

CARCINOMA OF THE GALLBLADDER AT THE NNAMDI AZIKIWE UNIVERSITY TEACHING HOSPITAL – A 5-YEAR RETROSPECTIVE STUDY

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ABSTRACT

Background: Carcinoma of the gallbladder is often missed because of the low index of suspicion.

Aims and Objectives: To review the incidence, pattern and outcome of carcinoma of the gallbladder in our center and to highlight the need for early diagnosis.

Design: Retrospective survey of all cases of carcinoma of the gallbladder.

Setting: Nnamdi Azikiwe University Teaching Hospital serving rural, semi-urban and urban communities.

Patients And Methods: Patients who had histologically confirmed carcinoma in the general surgical units of the Nnamdi Azikiwe University Teaching Hospital over a 5-year period were reviewed and, from their case notes, the following information on sex, age, mode of presentation, time of diagnosis, stage of disease, treatment given and outcome were extracted.

Results: Twenty-one cases of gallbladder carcinoma were seen out of a total of 692 cases of different types of cancers seen in the general surgical units, giving an incidence of 3.04%. Six were males and 15 were females, age ranged between 39 and 72 years, a mean of 55; with the peak age in the 7th decade of life. Eleven patients (52.4%) presented with features of chronic cholecystitis and had cholecystectomy. Ten patients presented with obstructive jaundice in a stage too advanced for any form of palliative surgical treatment. The outcome was good in patients who presented with features of cholecystitis but who turned out to be cases of early carcinoma of the gallbladder because after five years of follow-up, none of them has shown any features of recurrence. There was no mortality in this group and the patients have remained in good health. However, the prognosis was poor in those patients who presented with obstructive jaundice. They remained very ill, with worsening general condition. They were discharged home on request of their relations and were lost to follow-up.

Conclusions: Carcinoma of the gallbladder may present as cholecystitis. It is advisable for clinicians to have this in mind before, during and after cholecystectomy. Early presentation to hospital by patients would avert delay and improve early diagnosis, early treatment, and better outcome.

KEYWORDS: Carcinoma, gallbladder, Nigeria.

INTRODUCTION

The overall incidence of carcinoma of the gallbladder in the general population is 3-4%.^{1,2} The incidence of this cancer in women is three to four times that for men, and this is in contrast to the predominance of cancer of the bile ducts in men.² The highest incidence of cancer of the gallbladder occurs in American-Indian women, and there is a well-established association between this cancer and gallstones.^{1,2} The incidence increases with age, majority of the patients being at least 50 years of age.¹

Because this condition is often associated with cholelithiasis, majority of the patients present with

clinical features of gallstones and obstructive jaundice. The diagnosis of this disease is often incidental except in advanced cases. It was such incidental diagnosis of carcinoma of the gallbladder in some patients who had cholecystectomy for what was thought to be 'innocent' cholecystitis in our center that prompted this study.

PATIENTS AND METHODS:

Patients who had histologically confirmed carcinoma of the gallbladder in the general surgical units of the Nnamdi Azikiwe University Teaching Hospital, Nnewi Nigeria between February 1998 and February 2003 were identified from the operations register in theatre and ward records.

Their case notes were retrieved from the Medical Records department. From each patient's folder, the

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following data were extracted: sex, age, mode of presentation, time of diagnosis, stage of disease, treatment given and outcome. The data were analyzed, means determined and percentages calculated.

RESULTS:

A total of 271 cholecystectomies were performed during the five-year period under review. During the same period, 692 cases of different types of cancers were seen in our general surgical units. There were twenty-one cases of gallbladder carcinoma, giving an incidence of 3.04% of all the surgical cancers seen within the period under review. There were six males and 15 females, giving a male: female ratio of 1 : 2.5.

The age range was between 39 years and 72 years, with a mean of 55 years; the peak incidence was in the 7th decade of life.

Table 1: Ages of Patients

Age	No of Patients	Percentage
30-39	2	9.5%
40-49	1	4.8%
50-59	5	23.8%
60-69	12	57.1%
70-79	1	4.8%
Total	21	100.0%

Eleven of the 21 patients (52.4%) presented with symptoms and signs of cholecystitis: pain in the right hypochondrium that was aggravated by fatty food, occasional low grade fever, tender right hypochondrium and positive Murphy's sign. Ten of them with stones, and one without stone. The remaining 10 of the 21 patients (47.6%) presented with obstructive jaundice.

Table 2: Presentation, pre-operative diagnosis, and histology

No of patients	Presentation	Pre-operative diagnosis	Histology report
11	Epigastric/ right hypochondrial pain	Cholecystitis	Adenocarcinoma
10	Epigastric/ right hypochondrial pain; jaundice	Obstructive jaundice	Adenocarcinoma in 6; unspecified "carcinoma" in 4.

In 11 patients, the diagnosis of carcinoma of the gallbladder was neither suspected pre-operatively nor intra-operatively but was confirmed at histopathological examination. In the remaining 10 cases, obstructive jaundice secondary to common bile

duct stone was the pre-operative diagnosis in two cases while carcinoma of the head of the pancreas was the pre-operative diagnosis in the remaining eight cases.

These were supported by ultrasound examination but carcinoma of the gallbladder was suspected at operation and confirmed by histology. The disease was considered early in the 11 cases that presented with features of cholecystitis because of the favourable prognosis that they had. All the patients had laparotomy, with 10 cholecystectomies. In 11 cases, nothing was done because of the advanced stage of the disease. In these advanced cases, the organs that were involved included the liver and the porta hepatis as well as the bile duct and the hepatic flexure of the transverse colon. The respective lymph nodes were involved and lymph node biopsies were taken.

The outcome was good in patients who presented with features of cholecystitis but who turned out to be cases of early carcinoma of the gallbladder because after five years of follow-up, none of them has shown any features of recurrence. There was no mortality in this group and the patients have remained in good health. However, the prognosis was poor in those patients who presented with obstructive jaundice. They remained very ill, with worsening general condition. They were discharged home on request of their relations and were lost to follow-up.

Table 3: TNM staging for gallbladder cancer²

- T1: Tumor invades lamina propria (T1a) or muscular layer (T1b).
- T2: Tumor invades peri-muscular connective tissue; no extension beyond the serosa or into the liver.
- T3: Tumor perforates the serosa or directly invades into one adjacent organ, or both (Extension 2 centimeters or less into the liver)
- T4: Tumor extends more than 2 centimeters into the liver and/or into two adjacent organs (stomach, duodenum, colon, pancreas, omentum, extra-hepatic bile ducts, any involvement of liver).
- N0: No lymph node metastasis
- N1: Metastasis in cystic duct, pericholedochal and/or hilar lymph nodes.
- N2: Metastasis in pancreatoduodenal, portal, celiac, or superior mesenteric nodes.
- M0: No distant metastasis.
- M1: Distant metastasis.

DISCUSSION

Gallbladder carcinoma is the commonest carcinoma of the biliary tree.³ From our study, carcinoma of the gallbladder masqueraded as 'cholecystitis' in the majority of the cases we saw (52.4%), and the diagnosis was made only after receiving the histology report of the gallbladder which

had been removed in the operation of simple cholecystectomy. A number of workers have reported the fact that gallbladder carcinoma is often an incidental finding.^{4,6}

A good number of our patients (47.6%) presented with late cancer of the gallbladder and often, the lesion was too far advanced for any type of curative surgery. This fact was also reported by Florio et al.⁵ All the advanced cases in this study had obstructive jaundice from obstruction of the common bile duct by metastatic tumour. Thus, jaundice in association with carcinoma of the gallbladder may indicate inoperability. Yan et al⁷ in their work had 34 patients with advanced carcinoma of the gallbladder, all of whom also had obstructive jaundice.

In this study, diagnostic work-up included ultrasound scans in the investigation of the gallbladder and the common bile duct. Other diagnostic tools that would have guided us include computed tomography scan (CT-scan) and magnetic resonance imaging (MRI). Unfortunately, these tools are not available in our center. Ultrasound scans with good resolution and appropriate expertise, especially real-time gray-scale scanning machines, would go a long way in properly investigating the gallbladder and, indeed in studying the extra-biliary system for precise pre-operative TNM staging.⁸ The availability of dedicated biliary scanning experts is highly desirable. Kokudo et al⁸ posited that precise pre-operative TNM staging for gallbladder cancer is difficult and that the most accurate staging before resection is possible by integrating a number of diagnostic tools. TNM staging of gallbladder carcinoma is very important for on it hinge both treatment and prognosis. In the 11 patients who presented with features of cholecystitis, the disease was considered to be at an early stage considering the absence of a palpable tumour at surgery, and the favourable outcome that the patients have continued to enjoy even after five years of follow up. In the remaining 10 patients in whom carcinoma of the gallbladder was suspected intra-operatively, intra-operative staging revealed that they were all metastatic, with involvement of the liver and porta hepatis as well as the transverse colon and the adjacent lymph nodes. The treatment of carcinoma of the gallbladder depends on the stage. Early gallbladder carcinoma (T_{1a} or TIS) can successfully be managed by simple cholecystectomy, either laparoscopically or by the open method.⁴ If facilities for frozen section are available, it is possible to do wedge resection of liver bed if the gallbladder is malignant.⁴ We did not carry out any re-operation in any of the 11 patients in whom the diagnosis of gallbladder carcinoma was made after histology because we did not see the need for that. Wakai et al¹¹ believe that radical second resection provides survival benefit for patients with T₂ gallbladder carcinoma.

Trocar site metastasis in patients who had laparoscopic cholecystectomy and in whom carcinoma of the gallbladder was not diagnosed pre-operatively has been reported.¹² The authors of this report believe that a second or converted open radical surgery is necessary in such cases.

Miyazaki et al¹³ reported offering hepatopancreatoduodenectomy for squamous and adenosquamous carcinoma of the gallbladder. Yan et al⁷ reported their experience with surgical treatment of advanced gallbladder cancer. In their series, they performed extended radical cholecystectomy in 11 cases in whom the tumour was locally advanced but with no distant metastasis. Survival was between 8 and 32 months (average 18.8). They performed palliative operations in 29 cases with distant metastasis.

These later patients all died within one year. These authors advocate extended radical cholecystectomy for advanced gallbladder cancers. In this study, none of our advanced cases was suitable for any form of palliative surgery because the tumors were so extensively metastatic that the entire region was almost frozen, with widespread lymph node metastasis and the primary tumor fixed to the liver.

Tsukada et al¹⁴ reported that the presence of lymph node metastasis is strongly influenced by the depth of invasion of the primary tumour. These authors also believe that standard radical surgery contributes to patient's survival and is therefore recommended in patients with locally advanced gallbladder carcinoma. Reports dealing with chemotherapy and/or radiotherapy in the treatment of carcinoma of the gallbladder suggest that the benefit of these modalities is questionable.²

Majority of our cases were adenocarcinoma, although some workers have reported a combination of squamous cell carcinoma and adenocarcinoma in the same lesion.^{9,10}

Late presentation of diseases has remained a persistent problem in our community. This is very worrisome because these patients present when they cannot obtain any curative help. Many workers¹⁵⁻¹⁸ have attributed this late presentation to illiteracy, religious or cultural beliefs, and poverty.

Most of the long-term survivors of carcinoma of the gallbladder are those in whom the surgeon was unaware of the presence of the tumour at the time of cholecystectomy, with the diagnosis being made by the pathologist.² Survival in patients is strongly influenced by the pathologic stage at presentation. Stage T_{1a} has uniformly excellent prognosis (Table 3)².

Most patients have advanced unresectable disease at the time of presentation. As a result, fewer than 15% of all patients with gallbladder carcinoma are alive after five years. Median survival for any T + N₂ M₀ or any T + any N + M₁ is only one to three months.²

In our series, those patients in whom the diagnosis was made by the pathologist have survived for more than five years now. Considering the rate at which those patients who presented late were deteriorating before they were taken home by their relatives, they were unlikely to have survived for more than three months from the time we made the diagnosis.

CONCLUSION

Carcinoma of the gallbladder is commoner in our community than previously thought. In most cases, the diagnosis is incidental, or patients report late to hospital, with metastatic disease. Sustained enlightenment is necessary, so as to encourage patients to report early to hospital whenever they feel unwell.

A high index of suspicion amongst clinicians will avert delay in instituting appropriate management. The use of modern diagnostic tools will increase the diagnostic yield of this disease. We believe that these measures would go a long way towards improving early diagnosis, early treatment, and better outcome.

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