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Diagnosis of Incidental Gallbladder Cancer after Cholecystectomy in Cotonou: A Case Report and Literature Review

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Abstract

Background: Gallbladder cancer (GBC) is a rare tumor with a poor prognosis, often diagnosed late. It is discovered incidentally during pathological examination of a cholecystectomy specimen. **Observation:** We report a case of incidental primary gallbladder adenocarcinoma in a 50-year-old female patient operated for acalculous cholecystitis. **Conclusion:** Through this observation, we discuss the risk factors, diagnostic and therapeutic difficulties of incidentally discovered gallbladder cancers based on literature data.

Keywords

Diagnosis, Cancer, Gallbladder, Cholecystectomy

1. Introduction

Incidental gallbladder cancer refers to a cancer diagnosis made unexpectedly, often during or after a cholecystectomy performed for a condition initially presumed to be benign. Gallbladder cancer (GBC) represents the most frequent malignant tumor of the biliary tract. Although rare and associated with a severe and guarded prognosis, it ranks fifth among digestive cancers, accounting for 3 to 4% of cases, with a marked female predominance [1]. It is frequently associated with gallstone disease in 70% to 92% of cases and constitutes the main risk factor for its development. It is mostly discovered postoperatively, as the diagnosis of malignancy is rarely established preoperatively and is often an incidental finding dur-

ing histopathological report. Adenocarcinoma represents the most common histological type, observed in 87.7% of cases. Clinically, gallbladder cancer often manifests with vague and non-specific symptoms, making early diagnosis challenging [2]. The diagnosis is then made incidentally through the histopathological analysis of a cholecystectomy specimen initially performed for a presumed benign condition. We report a case of primary gallbladder adenocarcinoma incidentally discovered on histological examination after an open cholecystectomy.

2. Observation

We report the case of a 50 years old female patient, with no significant past medical history, who sought medical attention for hepatic colic evolving over the previous two weeks, without associated symptoms. She reported intermittent pain in the right hypochondrium for more than six months, along with undocumented epigastric pain. On physical examination, the patient was in good general condition, afebrile, with stable vital signs; the abdominal examination revealed tenderness in the right hypochondrium without guarding, raising suspicion of acute cholecystitis. Abdominal ultrasound showed a gallbladder with a thickened wall without gallstones. Inflammatory and liver function tests were within normal limits. A diagnosis of acute acalculous cholecystitis was made, and the patient underwent open cholecystectomy.

At the time of opening the surgical specimen, the gallbladder was found to be almost entirely filled by a whitish, firm tumor located in the fundus (**Figure 1**). It was approximately 1 cm from the cystic margin. Postoperative recovery was uneventful. Histopathological analysis revealed a moderately differentiated adenocarcinoma of the gallbladder infiltrating the muscularis layer (**Figure 2**), classified as pT1b (2017 TNM classification, AJCC 8th edition). No vascular emboli or perineural invasion were found, and surgical margins were clear. A staging work-up including thoracoabdominal-pelvic computed tomography (CT) was done and showed no metastases or lymphadenopathy. Multidisciplinary team

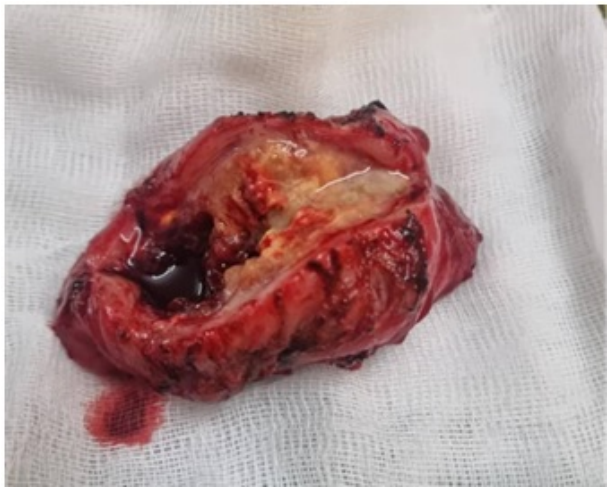

Figure 1. Macroscopic appearance of a budding neoplastic mass at the fundus of the gallbladder (arrow).

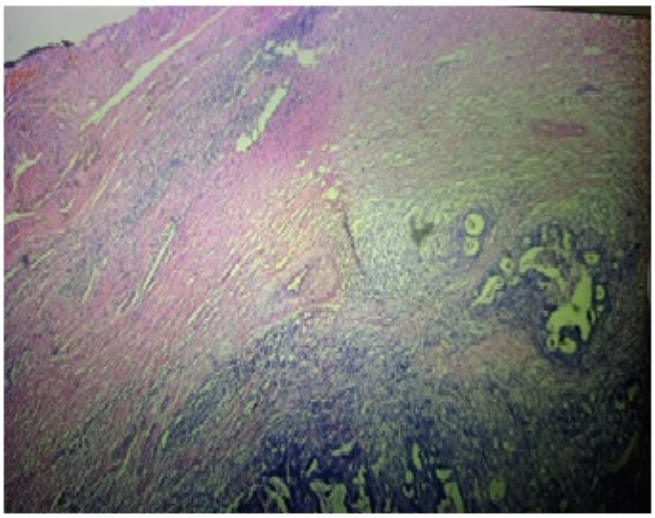

Figure 2. Histological section of a biliary-type adenocarcinoma showing a carcinomatous proliferation with glandular architecture.

meeting recommended adjuvant chemotherapy with oral Capecitabine (2000 mg twice daily for two weeks, followed by a one-week rest, repeated over six months). However, the patient did not comply with the treatment. At two-year follow-up, clinical outcomes were favorable.

3. Discussion

Gallbladder cancer represents only 3% of all cancers and is associated with a poor prognosis [3]. Its incidence peaks between the ages of 50 and 60 [4]. Unlike most digestive tract cancers, it predominantly affects women [5]. In our case, the patient is a 50-year-old woman. This is likely due to the higher prevalence of gallstones in this population which constitutes the main risk factor for GBC. Gallstones contribute to chronic mucosal irritation and delayed gallbladder emptying, creating a dysplastic environment. Indeed, the cholesterol contained in bile, in combination with other contributing factors, can lead to dysplasia of the gallbladder wall epithelium, with the emergence of Goblet cells, Paneth cells, excessive mucus secretion with unusual expression of lysozymes, and the appearance of endocrine (argyrophilic) cells. Such changes are found in nearly 50% of cases of malignant transformation to adenocarcinoma. In the series by Moukhchane O. [5], 100% of patients underwent cholecystectomy for gallstone disease, confirming cholelithiasis as a major causal factor for GBC. In our case, however, the patient had acalculous cholecystitis, suggesting chronic bacterial infection as a possible etiology. Chronic carriers of Salmonella Typhi and *S. paratyphi* have a relative risk of developing GBC ranging from 0.9 to 8.5%. Similarly, chronic infections with *Helicobacter pylori* and Helicobacterbilis have been implicated in gallbladder malignancy. In our endemic context, this infectious hypothesis appears highly plausible. Chronic gallbladder infections cause sustained mucosal irritation and the production of carcinogenic substances. This risk increases significantly with the chronic-

ity of the infection. In a study involving 471 individuals with chronic Salmonella Typhi infection, 5.5% of men and 1.3% of women died from gallbladder cancer. Additional risk factors include:

- Anomalous pancreaticobiliary junctions (APBJ)
- Porcelain gallbladder
- Adenomas with a risk of malignant transformation that increases with age (>50 years)
- Gallbladder adenomyomatosis
- Occupational exposure to carcinogens: GBC incidence is higher among workers in the rubber, paper, footwear, industrial textile, automotive, and metallurgy industries, as well as those handling Benzidine and Beta-naphthylamine.
- Familial and genetic predispositions are suspected but remain unconfirmed [5].

Epidemiologic characteristics and risk factors for GBC remain poorly defined in our setting. They require further investigations to identify at-risk populations who may benefit from prophylactic cholecystectomy and to establish an approach for earlier diagnosis.

The clinical presentation of GBC is often vague and nonspecific, complicating early diagnosis [6]. However, Sana Ben Slama *et al.* [2] reported that most GBC cases were diagnosed at early stages (0, I, or II), with a higher survival rate, which also represents an ideal situation allowing for curative resection and, consequently, ensuring a better prognosis. Our patient followed this pattern, as the cancer was at an early stage. Pain on palpation of the right hypochondrium was the main symptom observed. Other signs reported in the literature, such as jaundice, pruritus, and weight loss generally indicate advanced disease.

Given the nonspecific nature of gallbladder cancer symptoms, early detection of malignancy poses a significant challenge for radiologists. Ultrasound and CT scan are generally the most commonly used imaging modalities. Ultrasound is the first-line investigation for gallbladder pathology and can diagnose up to 80% of GBC cases [7]. Despite its accessibility and low cost, ultrasound is operator-dependent and failed to detect the fundal tumor in our patient. Several factors make diagnostic confirmation difficult with ultrasound. We can list polyps and gallbladder carcinomas that exhibit echogenicity identical to that of the normal gallbladder wall, making the diagnosis of small lesions difficult. For more advanced lesions, the margins are not well-defined, and it can be challenging to exclude a lesion of hepatic origin. Intravesicular tumors often harbor stones and wall calcifications, further complicating the diagnosis. The cancer may also present an infiltrative form with diffuse or localized thickening of the gallbladder wall. This appearance can pose a differential diagnostic challenge with cholecystitis; however, the irregular and asymmetrical nature of the wall thickening, especially when the thickness exceeds 1 cm, should raise suspicion for gallbladder cancer rather than cholecystitis [8]. The rare sclerotic-atrophic form is also diagnostically challenging.

The diagnosis of gallbladder cancer (GBC) prior to cholecystectomy is rare and challenging because these are usually small, asymptomatic lesions and clinical signs such as jaundice or general health deterioration are generally absent in incidentally discovered cancers. Therefore, it is primarily radiological signs that may raise suspicion, such as:

- Focal or irregular gallbladder wall thickening.
- A polyp larger than 10 mm, considered a precancerous lesion, especially if it is sessile, iso- or hypoechoic, with Doppler signal.
- Non-visualized gallbladder on ultrasound or replaced by a subhepatic mass.
- Pedicular or distant lymphadenopathy.
- Atypical perivesicular or hepatic abscess.
- Porcelain gallbladder with calcified wall, though rare.

CT is requested as a second-line investigation to complement ultrasound when MRI is unavailable. In addition to establishing the diagnosis, CT allows for staging assessment.

The surgeon must be alert during cholecystectomy, whether by laparotomy or laparoscopy, to an infiltrated or thickened appearance of the gallbladder, an abnormally enlarged Mascagni lymph node, pedicular infiltration, or a cholecystitis-like appearance in the absence of an infectious syndrome. The tumor frequently involves the fundus of the gallbladder (80%), followed by the body (30%) and the neck (10%) [9]. We performed a cholecystectomy via an open local approach, as laparoscopy remains unavailable in our setting. Intraoperatively, there was no evidence of pedicular infiltration, the Mascagni lymph node appeared normal, and there was no induration of the hepatic bed. The fundus is the preferential site of gallbladder carcinoma; this was the location in our case. Regarding the histological type, it was an adenocarcinoma, which is consistently the most frequent type. It is found in 88% to 100% of cases [10]. Immunohistochemistry could not be realized, as it represents an additional cost for the patient, who no longer had financial resources, given that universal health coverage has not yet been implemented in our country. This technique is used in the diagnosis and characterization of gallbladder cancers to identify specific proteins (markers) on the surface of cancer cells; it helps to better understand the nature, the aggressiveness of the tumor and to guide therapeutic decision-making.

Treatment is essentially based on surgical resection. Chemotherapy and radiotherapy are reserved for palliative care. The prognosis is determined by several factors, primarily the stage of disease, which constitutes the main prognostic factor for gallbladder carcinoma [6]. The treatment is primarily based on surgical resection, as was the case with this patient, with surgical margins extending into healthy tissue, which improves the prognosis. The TNM classification allows for the adaptation of management.

The prognosis depends on the stage of disease. The 5-year survival rate is estimated at over 80% for stage pT1a, compared to less than 10% for advanced stages. An incidentaloma remains an opportunity for curative diagnosis if appropriate

management is initiated promptly. Adjuvant chemotherapy, as decided during a multidisciplinary team meeting, is supported by the BILCAP trial, which concluded that adjuvant treatment with capecitabine "could be considered a standard of care," significantly improving recurrence risk and overall survival [11]. More, it is recommended to offer adjuvant chemotherapy with capecitabine for six months following R0 or R1 surgical resection of a cholangiocarcinoma, provided the patient has a preserved general condition (WHO performance status 0 - 1) and the postoperative delay does not exceed 16 weeks (AFEF and TNCD guidelines). The administration of this adjuvant therapy is not conditioned by tumor location nor by the presence of poor prognostic factors such as N1 or R1 status [12]. In our study, the absence of adjuvant treatment represents a poor prognostic factor, exposing the patient to a high risk of recurrence, even though the clinical outcome has remained favorable over a two-year follow-up. The rarity of gallbladder cancer limits the generalizability of the findings from this observation to the broader population in terms of demographic characteristics, risk factors, and clinical presentation. This case is valuable in generating hypotheses related to the potential risk factors associated with this disease. A prospective or retrospective cohort study would be necessary to define the risk factors for gallbladder cancer and to identify the at-risk population in order to develop effective prevention and screening strategies in our context.

4. Conclusion

The incidental diagnosis of gallbladder adenocarcinoma highlights the importance of systematic histopathological examination of all cholecystectomy specimens, even in the absence of macroscopic lesions. Early diagnosis allows for a curative therapeutic strategy, especially in the early stages. The two-year outcome was favorable despite the patient's inability to access adjuvant chemotherapy due to financial constraints.

Patient Consent

Informed consent was obtained from the patient for publication.

Author Contributions

All authors contributed to the writing and editing of the article. All authors have read and approved the final version of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest.

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