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Delayed Bladder Metastasis from Extrahepatic Cholangiocarcinoma: Case-Based Update with Literature Review

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Abstract

Cholangiocarcinoma is a rare and aggressive malignancy of the biliary tract that most commonly metastasizes to the liver, lungs, peritoneum, or lymph nodes. Metastatic involvement of the urinary bladder is exceptionally rare, with only a limited number of cases reported in the literature. Herein, we present the case of a 70-year-old woman with a history of extrahepatic cholangiocarcinoma who developed painless gross hematuria five years after completion of her initial treatment. Imaging studies revealed a lesion involving the bladder wall, and transurethral resection of the bladder tumor confirmed the presence of adenocarcinoma consistent with her previous primary malignancy. Histopathological and immunohistochemical evaluation demonstrated tumor positivity for CK7, CK19, CA 19-9, and carcinoembryonic antigen (CEA), with negative staining for GATA3 and CK20, supporting the diagnosis of metastatic cholangiocarcinoma rather than a primary urothelial tumor. This case underscores that cholangiocarcinoma may give rise to delayed and unexpected metastatic patterns, including isolated bladder involvement, even years after apparently curative treatment. In patients with a history of biliary tract malignancy presenting with hematuria, metastatic disease should remain an important diagnostic consideration.

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Introduction

Cholangiocarcinoma is a rare but aggressive malignancy arising from the epithelial cells of the intrahepatic or extrahepatic bile ducts. Owing to its insidious onset and nonspecific clinical presentation, the disease is frequently diagnosed at an advanced stage, thereby limiting the feasibility of curative surgical intervention [1]. Consequently, adjuvant treatment modalities, including chemotherapy and radiotherapy, play a pivotal role in disease management [2].

Metastatic spread of cholangiocarcinoma most commonly involves the liver, peritoneum, regional lymph nodes, lungs, and bones [3]. Nevertheless, rare cases of dissemination to atypical anatomical sites have been described, including isolated reports of renal involvement and ureteropelvic junction obstruction caused by metastatic lesions, further expanding the spectrum of its unusual metastatic behavior and posing diagnostic challenges in clinical practice [4,5]. Within the urinary system, metastatic involvement of the bladder is exceedingly uncommon. Although primary bladder tumors are predominantly of urothelial origin, the emergence of a new bladder lesion in patients with a known oncologic history should prompt consideration of secondary metastatic disease [6].

Herein, we report a rare case of a patient with a prior diagnosis of cholangiocarcinoma who underwent curative surgical resection followed by adjuvant therapy. Approximately five years after the initial diagnosis, the patient presented with gross hematuria, and histopathological evaluation of the bladder lesion confirmed metastatic cholangiocarcinoma. Although the exact incidence remains unknown, only a limited number of bladder metastases originating from cholangiocarcinoma have been reported in the literature, underscoring the exceptional rarity of this presentation [7]. This case highlights the importance of including metastatic disease in the differential diagnosis of bladder lesions in patients with a history of cholangiocarcinoma.

Case Presentation

In 2019, a 70-year-old woman presented with abdominal pain and unintentional weight loss. Diagnostic imaging combined with histopathological evaluation confirmed a diagnosis of cholangiocarcinoma originating from the extrahepatic bile ducts. The patient underwent left hepatectomy, extrahepatic bile duct resection, and portal vein resection. Final pathological examination revealed a gastric foveolar-type adenocarcinoma staged as T2bN0. Adjuvant chemotherapy with capecitabine was planned for eight cycles; however, the final cycle was omitted due to the development of thrombocytopenia and fever. The patient subsequently completed a course of radiotherapy between March and April 2020.

In 2022, disease progression with local recurrence was detected, and systemic chemotherapy with cisplatin and gemcitabine was administered for three cycles. Her medical history was notable for hypertension, a prior cerebrovascular accident requiring carotid artery stenting, and a postoperative incisional hernia.

In 2024, the patient experienced two episodes of painless gross hematuria with clot passage in March and July. She denied lower urinary tract symptoms and had no history of prior urologic surgery. During hospitalization for diagnostic evaluation, ultrasonography and contrast-enhanced computed tomography (CT) revealed a 37 × 12 mm mobile echogenic lesion within the bladder, initially interpreted as a possible intravesical hematoma (Figure 1). Subsequent cystoscopic evaluation identified a suspicious bladder lesion, and transurethral resection of the bladder tumor (TUR-B) was performed for diagnostic purposes (Figure 2).

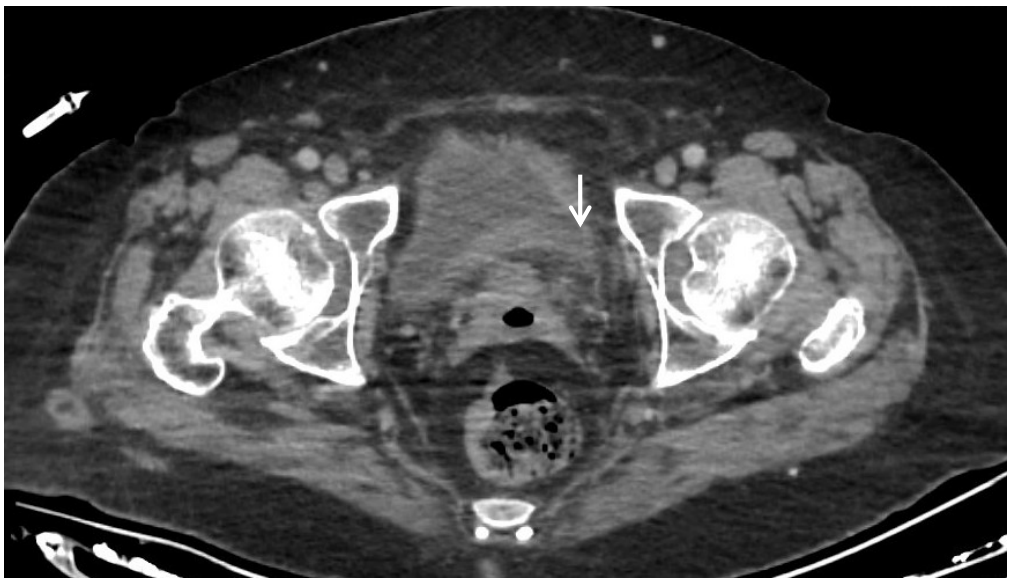

Figure 1. Axial contrast-enhanced computed tomography (CT) image demonstrating focal thickening and enhancement of the posterior bladder wall (white arrow), with no evidence of upper urinary tract involvement.

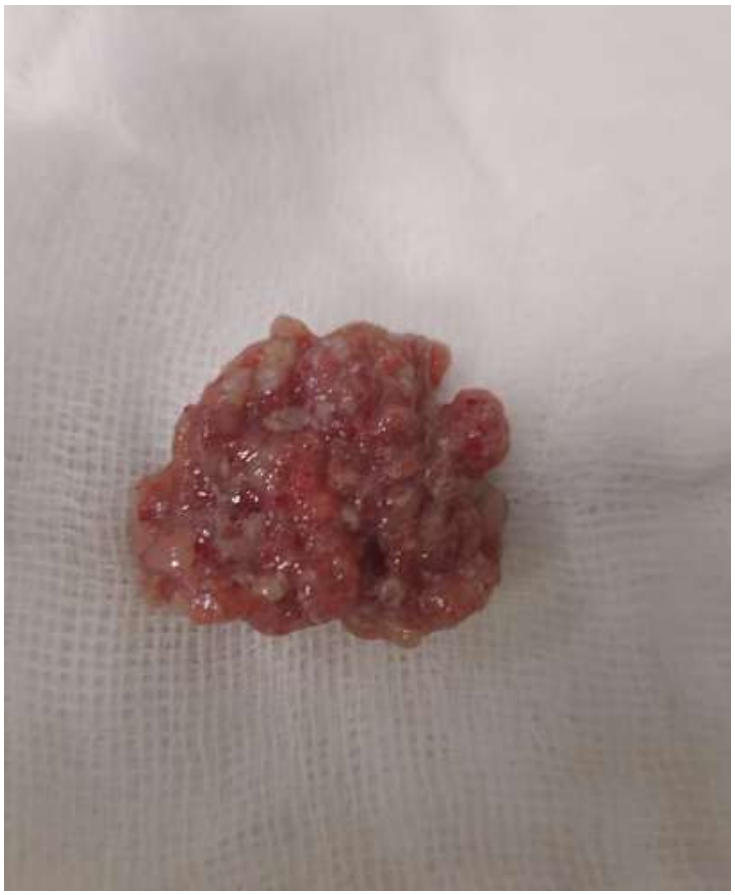

Figure 2. Macroscopic view of the bladder tumor specimen resected during transurethral resection of the bladder tumor (TUR-B).

Histopathological examination of the resected tissue revealed a mucin-rich neoplastic proliferation composed predominantly of columnar epithelial cells arranged in glandular structures (Figure 3).

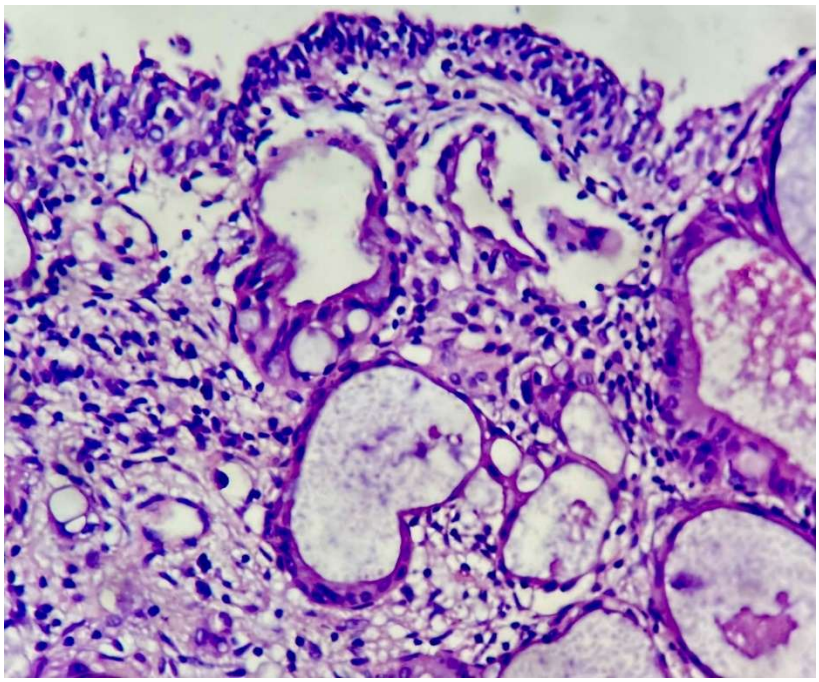

Figure 3. Hematoxylin and eosin (H&E)–stained section demonstrating infiltrative glandular structures composed of columnar epithelial cells with abundant cytoplasm and basally located nuclei.

Immunohistochemical profiling demonstrated tumor positivity for cytokeratin 7 (CK7), cytokeratin 19 (CK19), carbohydrate antigen 19-9 (CA 19-9), and carcinoembryonic antigen (CEA), while special AT-rich sequence-binding protein 2 (SATB2), GATA3, and cytokeratin 20 (CK20) were negative. This staining profile, particularly the dual positivity for CK7 and CK19 combined with negativity for urothelial markers such as GATA3 and CK20, supported the diagnosis of metastatic adenocarcinoma of biliary origin, consistent with the patient's known history of cholangiocarcinoma (Figure 4).

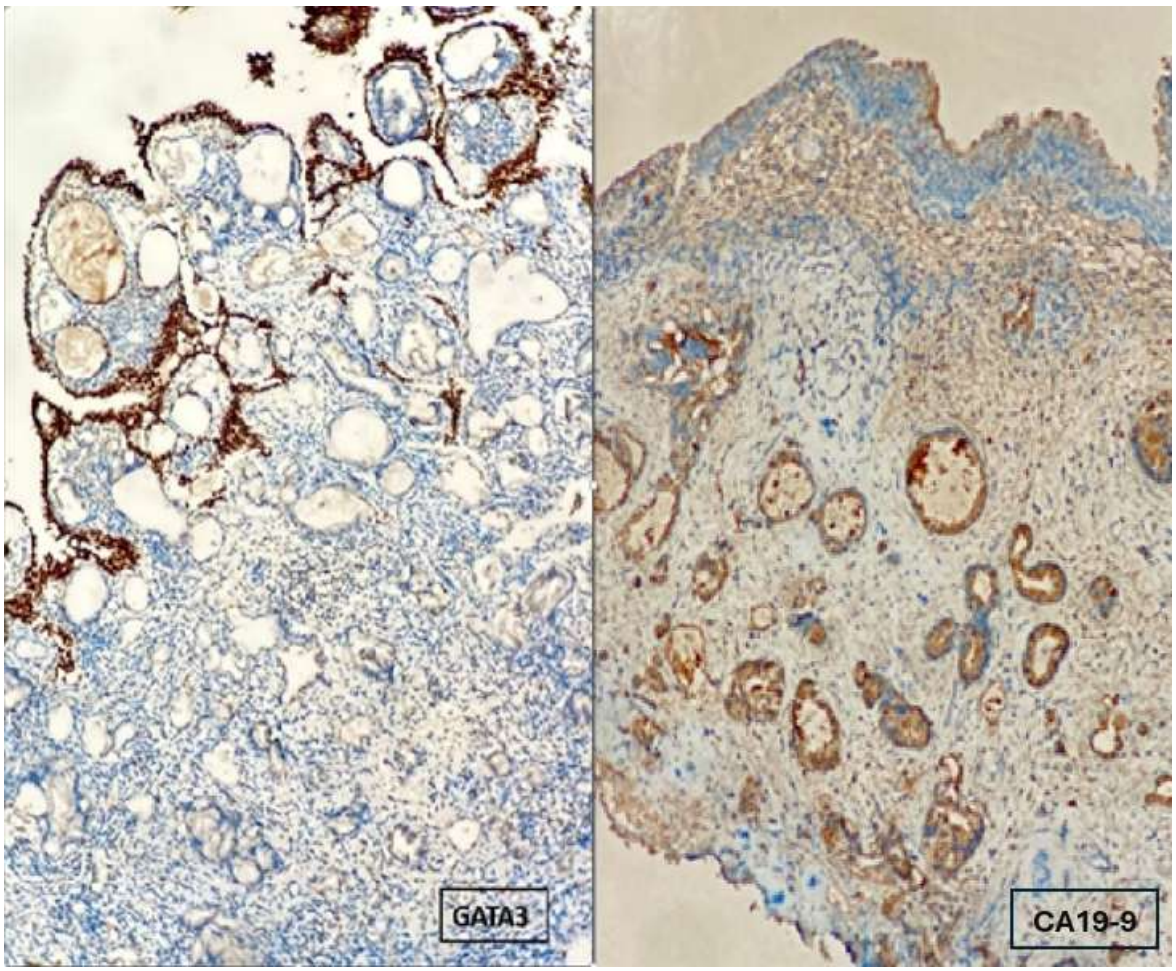

Figure 4. Immunohistochemical staining demonstrating negative GATA3 expression (left) and positive CA 19-9 expression (right) in tumor glands. GATA3 negativity helps exclude a primary urothelial carcinoma, whereas CA 19-9 positivity supports a biliary origin of the metastatic adenocarcinoma.

Following transurethral resection of the bladder tumor (TUR-B), immunotherapy was considered as a potential treatment option. However, owing to the patient's declining performance status and overall frailty, immunotherapy could not be initiated. The patient was subsequently managed with supportive and palliative care measures. Despite these interventions, the patient died seven months after the diagnosis of bladder metastasis.

This case underscores the importance of maintaining a broad differential diagnosis when evaluating hematuria in patients with a known history of malignancy, particularly in the absence of typical urological causes.

Discussion

Cholangiocarcinoma is a rare but highly aggressive malignancy arising from the biliary epithelium and is frequently diagnosed at a locally advanced or metastatic stage [8]. Although surgical resection remains the only potentially curative treatment option, the majority of patients present with unresectable disease [9]. The most common metastatic sites include the liver, peritoneum, lungs, lymph nodes, and bones. Nevertheless, in rare instances, cholangiocarcinoma may disseminate to atypical anatomical locations, including the urinary system. Among these, metastatic involvement of the urinary bladder is exceedingly uncommon.

Isolated reports have described cholangiocarcinoma metastasizing to other components of the urinary tract, such as renal metastases managed surgically, ureteropelvic

junction obstruction caused by metastatic lesions, and epididymal involvement confirmed by histopathological examination [4,5,10]. These unusual presentations collectively suggest that cholangiocarcinoma may exhibit unpredictable metastatic behavior within the urinary system, thereby posing significant diagnostic and therapeutic challenges.

The vast majority of bladder tumors are primary urothelial carcinomas, which typically present with painless hematuria and are most frequently observed in older male patients [11]. These malignancies are strongly associated with environmental risk factors, tobacco exposure, and characteristic molecular alterations [12]. In contrast, secondary metastatic tumors of the bladder are rare and most commonly originate from primary malignancies such as breast, gastric, or lung cancer, as well as melanoma, usually via hematogenous dissemination. Clinically and morphologically, metastatic lesions may closely mimic primary bladder tumors, making accurate diagnosis heavily dependent on thorough histopathological and immunohistochemical evaluation [13].

Beyond the urinary system, cholangiocarcinoma has also been reported to metastasize to other rare anatomical sites, including the cerebrospinal fluid, pleural cavity, peritoneum, and mesenteric lymph nodes. Metastatic involvement of the cerebrospinal fluid represents an uncommon manifestation [14], while malignant cholangiocarcinoma cells have been identified in pleural effusions [15]. Additionally, cases of peritoneal dissemination following immunotherapy [16] and mesenteric lymph node involvement after complicated liver biopsy procedures [17] have been described, further illustrating the heterogeneous metastatic potential of this malignancy.

The pathophysiological mechanism underlying bladder metastasis from cholangiocarcinoma remains poorly understood due to the extreme rarity of this phenomenon. In the absence of direct anatomical continuity or peritoneal dissemination, hematogenous spread appears to be the most plausible route in the present case. The posterior bladder wall localization may support this hypothesis, as this region is relatively well vascularized and potentially susceptible to hematogenous tumor seeding. Moreover, the prolonged interval of approximately five years between the initial diagnosis and the detection of bladder involvement raises the possibility of tumor dormancy, whereby disseminated micrometastatic cells remain clinically silent for extended periods before reactivation. Such delayed metastatic presentations have been described in other solid malignancies and may reflect complex interactions between tumor biology, host immune surveillance, and microenvironmental factors [18].

To date, only a limited number of cases describing metastatic spread of cholangiocarcinoma to the urinary bladder have been reported. In one early report, an 88-year-old male patient with hilar cholangiocarcinoma developed bladder wall involvement during follow-up, which was histopathologically confirmed based on CA 19-9 positivity [19]. In another exceptionally rare case, a 34-year-old female patient with intrahepatic cholangiocarcinoma presented with synchronous bladder trigone involvement, accompanied by gastric and psoas muscle metastases, with diagnosis supported by strong CK7 and CK19 immunoreactivity [7].

In the present case, a patient with a known history of extrahepatic cholangiocarcinoma presented with painless gross hematuria five years after initial treatment. Cystoscopic evaluation revealed an isolated, hyperemic lesion on the posterior bladder wall, and transurethral resection of the bladder tumor (TUR-B) was performed for diagnostic confirmation. Radiologic evaluation demonstrated no evidence of upper urinary tract involvement, supporting a hematogenous or lymphatic route of dissemination rather than direct local extension.

Table 1. Reported cases of bladder metastasis originating from cholangiocarcinoma compared with the present case.

Author (Year)	Age / Sex	Primary Cholangiocarcinoma Site	Bladder Involvement	Other Metastatic Sites	Time to Bladder Metastasis	Management / Outcome
Okumura et al. (2018)	88 / M	Hilar	Bladder wall	None reported	Not specified	Palliative biliary drainage
Banerjee et al. (2018)	34 / F	Intrahepatic	Bladder trigone	Stomach, psoas muscle	Synchronous	Palliative chemotherapy
Present case	70 / F	Extrahepatic	Posterior bladder wall	None at time of bladder metastasis	5 years	TUR-B, palliative care

This case not only provides unique clinical and academic insight into an exceptionally rare metastatic pattern but also reinforces the importance of maintaining a broad differential diagnosis when evaluating bladder lesions in patients with a known oncologic history.

Conclusion

This case highlights the potential for cholangiocarcinoma to metastasize to the urinary bladder, an exceedingly rare occurrence with only a limited number of cases previously reported in the literature. Bladder lesions should not be presumed to represent primary malignancies, particularly in patients with a known oncologic history. Delayed bladder metastasis should be considered even in long-term survivors of cholangiocarcinoma presenting with hematuria, as awareness of this possibility is essential for accurate diagnosis and appropriate clinical management.

Ethical Approval and Consent

Ethical approval was not required for this case report in accordance with institutional and national guidelines.
Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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Conflict of Interest

The authors declare that they have no conflicts of interest.

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