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Incidentally Detected Gallbladder Carcinoma in Routine Cholecystectomy Specimens: A Retrospective Observational Study of Frequency and Histopathological Spectrum at a Tertiary-Care Teaching Hospital in North India

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Abstract

Background: Gallbladder carcinoma is the most common malignancy of the biliary tract and is frequently detected only on histopathological examination of gallbladders removed for presumed benign disease. We examined the frequency, histological spectrum and clinicopathological features of incidentally detected gallbladder carcinoma at a tertiary-care teaching hospital in North India. **Materials and Methods:** All cholecystectomy specimens reported between 30 June 2022 and 30 May 2026 were reviewed retrospectively. Gallbladder neoplasms were identified and, where reports were retrievable, characterized for age, sex, pre-operative clinical suspicion, histological subtype, grade, tumor (pT) stage, lymphovascular and perineural invasion and margin status. Lesions carrying a documented pre-operative suspicion of malignancy were classified separately and not counted as incidental. **Results:** Of 964 cholecystectomies, 14 (1.5%) were flagged as gallbladder neoplasms; detailed reports were retrievable for 11. One specimen showed a benign gallbladder with a separate peritoneal adenocarcinoma and was excluded. Of the remaining ten gallbladder neoplasms, seven were invasive carcinomas and three pre-invasive; three carcinomas carried a pre-operative suspicion of malignancy and were analysed separately, leaving four incidental invasive carcinomas and three incidental pre-invasive lesions. Women predominated (nine of ten) and ages ranged from 41 to 77 years. All four incidental invasive carcinomas were tumor stage pT2, with perineural invasion in three, lymphovascular invasion in two and margin involvement in three, and spanned four different morphologies – signet-ring cell, mucinous, mucin-rich biliary-type and intestinal-type adenocarcinoma. The clinically suspected group included an adenosquamous (collision) carcinoma staged pT3N1. **Conclusion:** Gallbladder neoplasia was found in approximately 1.5% of routine cholecystectomies. Incidental carcinomas were uniformly pT2 rather than early, with frequent adverse pathological features, and an unusually broad range of aggressive morphologies was encountered in a small number of cases. A structured approach that includes histopathological examination of every cholecystectomy specimen, careful subtyping of any neoplasm, and prompt staging when invasive carcinoma is found is essential to avoid understaging and to guide further management.

Keywords: Biliary intraepithelial neoplasia, Cholecystectomy, Gallbladder carcinoma, Histopathology, Incidental finding, Mucinous adenocarcinoma, Signet-ring cell carcinoma

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Introduction

Gallbladder carcinoma is the most common malignancy of the biliary tract and generally carries a poor prognosis, largely because most patients present at an advanced stage. A distinct and clinically important subset is discovered unexpectedly – incidental gallbladder carcinoma – when a gallbladder removed for a presumed benign indication, most often symptomatic cholelithiasis or cholecystitis, is found on histopathology to harbor neoplasia. Reported frequencies in cholecystectomy series range from roughly 0.2 to 3%, varying with geography, gallstone burden and pathological sampling practice.[1,2]

The distinction is clinically consequential. An incidental diagnosis alters management: Depending on tumor (T) stage, patients require formal staging and, frequently, radical re-resection, and the interval to re-resection influences survival.[3] Because malignancy is by definition unsuspected before operation, and because pre-invasive lesions such as biliary intraepithelial neoplasia and dysplasia, as well as uncommon aggressive variants such as mucinous and signet-ring/poorly cohesive carcinoma, occur within this spectrum, histopathological examination of every cholecystectomy specimen has been advocated, although selective policies remain debated.[2,4-6]

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Against this background, and in a North Indian population with a substantial burden of gallstone disease, we reviewed our institutional cholecystectomy experience to determine the frequency, histological spectrum and clinicopathological features of incidentally detected gallbladder neoplasia.

Materials and Methods

Study Design and Setting

This was a retrospective observational study conducted in the Department of General Surgery in collaboration with the Department of Pathology, SGT Medical College, Hospital and Research Institute, Gurugram, a tertiary-care teaching hospital. All cholecystectomy specimens reported between 30 June 2022 and 30 May 2026 were reviewed. The study was conducted in accordance with the Declaration of Helsinki and institutional ethical requirements for the retrospective review of anonymized records.

Definitions

Incidental gallbladder carcinoma was defined as neoplasia identified on histopathological examination of a gallbladder removed for a clinically and radiologically presumed benign indication, without pre-operative or intraoperative suspicion of malignancy. Cases carrying a documented pre-operative suspicion of malignancy were classified separately as clinically suspected and were not counted as incidental. Invasive carcinoma and pre-invasive neoplasia (biliary intraepithelial neoplasia and high-grade dysplasia) were recorded separately. Histological subtyping followed the World Health Organization classification and staging the AJCC/UICC eighth edition.[5]

Data Collection and Analysis

Gallbladder neoplasms were identified from departmental histopathology records. For each case with a retrievable report, the age, sex, pre-operative clinical indication, histological diagnosis and subtype, grade, tumor (pT) stage, lymphovascular and perineural invasion, and margin status were recorded. Detailed reports could not be retrieved for three of the fourteen flagged neoplasms. Crude frequency was calculated as the number of neoplasms divided by the total number of cholecystectomies; categorical data are expressed as frequencies and percentages and continuous data as median and range. The denominator was the total number of cholecystectomies performed for presumed benign disease during the study period (964).

Results

Frequency and Case Ascertainment

During the study period, 964 cholecystectomy specimens were examined, of which 14 (1.5%) were flagged as gallbladder neoplasms on histopathology. Detailed reports were retrievable for 11. One specimen, clinically a mucocele, showed a benign gallbladder – chronic cholecystitis – with a separate peritoneal-wall adenocarcinoma, and was excluded as not representing a primary gallbladder neoplasm. The remaining ten gallbladder neoplasms comprised seven invasive carcinomas and three pre-invasive lesions and form the basis of the clinicopathological description [Table 1]. Three of the carcinomas carried a pre-operative clinical suspicion of malignancy and are reported separately, leaving seven incidental lesions – four invasive carcinomas and three pre-invasive. Women predominated (nine of ten); the single man had a pre-invasive lesion. Ages ranged from 41 to 77 years.

Incidental Invasive Carcinomas

Four of the seven incidental lesions were invasive carcinomas. Notably, all four were tumor stage pT2 – locally advanced, with invasion of the perimuscular connective tissue – despite being clinically unsuspected. Perineural invasion was present in three, lymphovascular invasion in two, and the resection margin was involved in three of the four. The morphology was strikingly heterogeneous for so small a group: one signet-ring cell carcinoma (G3), one mucinous adenocarcinoma (G1), one biliary-type adenocarcinoma with extracellular mucin pools (G2) and one intestinal-type adenocarcinoma (G2).

Incidental Pre-invasive Lesions

The remaining three incidental lesions were pre-invasive: Two cases of biliary intraepithelial neoplasia (one low-grade and one high-grade) and one of focal high-grade dysplasia arising in a background of chronic or follicular cholecystitis. All were confined to the mucosa, with uninvolved margins assessed, and each occurred in a gallbladder removed for gallstone disease.

Clinically Suspected Carcinomas

Three documented carcinomas carried a pre-operative suspicion of malignancy and therefore lie outside the incidental definition: A fundal-mass biopsy reported as adenocarcinoma; a mixed gastric-foveolar-and-biliary adenocarcinoma (pT2b) resected by radical cholecystectomy; and an adenosquamous (collision) carcinoma – the most advanced tumor in the series at pT3N1, a 7.5 cm fungating fundal mass combining keratinizing squamous and biliary adenocarcinoma components, with lymphovascular and perineural invasion and periportal nodal involvement. These are reported for completeness but excluded from the incidental group.

Discussion

In this 4-year single-institution experience, a gallbladder neoplasm was found in approximately 1.5% of routine cholecystectomies, within the internationally reported range for incidental gallbladder carcinoma.[1,2] This figure also aligns closely with the pooled incidence of 0.95% (95% confidence interval 0.51–1.51) that we derived from Indian cholecystectomy series in a companion systematic review and meta-analysis, situating the present single-center experience within the wider national picture. The more important observation, however, concerns the nature of these tumors rather than their frequency. All four incidental invasive carcinomas were pT2, and perineural invasion, lymphovascular invasion, and margin involvement were each common. In other words, incidental did not mean early in this cohort – a finding with direct implications for the need for staging and consideration of radical re-resection once such a diagnosis is returned, the timing of which is itself associated with survival.

The value of examining every specimen is underscored by our detection of both unsuspected invasive carcinoma and pre-invasive neoplasia in gallbladders removed for benign disease. Although routine histopathology of all cholecystectomy specimens has been questioned on resource grounds, and risk-targeted selective policies have been proposed, unsuspected

Table 1: Clinicopathological details of the documented gallbladder neoplasms and the excluded case (*n*=11)

#	Age/sex	Pre-operative indication	Histological diagnosis	Grade	pT	LVI/PNI	Margin
			Incidental invasive carcinomas (n=4)				
1	62/F	Xanthogranulomatous cholecystitis	Signet-ring cell carcinoma	G3	pT2a	–/+	Involved
2	77/F	Cholelithiasis	Adenocarcinoma, biliary type, mucin pools	G2	pT2a	+/+	Involved
3	64/F	Chronic cholecystitis	Mucinous adenocarcinoma	G1	pT2	+/+	Serosa 0.1 mm; neck free
4	47/F	Cholelithiasis; Mirizzi syndrome	Adenocarcinoma, intestinal type	G2	pT2a	–/–	Cystic duct positive
			Incidental pre-invasive lesions (n=3)				
5	63/F	Gallstone disease	Focal high-grade dysplasia (BilIN)	–	Pre-inv.	–/–	Free
6	41/F	Cholelithiasis	Biliary intraepithelial neoplasia, low grade	–	Pre-inv.	–/–	–
7	50/M	Cholelithiasis	High-grade dysplasia (BilIN)	–	Pre-inv.	–/–	Free
			Clinically suspected carcinomas (n=3)				
8	50/F	Suspected carcinoma gallbladder	Adenocarcinoma, mixed foveolar+biliary	G2	pT2b	–/+	Free
9	54/F	Suspected carcinoma gallbladder	Adenocarcinoma (fundal-mass biopsy)	–	n/a	–/–	–
10	46/F	Suspected carcinoma gallbladder	Adenosquamous (collision) carcinoma	G2	pT3N1	+/+	Free
			Excluded — gallbladder benign (n=1)				
11	63/F	Mucocele/abdominal mass	Gallbladder benign; peritoneal adenocarcinoma	–	n/a	–/–	–

BilIN: Biliary intraepithelial neoplasia, LVI: Lymphovascular invasion, PNI: Perineural invasion, +: Present, –: Absent or not identified, n/a: Not applicable. Detailed reports for three further flagged neoplasms could not be retrieved

malignancy of the kind seen here supports a low threshold for complete histological examination, particularly where gallstone disease and gallbladder cancer are prevalent.[2-4]

A second observation is the histological diversity of the disease encountered. The four incidental invasive carcinomas alone spanned four different morphologies – signet-ring cell, mucinous, mucin-rich biliary-type and intestinal-type adenocarcinoma – and the clinically suspected group added an adenosquamous (collision) carcinoma, an uncommon and aggressive entity. Several of these variants are recognised as biologically aggressive: mucinous carcinomas of the gallbladder are typically large and advanced tumors,[7] a signet-ring component within a mucinous tumor independently predicts worse survival,[8] and signet-ring or poorly cohesive carcinoma is itself independently associated with higher stage, nodal metastasis and inferior survival in population-based data.[9] Their appearance among incidental specimens reinforces that unsuspected gallbladder cancer cannot be assumed to be indolent and that careful subtyping is prognostically relevant.

The pre-invasive lesions detected – biliary intraepithelial neoplasia and high-grade dysplasia – represent recognised steps in the metaplasia–dysplasia–carcinoma sequence of the gallbladder, and their identification only on histopathology further argues for thorough examination and sampling of cholecystectomy specimens.[6]

This study has limitations. It is small, retrospective, and single-center. Detailed pathology reports were retrievable for 11 of the 14 flagged neoplasms, so the clinicopathological description reflects a documented subset and the full distribution of subtype and stage across all cases cannot be stated; this also precludes a clean definition-based incidence of strictly incidental carcinoma. Survival follow-up was not available. Larger and complete datasets would permit stage-stratified and outcome analysis.

Conclusion

Gallbladder neoplasia was identified in approximately 1.5% of routine cholecystectomy specimens at our institution. The incidental carcinomas were uniformly pT2 with frequent adverse pathological features, and an unusually broad range of aggressive morphologies – signet-ring, mucinous, mucin-rich, intestinal-type and, among suspected tumors, adenosquamous – was encountered in a small number of cases. These findings argue for histopathological examination of every cholecystectomy specimen, careful subtyping of any neoplasm identified, and prompt staging with consideration of radical re-resection when invasive carcinoma is found.

Ethical Approval

The study was conducted in accordance with the Declaration of Helsinki and institutional ethical requirements. As a retrospective analysis of fully anonymized histopathology records, a separate ethics-committee approval number was not assigned.

Informed Consent

Given the retrospective design and the use of fully anonymized histopathology records, individual patient consent was not required. All identifying information has been removed.

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