

Case Report

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# The Other Bladder: A Case of Prostatic Adenocarcinoma Metastasis to the Gallbladder

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## Abstract

Prostate cancer metastasis to bone and lymph nodes is common, but metastasis to the gallbladder is rare. We report a case of a 72 year-old-male with a three month history of weight loss and nausea. On further evaluation he was found to have an elevated alkaline phosphatase and radiographic evidence of prostate cancer, skeletal metastases, and a gallbladder mass concerning for concomitant gallbladder carcinoma. Prostate biopsy confirmed high-grade prostatic adenocarcinoma. The patient underwent laparoscopic cholecystectomy and pathologic evaluation of the gallbladder revealed metastatic prostatic adenocarcinoma without evidence of gallbladder carcinoma. This case demonstrates a possible association between prostatic adenocarcinoma and the gallbladder.

**Keywords:** Adenocarcinoma; Gallbladder; Laparoscopic cholecystectomy

## Introduction

Prostate cancer is one of the most common malignancies in the United States. In 2014, it is estimated that 233,000 men were diagnosed with prostate cancer, encompassing 14% of all new cancer cases, and 29,480 men died from the disease [1]. Prostate cancer most commonly metastasizes to regional lymph nodes and bone. A post-mortem survey characterizing the extra nodal metastatic sites of prostate cancer demonstrated that irrespective of clinical symptoms, the more commonly involved sites included bone, lung, liver, pleura, adrenal glands, peritoneum and meninges, however 0.5% of patients were found to have gallbladder metastases [2-4]. Different malignancies have been reported to metastasize to the gallbladder, including melanoma, renal cell carcinoma, and non-small cell lung carcinoma, and in most cases these patients present with acute cholecystitis [3-11].

Herein, we report a case of metastatic prostatic adenocarcinoma to the gallbladder presenting with weight loss and nausea and without acute cholecystitis.

## Case Report

A 72-year-old Caucasian male was referred from the outpatient setting for evaluation of weight loss, nausea, and an elevated alkaline phosphatase of 1,287 IU/L. His symptoms were concerning for a gastrointestinal malignancy, thus computed tomography of the abdomen and pelvis was obtained and showed a distended gallbladder with an enhancing soft tissue mass in the gallbladder neck measuring 1.1 cm×0.9 cm (Figure 1A) with no pericholecystic fluid to suggest acute cholecystitis. A 1 cm lymph node was visualized adjacent to the gallbladder neck (Figure 1B). Also, an enlarged, heterogeneously enhancing prostate gland was present, in addition to multiple sclerotic lesions within the bilateral proximal femurs and pelvis (Figures 2A and 2B). Imaging studies were concerning for metastatic prostate cancer and concomitant gallbladder carcinoma versus gallbladder polyp.

The patient had previously undergone a transurethral resection of the prostate in 2000, following hospitalization for acute urinary retention. Post-operatively, he continued to have poor bladder emptying requiring occasional clean intermittent catheterization. His medical history was also pertinent for pulmonary embolism four years prior for which he had an inferior vena cava filter and required six months of warfarin. At the time of evaluation, he was not taking any prescribed medications or supplements. His social history was negative

for tobacco, alcohol, or illicit drug use. He had no family history of prostate, gastrointestinal, or other malignancy.

On physical examination, he was a thin male and was not jaundiced.



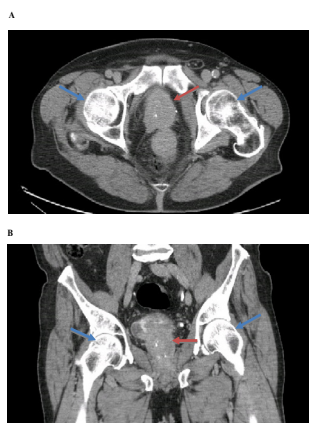
**Figure 1:** CT abdomen demonstrates a distended gallbladder with no pericholecystic inflammation to suggest acute cholecystitis. (a) There is an enhancing soft tissue mass measuring 1.1×0.9 cm in size identified within the gallbladder neck (arrow). (b) A 1 cm lymph node is visualized adjacent to the gallbladder (arrow).

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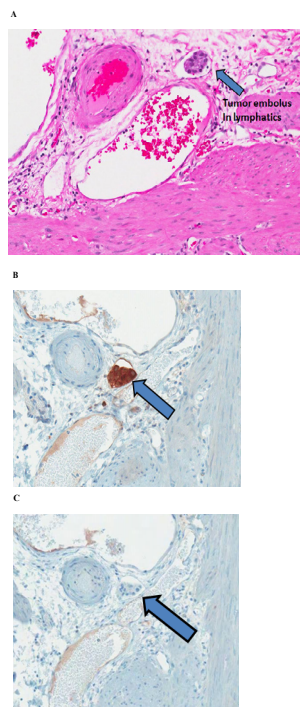
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**Figure 2: a and b:** CT pelvis sections (a–transverse, b–coronal) demonstrate heterogeneous enhancement and thickening of the posterior bladder wall. Furthermore, an enlarged heterogeneously enhancing prostate gland indents the posterior bladder wall and contacts the anterior rectal wall (red arrow). Multiple sclerotic lesions are identified within the bilateral proximal femurs and pelvis, consistent with multifocal osseous metastatic disease (blue arrows).



**Figure 3: (a)** H&E stain and **(b)** PSA stain of the gallbladder with lymphovascular involvement by prostatic adenocarcinoma (arrow). PSA staining of tumor embolus suggests prostatic origin. **(c)** Cytokeratin 7 stain of the gallbladder specimen confirms gallbladder epithelium. A lack of cytokeratin 7 stain suggests that tumor embolus is not of gallbladder origin (arrow).

His abdominal exam did not elicit tenderness on palpation and included a negative Murphy's sign. There was no palpable lymphadenopathy or vertebral tenderness. Genitourinary exam revealed normal external male genitalia. Digital rectal examination revealed a large, irregular, and rock hard prostate. Prostate Specific Antigen (PSA) at the initial visit was 240.64 ng/mL.

He subsequently underwent a prostate biopsy, repeat transurethral resection of the prostate and laparoscopic cholecystectomy. The operation and postoperative course were uncomplicated. Prostatic biopsies revealed Gleason 4+5=9 prostatic adenocarcinoma. Evaluation of the gallbladder specimen demonstrated a grossly distended gallbladder, chronic inflammation and hyper vascularity, and no identifiable mass. Histologic evaluation revealed prostatic adenocarcinoma with lymphovascular invasion, without pathologic evidence of gallbladder carcinoma. This was confirmed by tumor embolus visualized within the gallbladder (Figure 3A) that stained positive for PSA (Figure 3B), and negative for cytokeratin7 (Figure 3C), a molecule expressed in normal gallbladder epithelium. Postoperatively, combined androgen blockade was initiated with bicalutamide and leuprolide for metastatic prostatic adenocarcinoma. At 5 months post-operative, his PSA was 4.10 ng/mL and he was started on denosumab.

## Discussion

Although prostate cancer metastasis to bone and regional lymph nodes is common, metastasis to the gallbladder is exceedingly rare. To our knowledge, there are only two reports in the literature of prostate cancer metastasis to the gallbladder. Bubendorf et al. conducted an autopsy series between 1967 and 1995 on men older than 40 years. Of the 19,316 autopsies performed, 1,589 men were found to have prostate cancer with hematogenous metastatic spread detected in 556 patients. In these subjects, the most common sites of extranodal metastasis were bones, lungs, liver, pleura and adrenals, with gallbladder metastasis incidentally found 0.5% of males. Maxwell et al. presented a case report of an 83 year old male with a history of Gleason 8 prostatic adenocarcinoma, who elected watchful waiting, that presented with signs and symptoms consistent with acute cholecystitis. Following cholecystectomy, histopathologic examination of the specimen revealed metastatic prostate cancer. Interestingly, bone scans and other metastatic evaluation were negative, thus representing an isolated metastatic focus of prostate cancer to the gallbladder. In contrast with the other two reports, our report describes a case of prostate cancer metastasis to the gallbladder presenting on imaging studies as gallbladder carcinoma. Thus, these reports demonstrate that there may be an association between prostatic adenocarcinoma and the gallbladder.

Prostate Stem Cell Antigen (PSCA), a GPI-anchored cell signaling protein, has been investigated for its role in the pathogenesis of prostate cancer. PSCA is expressed in 90% of prostate cancer specimens, and current clinical utility is under investigation, with potential for use in diagnosis, prognosis and treatment of prostate cancer. Increased expression is correlated with high-grade prostatic intraepithelial neoplasia and progression to adenocarcinoma. High levels of PSCA are thought to be directly proportional to Gleason score, risk of metastasis and androgen independence, and effective treatment may decrease expression of PSCA [12-18]. PSCA has also been investigated as a target for immunotherapy in prostate cancer.

Unlike PSA, PSCA is expressed endogenously in other tissues, including normal gallbladder epithelium [12]. Dissimilar to its role in prostatic adenocarcinoma, PSCA may act as a tumor suppressor in gallbladder tissue. This may prevent gallbladder carcinoma, with decreased expression linked to biliary pathology such as gallbladder carcinoma, cholecystitis and cholelithiasis [13,14]. Thus, it is possible PSCA positive prostate cancer may have a protective effect against primary gallbladder cancer.

The endogenous expression of the cell signaling Protein Prostate

Stem Cell Antigen (PSCA) in both prostatic and gallbladder epithelial cells suggests a biochemical relationship between these seemingly unrelated organs. Future investigation is needed to determine if PSCA or other cell signaling pathways play a role in metastasis of prostatic adenocarcinoma to the gallbladder.

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