

Carcinoma of the gall bladder – can we do anything?

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Summary: A retrospective review of 143 cases of carcinoma of the gall bladder is presented. The disease was more common in females in the 5th and 6th decades. Pain, anorexia, weight loss and jaundice were the common presenting symptoms, and hepatomegaly and palpable gall bladder the common signs. Laboratory and radiological investigations were merely confirmatory as the diagnosis in a majority of the cases was clinically obvious. Aspiration cytology and laparoscopic biopsy were of help in obtaining histological diagnosis. Only 47 patients were considered fit enough to undergo laparotomy. In a majority of these patients biopsy alone was possible while palliative procedures were performed in the others. The operative mortality was 18% even in this selected group of patients, due to the poor general condition and the advanced stage of the disease at the time of diagnosis. Curative resection may be possible and long term survival is expected in incidentally found carcinoma at cholecystectomy. The only hope lies in prevention by prompt treatment of patients with benign biliary disease.

Introduction

Carcinoma of the gall bladder is the most common malignant lesion of the biliary tract and the fifth most common malignancy of the digestive tract.¹ The disease has remained a diagnostic and therapeutic challenge. This is due to the late presentation of the disease, so much so that 70% of the cases are unresectable at the time of exploration.² In spite of tremendous advances in the fields of surgery and anaesthesia the outlook for carcinoma of the gall bladder remains dismal.

We have reviewed the clinical records of our patients with carcinoma of the gall bladder and analysed the data to define the clinical features of this elusive disease, to study the role of biochemical and radiological investigations in the diagnosis and to assess the role of various surgical procedures in the management.

Materials and methods

A total of 143 cases of carcinoma of the gall bladder were seen during a period of 5 years at the All India Institute of Medical Sciences, New Delhi. The clinical records of these patients were reviewed to obtain the following data: age and sex, presenting symptoms with duration and signs, laboratory

and radiological findings, operative details, types of operative procedures and their complications and results.

Results

The age of the patients ranged from 28 to 76 years (mean 44 years) with a majority of the patients being in the age group of 40 to 60 years. Fifty-five patients were male. The male to female ratio was 1:1.6. The duration of symptoms varied from 1 month to 18 months (mean 6 months). However, the majority of the patients presented within 3 months of the onset of the symptoms. Pain in the right upper quadrant was the most common presenting symptom, followed by anorexia, weight loss and icterus. Some patients presented with features of gastric outlet or intestinal obstruction (Table I). Clinical examination revealed jaundice, hepatomegaly and palpable gall bladder in most of the patients. The general condition of a large number of the patients was poor (Table II). Laboratory investigations revealed anaemia (136 cases), elevated serum alkaline phosphatase (120 cases) and raised serum bilirubin (92 cases). The serum albumin levels were less than 30g/l in about half the patients, indicating their poor nutritional status.

In 43 patients with an obvious clinical diagnosis no further investigations were performed due to

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Table I Symptoms (143 cases)

| <i>Symptoms</i> | <i>No. of cases (%)</i> |
|------------------------|-------------------------|
| Pain | 115 (80) |
| Anorexia | 110 (77) |
| Weight loss | 108 (76) |
| Jaundice | 86 (60) |
| Fever | 24 (17) |
| Pyloric obstruction | 3 (2) |
| Intestinal obstruction | 3 (2) |

Table II Signs (143 cases)

| <i>Signs</i> | <i>No. of cases (%)</i> |
|------------------------|-------------------------|
| Jaundice | 88 (62) |
| Hepatomegaly | 86* (60) |
| Palpable gall bladder | 82 (57) |
| Poor general condition | 68 (48) |
| Ascites | 20 (14) |
| Pedal oedema | 16 (11) |

*44 of these were nodular.

their very poor general condition. The remaining 100 patients were further investigated to confirm the clinical diagnosis. The investigations included abdominal ultrasound showing mass in the gall bladder area (24 cases), radioisotope liver scan showing multiple space occupying lesions (17 cases) and percutaneous transhepatic cholangiogram showing block at the porta hepatis with non-visualization of the gall bladder (28 cases). Laparoscopy provided the diagnosis in 27 cases while in 25 cases fine needle aspiration cytology revealed the malignant nature of the lump.

No operative procedure was performed in 96 patients because of poor general condition and the advanced stage of the disease. Only 47 patients in good general condition and who were thought to have early disease underwent laparotomy. Only biopsy was possible in 20 patients as the tumour was unresectable. Cholecystectomy was performed in 11 patients. In 7 of these the tumour was localized to the wall of the gall bladder whereas in 4 cholecystectomy was palliative due to local spread. In 4 patients adjacent involved structures were also removed along with the gall bladder. Bypass procedures (biliary or intestinal) were performed in 12 patients.

The liver was the commonest site of spread, being involved in 113 cases, followed by porta hepatis lymph nodes (73 cases) and omentum and peritoneum (32 cases). Local infiltration into the stomach, duodenum, ascending colon and common bile duct was observed in many patients. Haematogenous spread with metastases in lungs, skull and

chest wall (1 case each) was also noted. Two patients had an enlarged left supraclavicular lymph node as well.

Histopathological diagnosis was obtained in 76 patients. Seventy-two of the tumours were adenocarcinoma (60 poorly differentiated and 12 well differentiated). There were two squamous cell carcinomas, one adeno-squamous carcinoma and one angiosarcoma.

Sixteen patients died in hospital. Four patients died even before any investigations could be performed. Percutaneous transhepatic cholangiography resulted in death in 4 patients due to biliary peritonitis. Eight out of 47 patients who underwent laparotomy died – a mortality of 18%.

Discussion

Carcinoma of the gall bladder is the most common malignant lesion of the biliary tract.² The disease is more common in the fifth and the sixth decades of life and, like benign disease of the gall bladder, is more frequent in females. Carcinoma of the gall bladder is frequently associated with cholelithiasis but their relationship is controversial. The aetiological role of cholelithiasis has been emphasized by Hart *et al.*³ who have found a greater incidence of stones in patients with carcinoma than in the general population. The clinical data available today has not established a causative role for gallstones in the development of carcinoma of the gall bladder, although the association is sufficiently frequent to suggest common antecedents or at least a facilitative role.⁴ We are not able to comment further on the relationship of carcinoma of the gall bladder with gallstones as cholecystectomy was performed in only 15 of our cases.

The symptoms of carcinoma of the gall bladder mimic benign gall bladder disease until persistent pain due to invasion of the surrounding structure gives a clue to the correct diagnosis. Anorexia, weight loss and jaundice are common but occur late in the disease. Hepatomegaly (often nodular) and a palpable gall bladder lump indicate an advanced stage of the disease. A review of more than 6000 cases of carcinoma of the gall bladder by Piehler and Crichlow⁵ also records similar experience.

Laboratory investigations reveal anaemia, hyperbilirubinaemia and raised levels of alkaline phosphatase. The association of elevated alkaline phosphatase without hyperbilirubinaemia with carcinoma of the gall bladder has been reported and 42% of these patients were found to have resectable lesions.⁶

Of the radiological investigations, oral and intra-

venous cholecystography could not be performed because of jaundice. Percutaneous transhepatic cholangiography only indicates the site of obstruction in the biliary tract. However, obstruction at the porta hepatis with non-visualization of the gall bladder is suggestive, though not specific, of carcinoma of the gall bladder. Ultrasound and computed tomographic (CT) scan also suggest the diagnosis by showing a mass filling, replacing or protruding into the gall bladder or asymmetrical thickening of irregularity of the gall bladder wall.⁷

Laparoscopy⁸ has been used for diagnosis. Nodules over the gall bladder or the adjacent liver edge and hard nodular gall bladder covered with omentum are laparoscopic features of carcinoma of the gall bladder. Cytology and/or biopsy confirm the diagnosis. Laparoscopy can also indicate inoperability thus avoiding the high morbidity and mortality of unnecessary surgery. In our experience, laparoscopy confirmed the diagnosis in 27 cases and helped in planning the treatment. Percutaneous aspiration cytology of the gall bladder mass or the liver nodule revealed the diagnosis in 25 of our cases, thus avoiding laparotomy for obtaining histological diagnosis alone.

Histologically, the majority of the cases were poorly differentiated adenocarcinomas, suggesting the aggressive nature of the disease. Presence of hepatic metastases and involvement of porta hepatis lymph nodes indicated the advanced stage of the disease at the time of diagnosis. This is further evident from the fact that some patients died in the hospital even before any investigations could be performed or after invasive radiological procedures. Only 33% of the patients were considered fit

enough to undergo laparotomy with a mortality of 18%. Similar has been the experience of Shukla *et al.*⁹ who reported an operation rate of 48% with a mortality of 20%. In the majority of these cases biopsy alone could be performed.

The prognosis of patients with carcinoma of the gall bladder continues to be poor. When cholecystectomy is performed for suspected benign disease and histopathological examination reveals malignancy, and in a small number of patients with localized tumour recognized at laparotomy, curative resection may be performed. The majority of the patients, however, have too advanced a lesion to be treated and undergo only palliative procedures for biliary or gastrointestinal obstruction. A review by Piehler and Crichlow⁵ of more than 3000 cases operated on for carcinoma of the gall bladder revealed that biopsy alone was performed in 34% patients and 13% underwent palliative diversion procedures.

Based on our experience and that of other reported series we observe that the diagnosis of carcinoma of the gall bladder is usually made when the disease is clinically obvious; this is too advanced a stage to offer any curative treatment. Palliative surgical procedures may be possible in some of these cases but are associated with high mortality. However, the disease may be prevented by prompt investigation of patients with symptoms suggestive of benign biliary disease and removal of all diseased gall bladders containing gallstones. All surgically removed gall bladders should be thoroughly examined histologically to rule out malignancy. A curative resection may be possible in such cases detected in the 'preclinical stage' and long term survival may be expected.

References

- Way, L.W. & Altman, D.F. Neoplasms of the gall bladder and bile ducts. In: Sleisinger, M.H. & Fordtran, J.S. (eds) *Gastrointestinal Disease*, 3rd edition. W.B. Saunders, Philadelphia, 1983, p. 1409.
- Shich, C.J., Dunn, E. & Standard, J.E. Primary carcinoma of the gall bladder. A review of a 16 years experience of the Waterbury Hospital Health Centre. *Cancer* 1981, **47**: 996-1004.
- Hart, J., Modan, B. & Shani, M. Cholelithiasis in the aetiology of gall bladder neoplasms. *Lancet* 1971, **i**: 1151-1153.
- Talwar, B.L., Kanta, C. & Gupta, N.M. Biliary carcinoma: an analysis of 209 personal cases. *Indian J Cancer* 1983, **20**: 241-246.
- Piehler, J.M. & Crichlow, R.W. Primary carcinomas of the gall bladder. *Surg Gynecol Obstet* 1978, **47**: 929-942.
- Vaitinen, E. Carcinoma of the gall bladder. A study of 390 cases diagnosed in Finland 1953-1967. *Ann Chir Gynec Fenn* 1970, **168** (Suppl.): 7.
- Weiner, S.N., Koenigsberg, M., Morehouse, H. & Hoffman, J. Sonography and computed tomography in the diagnosis of carcinoma of the gall bladder. *Am J Radiol* 1984, **142**: 735-739.
- Bhargava, D.K., Sarin, S., Verma, K. & Kapur, B.M.L. Laparoscopy in carcinoma of the gall bladder. *Gastrointest Endosc* 1983, **29**: 21-22.
- Shukla, V.K., Khandelwal, C., Roy, S.K. & Vaidya, M.P. Primary carcinoma of the gall bladder: a review of a 16 year period at the University Hospital. *J Surg Oncol* 1985, **28**: 32-35.