

## Editorial

### CARCINOMA OF THE GALLBLADDER

Primary carcinoma of the gallbladder is the most common malignant lesion of the biliary tract (Thorbjarnarson 1975). The current view about the diagnosis and therapy has been determined by reviewing 6,222 cases of carcinoma of the gall bladder reported in the English literature since 1960 (Piebler and Crichlow, 1978).

The frequency of gall bladder cancer varies in various populations. Burdette (1957) reported an incidence of 2.5 per 100,000 residents in the United States. In Pakistan the frequency varies from 6.0 per cent (Yaqin and Parmar, 1976) to 8.4 per cent (Hassan and Zuberi, 1978) of all the patients with biliary tract disease. The incidence in South West American Indians is six times that of the non-Indian population (Reichenbach 1967). Sievers and Marquis (1962) found it to be the second most common malignant disease of the gastro-intestinal tract. In the Israelis the incidence was found to be 27 per 100,000 (Hart et al., 1972). A high incidence has also been reported in Japanese immigrants to the United States.

Carcinoma of the gall bladder predominates in the female and according to one estimate 76.5 per cent were women of a total of 2998 patients (Piebler and Crichlow, 1978). In Pakistan also gall bladder malignancy predominates in the female with a ratio of 9 females to one male but the mean age was found to be low at 45.4 years (Hassan and Zuberi, 1978).

The exact aetiology of carcinoma gall bladder is not known although various possible causes have been proposed. Frequent association of cholelithiasis with gall bladder cancer is well known. Warren and Balch (1940) and Hart et al. (1972) have documented a greater incidence of stone in patients with carcinoma than in general population at all ages. In contrast 25 per cent gall bladder cancers develop with no evidence of cholelithiasis and experience in Uganda where a-calculous carcinoma with female predominance is seen points to a hormonal cause (Hutts and Anthony, 1973). A higher incidence of carcinoma gall bladder has been noticed in patients who have undergone previous surgery as the biliary tract (Piebler and Crichlow, 1978).

Methylcholanthrene, a carcinogen which is chemically similar to naturally occurring bile acids has been able to induce cancer in gall bladder of cats and dogs (Fortner and Norris, 1961). Similarly other chemicals such as O-aminoazotoulene and various nitrosamine have induced cancer. Rubber industry employees who are exposed to a number of chemicals known to be carcinogenic in animals, show a higher incidence and earlier onset of carcinoma gall bladder (Mancuso and Brennan, 1970).

Malignant transformation of a benign gall bladder tumours is rare. Selzer et al. (1962) and Elekema et al. (1962) have noted that the risk of a malignant degeneration in benign tumours without associated cholelithiasis is very small. Carcinoma of extrahepatic biliary tract occurs 5 to 10 times more frequently in the patients of ulcerative colitis of which some 13% are gall bladder cancers (Ritchie et al., 1974).

No remarkable differences were observed in the clinical and biochemical findings between benign and malignant gall bladder disease (Hassan and Zuberi, 1978). Most carcinomas of the gall bladder are unexpected findings and the lack of specific signs and symptoms prevents early detection. Generally speaking, carcinoma of the gall bladder presents as one of five clinical syndromes as reported in a review by Piebler and Crichlow (1978). 16% of patients presented with symptoms representing acute cholecystitis, while 43% presented with histories consistent with the diagnosis of ch. cholecystitis, 34% had symptoms suggesting biliary tract malignancy and 29% had symptoms suggesting a non-specific malignant disease. A small percentage presented with symptoms from extension of the disease.

The physical findings in patients of carcinoma gall bladder are generally non-specific and laboratory-cum-roentgenographic investigation have also proved to be of little aid. Levels of bilirubin, alkaline phosphatase and transaminases were found to be significantly higher in the malignant group as compared to a benign group of gall bladder diseases (Hassan and Zuberi, 1978). The association of elevated alkaline phosphatase without hyperbilirubinaemia in the gall bladder patients has been noted by several researchers (Hendrick et al., 1970; Vaittinen, 1970). Over 85% of patients with cancer of the gall bladder do not have visualisation of the gall bladder on oral cholecystography. Selective and highly

selective angiography have the highest degree of diagnostic accuracy (Piebler and Crichlow, 1978). Ogoshi and co-workers (1973) were able to pre-operatively diagnose two patients with carcinoma gall bladder, using endoscopic retrograde cholangio-pancreatography.

On gross examination there is usually a diffuse thickening of the gall bladder wall, though less frequently the tumour is found to be polypoid or papillary and occasionally calcification of the tumour is seen (Willis 1968). Histologically, 82.3% are adenocarcinomas, 6.9% are undifferentiated carcinomas, 3.3% are squamous carcinomas, 1.4% are adeno-acanthoma and 0.7% are carcinomas in situ.

Fahim and associates (1962) have emphasised the tendency of gallbladder cancers towards local invasion of the gallbladder and surrounding structures, until late in the course of the disease, when distant haematogenous metastases become evident. The spread in carcinoma of the gallbladder is via the lymphatic, vascular, neural, intra peritoneal and intra ductal routes.

The prognosis for patients with carcinoma gallbladder is poor and only a small percentage of patients with recognised tumours at laparotomy undergo successful resection. Fahim and associates (1963), Glenn and Hays (1954), Adison (1973) and others have advocated enbloc excision of the gallbladder with wedge resection of adjacent liver and regional lymphadenectomy of the adjacent hepatoduodenal ligament. Majority of cases are not treatable or only palliatively so. Chemotherapy may be of some palliative benefit and Watkins and Khazai (1966) have reported objective response to regional inter-arterial administration of 5-fluoro-uracil in 50% of their patients. The overall 5 years survival rate was 4.1% and one year survival rate was 11.8% and only 16.5% of patients with resected tumours survived five years (Piebler and Crichlow, 1978).

The low mortality of elective cholecystectomy raises the question of prophylactic surgical procedures in patients with gallbladder disease, to prevent the many complications of gallbladder dysfunction, one of which is cancer.

#### References

- Adison, M.A. (1973) Carcinoma of the gallbladder. *Surg. Clin. North Am.*, 53:1203.
- Burdette, W.J. (1957) Carcinoma of the gallbladder. *Ann. Surg.*, 145:832.
- Elekema, H.H., Hodgson, J.R. and Stauffer, M.H. (1962) Fifteen-year follow-up of polypoid lesions of the gallbladder diagnosed by cholecystography. *Gastroenterology*, 42:144.
- Fahim, R.B., McDonald, J.R., Richards, J.C. and Ferris, D.O. (1962) Carcinoma of the gallbladder; study of its modes of spread. *Ann. Surg.*, 156:114.
- Fahim, R.B., Ferris, D.O. and McDonald, J.R. (1963) Carcinoma of the gallbladder; an appraisal of its surgical treatment. *Arch. Surg.*, 86:334.
- Fortner, J.G. and Norris, W.P. (1955) Determination of the radioactivity of gall stones obtained from cases of gallbladder cancer. *Cancer*, 8:687.
- Glenn, F. and Hays, D.M. (1954) The Scope of radical surgery in the treatment of malignant tumours of the extrahepatic biliary tract. *Surg. Gynaecol. Obstet.*, 99:529.
- Hart, J., Shani, M. and Modan, B. (1972) Epidemiological aspects of gallbladder and biliary tract neoplasm. *Am. J. Public Health*, 62:36.
- Hassan, T.J. and Zuberi, S.J. (1978) Carcinoma of gallbladder. *JPMA*, 26:133.
- Hendrick, J., Beckers, J., Franssen, G. and Tanghe, W. (1970) Primary carcinoma of the gallbladder. *Gastroenterology*, 13:11.
- Hutts, M.S.R. and Anthony, P.P. (1973) Tumours of Liver, biliary system, and pancreas. *Recent Results, Cancer Res.*, 41:76.
- Mancuso, T.F. and Brennan, M.J. (1970) Epidemiological considerations of cancer of the gallbladder, bile ducts and salivary glands in the rubber industry. *J. Occup. Med.*, 12:333.
- Ogoshi, K., Niwa, M., Hara, Y. and Nebel, O.T. (1973) Endoscopic pancreatochole angiography in the evaluation of pancreatic and biliary disease. *Gastroenterology*, 64:210.
- Piebler, J.M. and Crichlow, R.W. (1978) Primary Carcinoma of the gallbladder. *Surg. Gynaecol. Obstet.*, 147:929.
- Reichenbach, D. (1967) Autopsy incidence of diseases among Southwestern American Indians. *Arch. Pathol.*, 84:81.
- Ritchie, J.K., Allen, R.N., Macartney, J., Thompson, H., Hawley, P.R. and Cooke, W.T. (1974) Biliary tract carcinoma associated with Ulcerative Colitis. *Quart. J. Med.*, 43:263.
- Selzer, D.W., Dockerty, M.B., Stauffer, M.H. and Priestley, J.T. (1962) Papillomas (so-called) in the non-calculous gallbladder. *Am. J. Surg.*, 103:472.
- Sievers, M.L. and Marquis, J.R. (1962) The Southwestern American Indian's Burden, biliary disease. *JAMA*, 182:570.
- Thorbjarnarson, B. (1975) Carcinoma of biliary tree. I. Carcinoma of gallbladder. *N.Y. State J. Med.*, 75:550.
- Vaitinen, E. (1970) Carcinoma of the gallbladder. A study of 390 cases diagnosed in Finland 1953-1967. *Ann. Chir. Gynaec. Fenn.*, 168:Suppl. 168:1+.
- Warren, R. and Balch, F.G., Jr. (1940) Carcinoma of gallbladder; etiological role of gall-stones. *Sur-*

gery, 7:657.

Watkins, E., Jr. and Khazci, A.M. (1966) Arterial infusion chemotherapy of liver cancer. *Bull. Soc. Int. Chir.*, 25:279.

Willis, R.A. *Pathology of Tumours*, 4th ed., London, Butterworth, 1968.

Yaqin, H. and Parmar, B.K. (1976) A comparative study of Biliary tract disease in Karachi (Pakistan) and Aylesbury (England). *JPMA*, 26:162.

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John Bryan — "Large numbers of world's people, perhaps more than half, have no access to health care at all. For many of the rest, the care they receive does not answer the problems they have."

David Morley — Three fourth of our population is rural yet three fourth of our resources are spent on the towns where three fourth of our doctors live; three fourth of people die from disease which could be prevented at low cost and yet three fourth of medical budgets are spent on curative services.