

# Pure Squamous Cell Carcinoma of the Gall Bladder: A Rare and Aggressive Cancer

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## Abstract

**Introduction:** Pure gall bladder squamous cell cancer comprises less than 1% of all gallbladder malignancies and prominent, well differentiated keratinization is a key histological feature.

**Presentation of Case:** This is a case report of an elderly male who presented with nausea and weight loss. His physical examination revealed significant hepatomegaly without jaundice. A CT scan of the abdomen revealed a large infiltrated mass in the liver with significant regional and distal enlarged lymph nodes. In comparison to a CT scan done 17 months ago - showing a normal gall bladder and liver - it was determined that this mass was likely gall bladder cancer with direct invasion into the liver. Histology via percutaneous biopsy showed pure squamous cell carcinoma, by evidence of prominent and well differentiated keratinization. He was staged as IIIb (T3N1M0) deeming the cancer unresectable with a poor prognosis.

**Conclusion:** Gall bladder cancer remains an uncommon cancer of a variety of histological types, in which pure squamous cell dysplasia is rare. This type of cancer is more aggressive than most other histological types and as a result is rapidly progressing, with a poor prognosis.

**Keywords:** gall bladder cancer; squamous cell carcinoma; pure squamous cell

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**Consent:** Consent was taken from the patient's next of kin for publication of this case report.

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## Introduction

Gallbladder cancer is a rare and aggressive tumor that is commonly associated with a poor prognosis. Patients present with nonspecific symptoms and signs leading to an often incidental and late diagnosis. Pure gall bladder squamous cell cancer comprises of less than 1% of all gallbladder malignancies and prominent, well differentiated keratinization is a key histological feature. We present a case of an elderly male with initial symptoms of nausea and weight loss, who was later found to have stage IIIB (T3N1M0) pure squamous cell gall bladder – developed within 17 months of last known normal imaging.

## Case Report

We present an 88 year old African American male with a past medical history of hypertension and benign prostatic hypertrophy, who presented to the emergency department with a three day history of nausea without vomiting. This nausea was not affected by meals but was associated with early satiety and decreased appetite. He also reported a subjective weight loss. A review of symptoms was negative for abdominal pain or jaundice. He had no history of symptomatic gallstones. He smoked 1 cigarette weekly and occasionally drank alcohol.

His vitals were blood pressure 150/66 mmHg, pulse rate 72 beats/min, respiratory rate 18, and temperature 36.5°C with oxygen saturation 98% on room air. A physical examination was significant for a firm, smooth, non-tender right upper quadrant mass extending across the midline which was assessed as hepatomegaly. The patient was anicteric. Other systems were normal.

Initial lab investigations on admission showed normocytic anemia (hemoglobin 8.3 g/dL, mean corpuscular volume 85 fl) with mild leukocytosis (white blood cell count 13300/uL) without bands and thrombocytosis (platelets 522 k/UL). Complete metabolic profile did not show evidence of significant cholestasis (total bilirubin 1.1, alkaline phosphatase 123) with other liver function tests within normal limits.

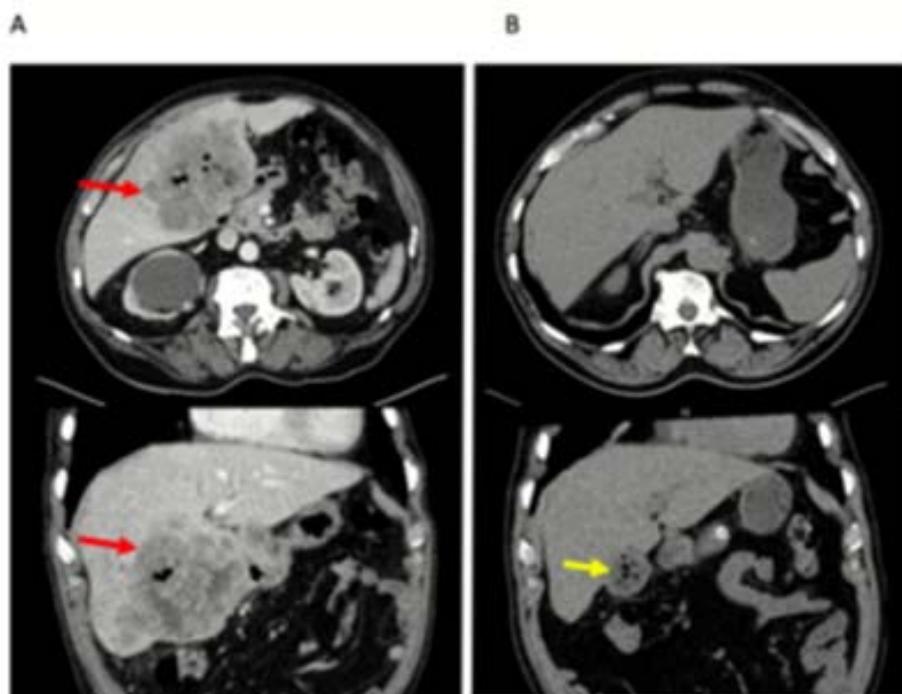
A CT scan of the abdomen and pelvis with contrast revealed a large heterogeneous infiltrative mass in the liver in segments 5, 8, 4a and 4b with additional satellite nodules. There were multiple foci of air within the lesion as it abutted the distal stomach and the C-loop of the duodenum with mass effect. The gallbladder was not visualized. Pathological lymph nodes were noted anterior to the distal thoracic esophagus, anterior-superior to the pancreatic neck in the gastro-hepatic ligament region, superior to the left renal vessels and in the portocaval region. CA 19-9, alpha fetoprotein, and CA 125 were within normal limits. 17 months ago, an abdominal CT done for investigation of a different presentation showed normal liver and gallbladder, with multiple asymptomatic gallstones. On comparison of both of the images it was determined that this new aggressive lesion was likely gall bladder cancer directly invading the liver. Four core needle biopsies were taken from the liver, with subsequent histopathology showing a moderately differentiated, keratinizing squamous cell carcinoma. A staging CT of the chest showed para-esophageal nodes suspicious for metastatic disease as well as a 4 mm ground-glass nodule in the right upper lobe.

The patient was staged at IIIB (T3N1M0) which deemed the tumor inoperable. As his prognosis was poor, palliative care was instituted. He was subsequently discharged to a hospice care facility.

## Discussion

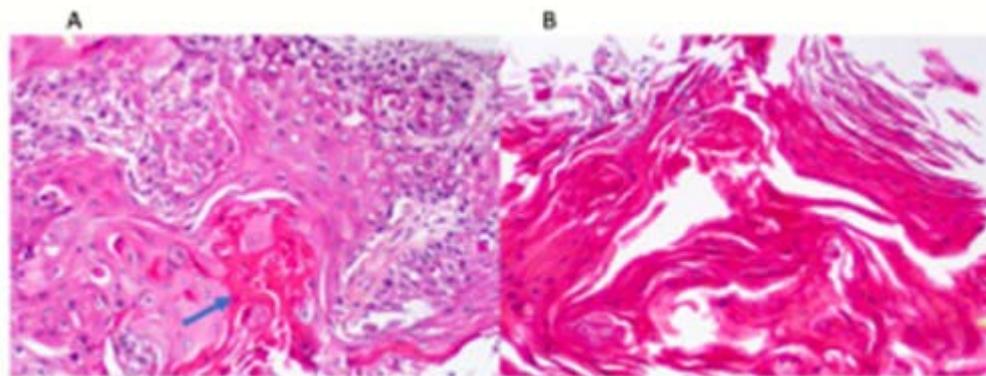
Cancers of the gallbladder are an uncommon occurrence, with an incidence of 1-2.5 cases per 100,000 [1]. Adenocarcinoma is the most common, making up about 95% of gallbladder cancers [2]. Pure squamous cell carcinoma (GCSCC) is very rare, with a frequency of  $\leq 1\%$  [2]. Cholelithiasis has the strongest association to date, being present in up to 85% of cases [1,5]. Larger stones ( $>1\text{cm}$ ) also increase the risk [3]. However the overall incidence of gallbladder cancer in patients with cholelithiasis is 0.2-3% [4,5]. With this low incidence therefore, prophylactic cholecystectomy in asymptomatic patients with cholelithiasis, without remarkable gallbladder changes (e.g. porcelain gall bladder) would be impractical.

The presentation of gall bladder cancer is variable, with non-specific but alarming signs; such as nausea, vomiting and weight loss. Incidental findings in patients with symptomatic gallstones are also common [1]. Symptoms and signs of obstructive jaundice were once the common clues to diagnosis [6]. However, as imaging became more available and frequently used, these presentations are becoming less common, and are indicative of a later stage and hence a poorer prognosis. These more telling symptoms and signs were not present in our patient. Therefore, it was only with the presence of the concerning CT scan findings (Fig. 1) that gall bladder cancer was entertained as a differential. In retrospect, it is also probable that the hepatomegaly felt on physical examination was that of a palpable gallbladder, as liver enlargement was not evident on imaging. More available and frequent imaging has also increased pre-operative diagnosis, which has currently occurred in 30% of cases [5] – our case being one of them (Fig. 1).



**Figure 1** CT scan showing large heterogeneous mass (red arrow) in the liver (A), without distinct visualization of gall bladder, compared to CT scan taken 17 months ago (B) with normal appearing gallbladder (yellow arrow)

One characteristic histological feature of squamous cell carcinoma is prominent and well differentiated keratinization [2] (Fig. 2), which differentiates it from the focal and ill-defined keratinization typical of adenosquamous carcinoma [2]. GBSCC is also stated to be more aggressive than most other types [2,7,8], and was proven to be so in our patient, as prior imaging taken 17 months before showed a normal appearing gallbladder.



**Figure 2** Histology showing pure squamous cell carcinoma (GCSCC) by evidence of prominent, well-differentiated keratinization (blue arrow in A, also seen in B)

Currently, histology does not play a major role in treatment or prognosis, as these are determined by cancer resectability, local infiltration and evidence of metastasis [5]. As most of gall bladder cancers are at an advanced stage at diagnosis, prognosis is generally poor. Our patient's stage at diagnosis was advanced (Stage IIIb/T3N1M0), making his tumor unresectable. In such cases palliative chemotherapy is optional and this was offered to our patient.

## Conclusion

Gall bladder cancer remains an uncommon cancer of a variety histological types, in which pure squamous cell dysplasia is rare. This type of cancer is defined by the presence of prominent keratinization, differentiating it from mixed histological types. This type of cancer is more aggressive than most other histological types and as a result is rapidly progressing, with a poor prognosis.

## Consent Statement

We confirmed that the patient has given informed consent to the publishing of this case.

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