

Bladder Perforation during Transurethral Resection of Bladder Tumor Is Not an Innocent Accident: Literature Review Based on a Clinical Case Experience

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Abstract

Urothelial Carcinoma (UC) is one of the most frequent cancers worldwide. Transurethral Resection of Bladder Tumor (TURBT) is a standard treatment in the disease's early stages, with bladder perforation being a possible and classical complication. However, extravesical tumor seeding resulting from perforation is a rare phenomenon. We hereby report the case of a 76-year-old man with a history of smoking diagnosed with high-grade T1 urothelial carcinoma. TURBT was performed and bladder perforation occurred during the procedure. Radical cystectomy after neoadjuvant chemotherapy failed to reveal an invasive tumor. However, the patient experienced peritoneal recurrence with liver metastasis 3 years following the operation. This case left physician wondering whether the bladder perforation and the resulting tumor seeding are the cause behind the late peritoneal recurrence of an early-stage urothelial carcinoma.

Keywords

Bladder Cancer, Transurethral Resection of Bladder Cancer, Bladder Perforation, Peritoneal Carcinomatosis

1. Introduction

With over 550,000 cases annually, bladder cancer is one of the ten most prevalent cancers worldwide [1]. Urothelial Carcinoma (UC), also known as transitional cell carcinoma, is by far the most common histologic subtype, accounting for 90% of bladder cancer cases [2]. Notable risk factors of UC include tobacco

smoking, occupational exposure to aromatic amines, or certain medical conditions and pharmaceutical agents, with men being more at risk [3]. Painless hematuria, lower urinary tract symptoms, flank pain, or pelvic mass are typical symptoms and signs [4]. Treatment options highly depend on tumor staging: they include a combination of surgical treatment, intravesical *Bacillus Calmette-Guérin* (BCG) instillations, intravesical or systemic chemotherapy, and/or immunotherapy [5].

Transurethral Resection of Bladder Tumor (TURBT) has become one of the most common surgical approaches to eradicate non-muscle invasive bladder tumors. While technically safe, bladder perforation can occur in 0.9% to 5% of cases and remains one of the most common complications [6]. Urologists consider bladder perforation a classical complication, easily managed by either supportive care or open surgery [6]. However, tumor seeding as a result of bladder perforation is a very rare form of recurrence and an infrequently reported entity.

We hereby report the case of a 76-year-old man with UC recurrence as, most probably, a result of tumor seeding following bladder perforation during transurethral resection.

2. Case Presentation

A 76-year-old man presented with painless hematuria in February 2019. Past medical history included hypertension and diabetes. Social history included smoking stopped ten years ago and a daily single glass of alcohol intake. He underwent TURBT which revealed a high-grade urothelial carcinoma infiltrating the bladder muscle. Bladder perforation occurred during the transurethral resection, leading to surgery the next day for bladder reparation. The patient received neoadjuvant chemotherapy consisting of 4 cycles of Gemcitabine and Cisplatin followed by radical cystoprostatectomy with an orthotopic neobladder in August 2019. The histologic study failed to show any invasive residual tumor albeit the persistence of superficial papillary foci in the anterior wall of the bladder. He did not receive any treatment after his surgery, and he was lost to follow-up.

In July 2022, the patient presented to our clinic with diffuse abdominal pain, nausea, anorexia, and spectacular weight loss. Total body CT scan showed diffuse hepatic and splenic metastasis, and peritoneal carcinomatosis (**Figure 1**). It also showed bilateral hydronephrosis and enlarged retroperitoneal lymphadenopathies (**Figure 2**). Transcutaneous biopsy of the liver masses showed a high-grade carcinoma with malpighian differentiation, compatible with the patient's primary bladder tumor (**Figure 3**). Serum creatinine was increased to 4 times the normal with a creatinine clearance of 15 ml/min, deemed irreversible despite bilateral pyelostomy. A nasogastric tube was placed to relieve gastric occlusion symptoms and the patient became progressively icteric. Immediate initiation of Pembrolizumab failed to stop disease progression and the occurrence of hepatic function insufficiency, resulting in patient death one month after his hospitalization.



Figure 1. CT scan showing diffuse hypodense metastatic nodules in the liver and the spleen. Micronodular aspect of the peritoneum compatible with peritoneal carcinomatosis (blue arrow).

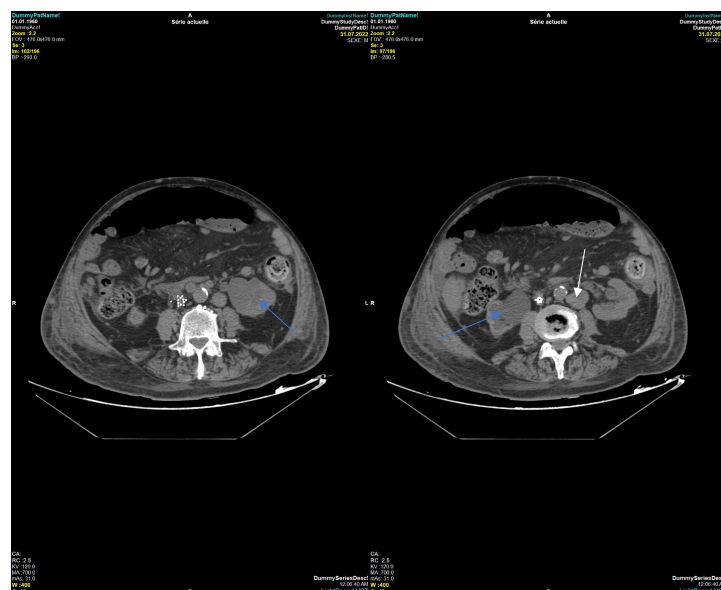


Figure 2. CT scan showing left and right hydronephrosis (blue arrows), and multiple retroperitoneal lymphadenopathies (white arrow).

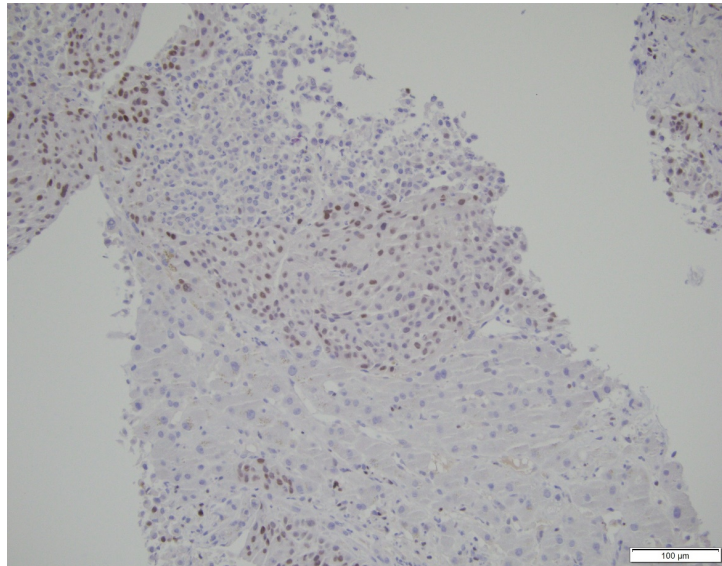


Figure 3. Liver biopsy with GATA3 immunohistochemical stain, a sensitive marker for UC.

3. Discussion

TURBT has become a standard diagnostic and therapeutic procedure in patients with non-muscle invasive bladder cancer. However, it is far from perfect as multiple complications can occur, such as bladder perforation, obturator nerve stimulation, or infection [6]. Bladder perforation, being one of the most common complications, is more frequent with risk factors such as low Body Mass Index, resection depth, and low surgical experience [7]. It is associated with an increased risk of urinary tract infection, fever, septicemia and transfusion, and a decreased 5-year survival rate [8].

In our patient's case, bladder perforation could have resulted in an extravesical tumor seeding, which is an uncommon form of recurrence in UC. Whether extravesical seeding increases the risk of recurrence is still controversial. In fact, Lonati *et al.* reported that only 7 cases out of 521 patients with bladder perforation experienced tumor seeding [7].

Moreover, a frequently discussed risk factor for extravesical tumor seeding is the requirement of open surgery. A retrospective study by Skolarikos *et al.* found that all 4 patients who required open surgery following bladder perforation presented extravesical recurrence. In comparison, none of the 30 patients who did not require open surgery experienced extravesical progression [9]. On the contrary, Golan *et al.* stated that bladder perforation requiring surgical repair does not significantly enhance the chance of extravesical recurrence [10]. Nevertheless, reoperation could therefore be a potential mechanism that increases tumor seeding risk in our patients.

Extravesical tumor seeding and metastasis may be seen at a higher frequency in patients with high-grade UC. While it could have increased the risk of recurrence in our patient, the initial excellent response and the delayed recurrence-free

interval further incriminate the initial perforation as a plausible cause of our patient's recurrence and metastasis.

Few cases resembling ours have been described in the literature by Kim *et al.*, Bus *et al.*, Corfitsen *et al.* and Lim *et al.* who reported one patient each with UC recurrence following bladder perforation [11] [12] [13] [14]. Sites of metastasis were unusual such as the adnexa [11] [12], the peritoneum [11], the pelvis [13] and the sigmoid colon [14]. Time elapsed between the perforation and the recurrence discovery in these patients ranged between 4 and 15 months. Our patient, on the other side, despite an initial impressive response to neoadjuvant chemotherapy, had mainly peritoneal carcinomatosis, and a relatively long recurrence-free interval, with more than 3 years elapsed between perforation and recurrence.

Intraperitoneal chemotherapy has been proven to be effective in preventing tumor spillage from bladder perforation in a rat model. Following laparotomy, rats treated with intraperitoneal Mitomycin showed no sign of tumor recurrence compared to rats who underwent lavage with water [15]. This experiment could provide positive insight for future treatment of this complication. However, this topic has never been investigated in a human study, and no decision or guideline has ever been issued, most likely because of the rarity of the situation.

4. Conclusion

UC is one of the most frequent cancers worldwide, and TURBT is increasingly being used as a treatment option. While many complications can occur, bladder perforation is regarded as an innocent event that can be managed successfully, but it could hide a real risk of extravesical tumor recurrence. This report highlights the importance of a good surgical technique, a high index of suspicion regarding perforation during the procedure, and the avoidance of such complications. It also highlights the possibility of implementing a close surveillance plan in patients who experience bladder perforation or suggest preventive intraperitoneal measures in the future.

Consent

Consent to report this case has been obtained from the patient's family.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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