Diagnostic and surgical therapeutic features of extrahepatic bile duct carcinoma without jaundice

Hui-Huan Tang, Shi Chang, Xian-Wei Wang, Yun Huang, Xue-Jun Gong, Jun Zhou

MATERIALS AND METHODS
From January 1984 to December 1999, two hundred and thirty-nine patients who were diagnosed as extrahepatic bile duct carcinoma were admitted to Xiangya Hospital. One hundred and one were operated and the diagnosis was confirmed by pathology. Patients with carcinomas of gallbladder, intrahepatic bile duct and ampulla of Vater were excluded from the study. The patients under studies consisted of 58 males and 43 females, aged 27 to 76 years (an average age of 61.7 years).

According to the level of serum total bilirubin (STB), the patients were divided into non-jaundiced group (17 patients, STB ≤ 2.0 mg/dl at the time of diagnosis) and jaundiced group (84 patients, STB > 2.0 mg/dl). Clinical data included symptoms, laboratory results, imaging findings, pathological results, treatments and resectabilities.

Statistical analysis
The difference between the two groups was compared using chi-square analysis and Student’s t test. P < 0.05 was considered statistically significant.

RESULTS
Symptoms and signs
Fifteen (88.2%) patients in the non-jaundiced group had anorexia or and vomiting, abdominal pain compared with 63 (75.0%) in the jaundiced group. Eight (47.1%) patients in the non-jaundiced group and fifty-seven (67.9%) patients in the jaundiced group were found to show positive signs in liver, spleen or gallbladder enlargement. (Table 1).

Laboratory examination
The patients showed no difference in the levels of abnormal serum albumin, alkaline phosphates (AKP), γ-glutamyltranspeptidase (γ-GT), except STB level (Table 2).

Image examination
All patients in the non-jaundiced group underwent sonography. The results showed segmental stenosis of extrahepatic bile duct, thickening of the bile duct wall, and dilatation of intra-or extra-hepatic bile duct proximal to the stenosis. Sixty-seven out of 78 patients showed stenosis or neoplastic space-occupying lesions within the extrahepatic bile duct.

Operation findings
During the operation, 59 patients had neoplasms located in the upper extrahepatic bile duct while 8 in the middle and 34 in the lower. There was no difference with regard to localization of the tumor between the two groups.

Pathological features
All patients were proved to have adenocarcinoma. The patients were categorized into three different grades by the degree of differentiation. The results showed that there was no difference between the patients with or without jaundice.

Treatment
Radical resection, biliary bypass, external drainage or biopsy.
were performed according to the surgical findings. There was no difference in tumor resectability between the two groups (P>0.05, Table 3).

Table 1 Symptoms and signs

| Symptom                  | Non-jaundiced | Jaundiced | P value |
|--------------------------|---------------|-----------|---------|
|                          | No.           | %         | No.     | %      |
| Abdominal discomfort     | 15            | 88.2      | 63      | 75.0   | >0.05  |
| Liver or gallbladder     | 8             | 47.1      | 57      | 67.9   | >0.05  |
| Palpable cholelithiasis  | 11            | 64.7      | 26      | 31.0   | <0.05  |

No significant difference was found between the two groups in the clinical symptoms and signs. In the non-jaundice group, the rate of combined cholelithiasis was obviously higher than in the jaundice group.

Table 2 Laboratory data

|                      | Non-jaundiced | Jaundiced | P value |
|----------------------|---------------|-----------|---------|
|                      | No.           | %         | No.     | %      |
| Descending of HB     | 8             | 47.1      | 45      | 53.6   | >0.05  |
| Ascending of AKP      | 8             | 72.7      | 56      | 86.2   | >0.05  |
| Ascending of γ-GT     | 4             | 66.7      | 28      | 93.3   | >0.05  |
| Descending of ALB     | 4             | 23.5      | 39      | 47.0   | >0.05  |

No significant difference was found between the two groups in laboratory data.

Table 3 Tumor location, pathological type, treatment

|                      | Non-jaundiced | Jaundiced | P value |
|----------------------|---------------|-----------|---------|
|                      | No.           | %         | No.     | %      |
| Upper                | 11            | 64.7      | 48      | 57.1   | >0.05  |
| Location middle      | 0             | 0.0       | 8       | 9.6    | >0.05  |
| Lower                | 6             | 35.3      | 28      | 33.3   | >0.05  |
| Good                 | 6             | 35.3      | 48      | 57.1   | >0.05  |
| Differential mild    | 8             | 47.1      | 27      | 32.1   | >0.05  |
| Poor                 | 3             | 17.7      | 9       | 10.8   |         |
| Biopsy               | 3             | 17.7      | 8       | 9.5    |         |
| Treatment drainage   | 9             | 52.9      | 43      | 51.2   | >0.05  |
| By pass              | 0             | 0.0       | 1       | 1.2    |         |
| Radical              | 5             | 29.4      | 32      | 38.1   |         |

No significant difference was found between the two groups in tumor locations, pathological types and treatment methods.

**DISCUSSION**

Jaundice is the early and main manifestation of extrahepatic bile duct carcinoma. It has been reported to be the initial sign in 83-97% of patients[5-9]. However, there are few patients coming to hospital before the appearance of jaundice. These patients were likely to be neglected during busy outpatient service. We found that, there were still some clues to the diagnosis of bile duct carcinoma for these patients without jaundice. Some laboratory parameters, such as hemoglobin, serum albumin, AKP and γ-GT may be suggestive.

Sonography is almost the first tool for the diagnosis of extrahepatic bile duct carcinoma because it is non-invasive and less expensive. Ninety-five of the patients underwent sonography in our study, of whom 84 (88.4%) had positive findings, such as duct stenosis, thickness of the bile duct wall or space-occupying lesions within the duct. The results were in accordance with those documented in the literature[10-12].

The relationship between cholelithiasis and bile duct carcinoma is still unclear. As reported, 6-37% of extrahepatic bile duct carcinomas were associated with bile duct stones[13]. In the present study the number of patients who suffered from cholelithiasis in the non-jaundiced group was significantly higher than that in the jaundiced group (P<0.05). Two factors may contribute to this finding. First, for patients with bile duct stones, the clinical manifestations were so typical that the doctor would pay more attention to the biliary system. Second, during the operation for cholelithiasis, we usually took the whole layer of bile duct wall for biopsy whenever there was stenosis, sclerosis or nodular change in the bile duct. Eight patients were diagnosed by this means and radical resection was performed.

It was reported that extrahepatic bile duct carcinoma without jaundice occurred in the early stage of the disease. The tumor was well differentiated and the resection rate was usually high[9]. However, there was no difference between the two groups in our study. The radical resection rate was 29.4% in the non-jaundiced group and 38.1% in the jaundiced group (P>0.05). Liver and/or intrabdominal lymph node metastases were found in 12 patients without jaundice. We suggest that the presence of jaundice cannot be taken as the major criterion to predict the tumor resectability or the extent of tumor progression.

**ACKNOWLEDGEMENT**

We are grateful to Professor Zhong-Shu Yan for his assistance in preparing this manuscript.

**REFERENCES**

1. Helling TS. Carcinoma of the proximal bile duct. J Am Coll Surg 1994; 178: 97-106
2. de Groen PC, Gores GJ, LaRusso NF, Gunderson LL, Nagorney DM. Biliary tract cancers. N Engl J Med 1999; 341: 1368-1378
3. Chamberlain RS, Blumgart LH. Hilar cholangiocarcinoma: a review and commentary. Ann Surg Oncol 2000; 7: 55-66
4. Tsujino K, Landry JC, Smith RG, Keller JW, Williams WH, Davis LW. Definitive radiation therapy for extrahepatic bile duct carcinoma. Radiology 1995; 196: 275-280
5. Chung C, Bautista N, O’Connell TX. Prognosis and treatment of bile duct carcinoma. Am Surg 1998; 64: 921-925
6. Miyazaki M, Ito H, Nakagawa K, Ambrus P, Shimizu H, Shimizu Y, Kato A, Nakamura S, Ohtomo H, Nakajima N, Kimura F, Suwa T. Aggressive surgical approaches to hilar cholangiocarcinoma: hepatic or local resection? Surgery 1998; 123: 131-136
7. Suzuki M, Takahashi T, Ouchi K, Matsumoto S. The development of combined cholelithiasis and bile duct carcinoma: a three-dimensional tumor mapping in the intrahepatic biliary tree visualized with the aid of a graphics computer system. Cancer 1989; 64: 658-666
8. Sugiyama M, Atomi Y, Kuroda A, Muto T. Bile duct carcinoma without jaundice: clues to early diagnosis. Hepatogastroenterology 1997; 44: 1477-1483
9. Tamada K, Sugano K. Diagnosis and non-surgical treatment of bile duct carcinoma: developments in the past decade. Gastroenterol 2000; 35: 319-325
10. Choi BI, Lee JH, Han MC, Kim SH, Yi JG, Kim CW. Hilar Cholangiocarcinoma: comparative study with sonography and CT. Radiology 1989; 172: 689-692
11. Chou FF, Sheen-Chen SM, Chen YS, Chen MC, Chen CL. Surgical treatment of cholangiocarcinoma. Hepatogastroenterology 1997; 44: 760-765
12. Looser C, Stain SC, Bahr HH, Triller J, Blumgart LH. Staging of hilar cholangiocarcinoma by ultrasound and duplex sonography: a comparison with angiography and operative findings. Br J Radiol 1992; 65: 871-877
13. Schoenthaler R, Phillips TL, Castro J, Efrid JT, Better A, Way LW. Carcinoma of the extrahepatic bile ducts. The university of California at san francisco experimence. Ann Surg 1994; 219: 267-274

Edited by Wang XL  Proofread by Xu FM