type	NCAM expression	
	(-)	(+)
Papillary	5	3
High diff.	10	12
Moderate diff.	8	16
Low diff.	3	21

$P=0.0267, \chi^2=9.20$

For further demonstration of the spread of cholangiocarcinoma cell along the perineural space, observations of computer assisted 3 dimensional reconstruction of the pathological section was performed in 2 cases, totally 110-200 slides were selected for reconstruction using a SHOW 3D image analysis system. The results showed that a dense net-work of small vascular and lymphatic channels together with a branching net-work of tumor infiltrates are in close relationship along the nerve fiber. By using the "wire framing" technique to visualize the structures, it was demonstrated that the tumor cells stayed sporadically in perineural space, lymphatics, and small vessels far from the primary focus of carcinoma. Probably, carcinoma cells involving a nerve at a place far from the original site must have reached there via lymphatics, vascular vessels or by direct invasion. These facts might be important in explaining the high recurrence rate of hilar bile duct carcinoma after conventional radical resections.

In a clinical pathological study of 40 resected hilar bile duct cancer specimens, a research group from the Third Military Medical University reported that 72.5% had near-by lymphatic invasion by the tumor, 77.5% showed blood vessels invasion within the tumor, 82.5% had perineural space invasion; the density of blood vessels inside the tumor and the perineural space infiltration index are positively correlated with metastasis of the cancer. In the presence of metastasis, 100% recurred within 3 years after the resection with an average of 9.6 months, while in the cases without metastasis, 64.3% recurred 3 years after the

resection with an average 17.5 months^[32].

INTRAHEPATIC LITHIASIS COMPLICATED WITH HEPATIC DUCT CARCINOMA

Since Sanes and McCallum (1942) first reported 2 cases of bile duct cancer complicating intrahepatic stones, sporadic cases reports were found in the world medical literatures. But, however, prevalence of bile duct cancer on the background of intrahepatic stones seemed to be increased in recent decade. Chijiwa from Japan reported 8 (7.3%) cases of hepatic duct carcinoma among 109 intrahepatic stones in 1973-1992^[33]. Chen (1993) from the Cheng Gang Hospital, Taipei reported 35 cases of bile duct carcinoma in 255 cases of intrahepatic stones in a period of 3 years duration (1988-1990)^[34]. In Mainland and China, hepatic duct carcinoma was found in 1.46% to 1.5% of intrahepatic stones operations as was reported by Huang (1981) and Guo (1995) from Chongqing. In the recent 6 series, of 661 cases of lobectomies for intrahepatic stones, 16 hepatic bile duct cancers were found, with a prevalence rate of 2.4%. Transition of hyperplasia and atypical hyperplasia from hyperplastic mucosa to bile duct cancer may be seen during pathological investigations^[35,36]. Carcinoma usually developed on the background of chronic biliary infection. Patients may have 10-40 years of biliary disease history and often had multiple operations including biliary enterostomy.

Hepatic duct carcinoma complicating intrahepatic lithiasis offered a very poor prognosis because of delay in diagnosis, and this is the another reason of advocating early resectional treatment of intrahepatic stones.

IMPACT OF LAPAROSCOPY ON CONVENTIONAL BILIARY SURGERY

Laparoscopic cholecystectomy was first introduced to China in February 1992. Presently, trained personnels and facilities are available in most parts of China. The largest series of patients treated by laparoscopic cholecystectomy in a single institution has been well over 20000. Almost 90% of gallbladder stone disease can be treated by laparoscopic cholecystectomy with minimal risk. In a review of 3986 cases of laparoscopic cholecystectomy from 28 institutes in 1992, the average bile duct injury rate (the most serious complication of cholecystectomy) was 0.31%. In a review of collected series of 39238 cases from 1992 to 1995 by Huang *et al*^[38] showed that the incidence of bile duct injuries was 0.32% and a biliary complication rate of 0.6%. Data of 142 946 laparoscopic cholecystectomies from 222 institutes collected in 1998 by Liu GL showed the bile duct injury rate dropped to 0.19% and the biliary

complication rate lowered to 0.14%. At present, the rapid development of medical technology, the tendency of minimally invasive operation and the application of laparoscopic cholecystectomy changed the leading position of conventional cholecystectomy as the "gold standard" of treatment for gallbladder stone disease since Carl Langenbuch in 1882^[38-40].

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