

Cancer of the gallbladder

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Incidence Gallbladder cancer is extremely variable by geographical region and racial-ethnic groups; the highest incidence is among Chileans, Native Americans and residents in parts of northern India, where it accounts for as much as 9% of all biliary tract disease. Women appear to have a higher incidence across all geographical areas. In western practice, gallbladder cancer accounts for less than 1% of new cancer diagnoses. The disease usually presents in the seventh or eighth decade. The aetiology is unclear but there is a suggested association with pre-existing gallstone disease, implying that chronic inflammation may play a role. Calcification of the gallbladder wall, presumably due to chronic inflammation (porcelain gallbladder), is also associated with a small increased risk of cancer (Figure 71.5). Chronic infection may promote the development of cancer and the risk in typhoid carriers is significantly increased over that of the general population. Patients with PSC, especially with concomitant IBD, and those with an abnormal pancreatic- biliary junction are at greater risk of gallbladder cancer. In patients with gallbladder polyps (Figure 71.40) the risk of malignant transformation increases with increasing size of the polyp. Summary box 71.9 Gallbladder cancer

Pathology The majority (90%) of tumours are adenocarcinomas. Squamous carcinomas may arise from areas of mucosal squamous metaplasia. At operation, localised carcinomas are difficult to differentiate from chronic cholecystitis; the tumour most commonly is nodular and infiltrative, with thickening of the gallbladder wall, often extending to the whole gallbladder. The tumour spreads by direct extension into the liver, seeding of the peritoneal cavity and involvement of the perihilar lymphatics and neural plexuses. At the time of presentation, the majority of tumours are advanced. Clinical features Patients may be asymptomatic; symptoms, if present, are usually indistinguishable from those of benign gallbladder disease such as biliary colic or cholecystitis, particularly in older patients. Jaundice and anorexia are late features, heralding a low resectability rate and even fewer negative margins. A palpable mass is a late sign. Investigation Laboratory findings are generally non-specific but may be consistent with biliary obstruction. Non-specific findings include anaemia, leukocytosis and a mild elevation in transaminases. Serum CA19-9 and carcinoembryonic antigen may be elevated in approximately 80% of patients. The preoperative diagnosis is often made on USG and confirmed by CT thorax, abdomen and pelvis or MRI/MRCP. Preoperative staging should aim to determine the local extent of disease and exclude the presence of distant metastases. Percutaneous biopsy under radiological guidance may be considered to obtain tissue for pathological examination, but only in unresectable disease prior to palliative treatment. Laparoscopic examination is useful in staging the disease. Laparoscopy can detect peritoneal or liver metastases, which would preclude further surgical resection (Figure 71.41). PET scanning has a role in detecting metastatic disease. Treatment and prognosis The majority of patients have advanced disease at presentation and are not candidates for surgical therapy. Staging

Rare Similar presentation to benign biliary disease (gallstones) Diagnosis by USG, CT, MRI/MRCP Most patients present with advanced disease Surgical resection in less than 10% – remainder receive palliative treatment Prognosis is poor Figure 71.40 Ultrasonography demonstrating a gallbladder polyp. Note the absence of an acoustic shadow (arrow).

laparoscopy is mandatory prior to formal laparotomy to detect occult metastases not picked up on imaging. Radical en bloc resection includes the gallbladder, wedge hepatectomy (2–5 cm of liver in the gallbladder bed or segments IVb and V if there is concomitant liver infiltration) or extended hepatectomy and bile duct resection if the bile duct is involved or the cystic duct margin is positive on intraoperative frozen section. Regional lymphadenectomy (paracholedochal portal, along the right hepatic artery and retroduodenal nodes) should be considered. The aim is to remove the tumour entirely and achieve negative histopathological margins. Some patients have the disease diagnosed following histopathological examination of the gallbladder after it has been removed. Summary box 71.10 Aims of staging gallbladder cancer (Table 71.10). In these cases, the need for further surgery is determined by the stage of disease. For early-stage disease confined to the mucosa of the gallbladder with a negative cystic duct margin and no evidence of recurrence on imaging, no further treatment is indicated. However, for transmural disease, a radical en bloc resection of the gallbladder fossa and surrounding wedge of liver along with the regional lymph nodes should be performed. If the initial procedure was performed laparoscopically, the surgeon should examine the laparoscopic port sites. Routine resection of port sites is no longer recommended. However, it is recognised that the finding of disease at the port sites is a sign of generalised peritoneal disease and carries a very poor prognosis. Adjuvant oral chemotherapy (capecitabine alone is preferred or in combination with gemcitabine/oxaliplatin) may derive survival benefit. Gallbladder cancer is a lethal disease with a grim prognosis; the median survival is less than 6 months and 5-year survival figures of 50% for localised gallbladder cancer (with chemotherapy) and 2–5% in patients with distant metastasis have been reported. For the majority of patients with advanced disease a non-operative approach to palliation is best. Obstructive jaundice can be relieved by endoscopic and/or percutaneous methods after discussion in the multidisciplinary team.

Figure 71.41 Laparoscopic staging in a patient with gallbladder cancer demonstrating gross peritoneal metastases. Assessment of local disease Detection of metastatic disease: Liver Peritoneum Lymphatics Extra-abdominal disease

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