Is there any justification for the routine histological examination of straightforward cholecystectomy specimens?

B DARMAS, S MAHMUD, A ABBAS, AL BAKER

Department of General Surgery, Wrexham Maelor Hospital, Wrexham, UK

ABSTRACT

INTRODUCTION Gall bladder carcinoma is a rare malignancy that carries a very poor prognosis. Laparoscopic cholecystectomy (LC) is established as the gold-standard treatment for symptomatic gall stones. The aim of the study was to assess the incidence of gall bladder carcinoma and the possibility of reducing the routine histological examination of gall bladder specimens.

PATIENTS AND METHODS Pathology laboratory data of gall bladder specimens over a period of 5 years (June 2000 to July 2005) were analysed retrospectively. The case notes were retrieved in all cases of malignancies.

RESULTS The total number of specimens was 1452. Four (0.27%) cases of primary gall bladder carcinoma, one case of primary B-cell lymphoma and one secondary carcinoma were detected as well as one case of intra-epithelial neoplasia. Operative notes revealed that there was a high index of suspicion of malignancy in all cases. Of the 4 primary gall bladder carcinomas, 3 were stage T2 and one T4. Pre-operative ultrasound suspected carcinoma in only one case but a thickened gall bladder wall was noted in all cases.

CONCLUSIONS All cases of gall bladder carcinoma were suspected pre-operatively or intra-operatively. Histological examination did not alter the management or outcome in any of the cases. We suggest that selectively sending specimens for histopathological examination would result in reduced demands on the histopathology department without compromising patient safety.

KEYWORDS

Gall bladder – Gall bladder cancer – Histopathology

CORRESPONDENCE TO

Borys Darmas, Department of General Surgery, Wrexham Maelor Hospital, Wrexham LL13 7TD, UK

T: +44 (0)1978 291100 bleep 5431; M: +44 (0)7891 075687; F: +44 (0)1978 727000; E: bdarmas@hotmail.com

Adenocarcinoma of the gall bladder is a rare but aggressive gastrointestinal malignancy. It carries a dismal prognosis, with a reported overall 5-year survival rate not exceeding 5%.¹ According to a large multicentre survey commissioned by the French Surgical Association, the overall median survival is just 3 months,² the main reason being late presentation. It mainly affects patients in their 7th and 8th decade and is about 5 times more common in females. It is estimated that in 85% of cases it is associated with gallstones³ but the only recognised pre-malignant condition is a 'porcelain gall bladder'. In the vast majority of patients who are diagnosed with gall bladder carcinoma, the first suspicion of malignancy arises during operation and is confirmed on histological examination of the specimen. Despite advances in radiological imaging, accurate pre-operative diagnosis is the exception rather than the rule. At present, all specimens, regardless of their macroscopic appearance, are being sent for histological examination. It

seems questionable whether the result of the histopathological examination of each gall bladder would alter management when it provides no advantage to the surgeon, patient or pathologist.

The aim of the study was to assess the necessity of routine histological examination of the gall bladder following simple cholecystectomy and its impact on the further management of the patients.

Patients and Methods

We analysed, retrospectively, the electronic database of histological reports of all gall bladder specimens after cholecystectomy in the last 5 years. In all cases of confirmed malignancy, we retrieved and reviewed, from patients notes and, when missing, from the hospital electronic database, results of pre-operative investigations such as: liver function tests, ultrasound scans or computed tomography

Table 1 Summary of the patients with gall bladder adenocarcinoma

Patient no.	Age (years)	M/F	Pre-operative suspicion	Open/LC	Operative findings	Type of tumour	Survival (months)
1	74	M	Yes, thick gall bladder wall, multiple stones, cholecystitis/malignancy	Open	Empyema, wall necrosis, difficult anatomy, mass	Poorly differentiated adenocarcinoma. T4 N0	4
2	70	M	No, multiple stones, thick wall, deranged LFT	LC	Inflammatory mass, thick shrunken gall bladder, subtotal cholecystectomy	Moderately differentiated adenocarcinoma T2 N0	3
3	46	F	No, multiple stones, dilated CBD, deranged LFT	Open	Inflammation, dilated CBD, clinically acute cholecystitis	Moderately differentiated adenocarcinoma T2 N0	60 still alive
4	78	M	No, large gall bladder with stones but no impaction	Open	Operated for gastric carcinoma. Incidental finding of shrunken gall bladder with mass	Well-differentiated adenocarcinoma T2	34 still alive
5	68	F	Suspicion of malignancy, large mass in the RUQ	Open	Mass involving gall bladder, stomach and colon	Poorly differentiated adenocarcinoma of the colon T4 N1 M1	5
6	75	F	No, thick wall, multiple stones ?cholecystitis	Open	Mass involving gall bladder	Low grade B cell lymphoma	60 still alive

LC, Laparoscopic cholecystectomy.
Patients 5 and 6 had other malignancies of the gall bladder.

and intra-operative findings from operation notes. We analysed all the findings to assess their usefulness in establishing pre-operative diagnosis of the gall bladder malignancy. All patients with a confirmed diagnosis of gall bladder carcinoma were followed up after the operation up to the present date or their death.

Results

A total of 1452 gall bladder specimens were subjected to histopathological examination within the last 5 years, approximately 290 per year. We found 4 cases (0.27%) of primary adenocarcinoma of the gall bladder, one case of low-grade B-cell lymphoma and one case of adenocarcinoma of the colon invading the gall bladder. Out of 4

patients with primary gall bladder carcinoma, 3 (75%) were males. In one case, the patient was operated on electively for gastric carcinoma and found to have a shrunken gall bladder with an adjacent mass. The gall bladder was resected and a histological diagnosis of T2 adenocarcinoma was made. One case of epithelial dysplasia was also detected. There were no cases of carcinoma *in situ*. Operation notes revealed that, in all cases of histologically confirmed invasive gall bladder carcinoma, there was a high index of suspicion of malignancy at the time of surgery and also that dissection was difficult because of an obvious mass. Out of 4 primary carcinomas of the gall bladder, 3 were stage T2 and one was stage T4. Pre-operative ultrasound scans gave suspected carcinoma in only one case, but a thickened wall of the gall bladder was noted in

all cases. Deranged LFTs were found in 2 cases. In patients with B-cell lymphoma and invasive adenocarcinoma of the colon there was evidence of obvious macroscopic abnormality both on pre-operative ultrasound scan as well as at laparotomy. Gallstones and histologically proven inflammation were present in 4 and 3 out of 4 cases, respectively. Only one gall bladder was removed by a laparoscopic procedure, this being a subtotal cholecystectomy. All patients were followed up to the present date or until death. (3–60 months). Two patients with T4 N0 and T2N0 disease stage died after 4 and 3 months, respectively (Table 1).

Discussion

At present, the only hope of a cure in the case of gall bladder adenocarcinoma is offered by surgery. The extent of curative R0 resection depends on the stage of the disease at the time of diagnosis. It ranges from simple cholecystectomy for Tis to pT2a and radical cholecystectomy including segment 4a and 5 of the liver and regional lymphadenectomy for pT2b.^{2,4,5} It is postulated that the incidental finding of gall bladder carcinoma during a laparoscopic cholecystectomy warrants conversion to an open procedure. This is to minimise the chance of port site and peritoneal metastases and to achieve accurate clearance as peritoneal seeding occurs especially when the gall bladder lumen is opened.^{2,4} However, Cuccinotta *et al.*⁶ showed that the overall outcome of the patients with unsuspected gall bladder adenocarcinoma is not related to the surgical approach and it is the tumour stage that is the most important factor.

Our findings confirm that accurate pre-operative diagnosis of gall bladder carcinoma is very difficult and it is during the operation that suspicion or clinical diagnosis of malignancy is made. However, in each case, a gross macroscopic abnormality of the gall bladder was easily identifiable and prompted the surgeon to send the specimen for histological examination. Previous reports in the literature clearly indicate that a more selective policy towards histological examination, *i.e.* only specimens which are macroscopically abnormal, is rational, effective and safe. These series confirm that there was not a single case of invasive adenocarcinoma of the gall bladder that would have been missed if only macroscopically abnormal specimens were examined.^{7–9}

In recent years, we have witnessed a significant increase in a consultant histopathologist's workload. In response to the mounting pressure on pathological services, the Royal College of Pathologists published guidelines on workload and safe staffing levels in pathology departments. The case-load has been estimated at 4000 specimens per year per consultant in a district general hospital. The same group identified factors contributing to the increase of workload: sub-specialisation, appointment of clinical staff without

consideration of the strain on pathological services and greater complexity of cases.¹⁰ The Royal College of Pathologists published a number of guidelines to help to manage this increasing demand. One of the proposed recommendations is to count the workload on the basis of the number of processed slides rather than 'requests'. This is a more sensitive way of estimating the varying complexity of specimens as some of them may require multiple slides or more specialist immunohistochemical techniques. The same working party advised a greater use of biomedical scientists in specimen dissection and sampling. The aim is to relieve consultants of some work pressures but not the overall responsibility for delegated tasks. In the *Royal College of Pathologists Guidelines August 2002*¹¹ on the subject of whether histopathological and cytological examination is of limited value, one reads: '[Gallbladders and appendices] should be examined as significant pathology may be present with normal gross morphology'. The revised edition of this document published in December 2005¹² again suggested that sampling of the gall bladder should continue. In drafting these recommendations, the authors quoted only one publication by HW Taylor suggesting the opposite. Review of the literature reveals that there are now 4 papers, including the present one, to refute this.

The cost-effectiveness of such an approach is open to debate. Out of a total of 1452 specimens, only 4 (0.27%) cases of primary gall bladder carcinoma were found. All looked suspicious to the operating surgeon and to the histopathologist on macroscopic examination. There were no cases of gall bladder adenocarcinoma in unsuspecting-looking specimens. Therefore, detailed microscopic examination should be indicated only in cases of abnormal gross appearance. As the incidence of gall bladder malignancy starts to rise after the age of 50 years, the threshold for histological examination may need to be lowered in this age group. On the basis of the macroscopic appearance of the gall bladder specimens received in our laboratory, as well as patient's age, it was estimated that at least half of them should not be processed (AH Burdge, consultant histopathologist, personal communication). The total cost of the preparation of a standard haematoxylin–eosin (H&E) slide, as well as the pathologist's time, was calculated at £15 per gall bladder specimen. This is the overall cost including all consumables and labour. It adds up to a total of £21,750 over the 5-year period. The cost of finding a gall bladder carcinoma was calculated at £5437.50 per case. Adopting a more selective approach would reduce the cost to £2719 and result in an overall saving of £10,875. The workload of the histopathologist would be reduced by about 3.5–4.0% per year if only selected gall bladder specimens were examined. Consultant time allocated to this examination is approximately 12 min per specimen.¹⁰ Implementing a selective policy of microscopic examination would save over 29 hours of consultant time per year.

Based on the above findings, we suggest that standard histological examination of all gall bladder, irrespective of their macroscopic appearance during operation, is neither justifiable, nor cost-effective and does not contribute to the management of the patient. As we have shown, adopting a more selective policy and examining only the macroscopically abnormal gall bladder proves to be equally sensitive, as no invasive carcinomas were missed. In this study, we have not found any case of early carcinoma within a normal looking gall bladder; however, as mentioned above, the management of such cases consists of a simple cholecystectomy.

Conclusions

All cases of invasive carcinoma of the gall bladder showed gross macroscopic abnormal appearance either pre- or intra-operatively. A more selective policy to histological examination of the gall bladder specimens would not miss any invasive malignancy. It would significantly reduce the workload for a consultant pathologist, be more cost-effective and still remain safe for the patients.

References

1. Levy AD, Murakata LA, Rohrmann CA. Gallbladder carcinoma: Radiologic-pathologic correlation. *Radiographics* 2001; **21**: 295–314.
2. Cubertaond P, Mathonnet M, Gainant A, Launois B. Radical surgery for gall bladder cancer. Results of the French Surgical Society survey. *Hepatogastroenterology* 1999; **46**: 1567–71.
3. Roa I, Araya JC, Villaseca M, Roa J, de Aretxabala X, Ibacache G. Gall bladder cancer in high risk area: morphological features and spread patterns. *Hepatogastroenterology*. 1999; **46**: 1540–6.
4. Wakai T, Shirai Y, Hatekayama K. Radical second resection provides survival benefit for patients with T2 gall bladder carcinoma first discovered after laparoscopic cholecystectomy. *World J Surg* 2002; **26**: 867–71.
5. Gomez Freijoso C, Acea Nebril B, Fraguera Marina J, Taboada Filgueira L, Freire Rodrigues D, Aguirrezabalaga Gonzalez J. Carcinoma *in situ* of the gall bladder. The prognostic and therapeutic implications. *Gastroenterol Hepatol* 1995; **18**: 457–9.
6. Cucinotta E, Lorenzini C, Melita G, Iapachino G, Curro G. Incidental gall bladder carcinoma: does the surgical approach influence the outcome. *Aust NZ J Surg* 2005; **75**: 795–8.
7. Bisgaard T, Hansen BF, Lassen AH, Rosenberg J. Histological examination of the gall bladder after cholecystectomy. *Ugeskr Laeger* 2001; **263**: 5025–8.
8. Dix FP, Bruce IA, Krypczyk A, Ravi S. A selective approach to histopathology of the gall bladder is justifiable. *Surgeon* 2003; **1**: 233–5.
9. Taylor HW, Huang JKC. 'Routine' pathological examination of the gall bladder is a futile exercise. *Br J Surg* 1998; **85**: 208.
10. Royal College of Pathologists. *Guidelines on staffing and workload for histopathology and cytology departments*, 2nd edn. London: Royal College of Pathologists, 2005.
11. Royal College of Pathologists. *Histopathology of limited or no clinical value. Report of working group of The Royal College of Pathologists*. London: Royal College of Pathologists, 2002.
12. Royal College of Pathologists. *Histopathology of limited or no clinical value. Report of working group of The Royal College of Pathologists*, 2nd edn. London: Royal College of Pathologists, 2005.