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Oncology

Unusual lymphatic spread: Autopsy report of rectal obstruction from high-grade micropapillary urothelial carcinoma in the urinary bladder

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A B S T R A C T

Bladder cancer commonly metastasizes to the lymph nodes. Rectal obstruction (RO) caused by bladder cancer has been reported rarely, and its underlying mechanism remains unclear. Herein, we present an autopsy case of a 67-year-old man with RO caused by urothelial carcinoma (UC) with a micropapillary variant in the bladder. The autopsy showed high-grade UC infiltrating the rectum via the bladder's lateral pedicle, and widely spreading within the retroperitoneum due to lymphatic dissemination. Given that RO caused by bladder cancer is typically diagnosed after it has become a systemic disease, it is crucial to consider systemic treatment for the patient.

1. Introduction

Bladder cancer is a commonly observed malignancy in older men. It has a common tendency to metastasize to the lymph nodes, liver, and lungs.[1] Rectal obstruction (RO) caused by bladder cancer has rarely been reported in case reports, and the mechanism through which bladder cancer leads to RO remains unclear.[2,3] In this report, we present an autopsy case of a 67-year-old man with RO due to bladder cancer, along with widespread systemic metastases due to lymphatic dissemination. The histopathological findings from this autopsy would aid in clarifying the underlying mechanism.

2. Case presentation

A 67-year-old male construction worker complaining of abdominal distention and hematuria was admitted to our urology department. He was a chronic smoker (Brinkman index of >600); as described by the patient, there was no history of malignancy, but he had not undergone medical examinations in the past few years. The patient appeared physically frail because of insufficient oral intake (only semi-solid foods) for a month due to abdominal distension; he had chronic nausea and significant difficulty in defecating.

Digital rectal examination indicated circumferential rectum stenosis. A cystoscopy indicated a bleeding nonpapillary bladder tumor with a broad base located from the bladder trigone to the prostatic urethra. A computed tomography (CT) scan indicated gastrointestinal obstruction due to RO, along with the accumulation of ascites and deformity of the bladder with wall thickening (Fig. 1). However, it did not show any signs of metastasis. The colonoscopy and gastroscopy did not indicate any gastrointestinal cancer. Urine cytology and ascites cytology indicated adenocarcinoma-like cancer cells. The patient's serum levels of carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9) were 17.2 ng/ml and 48.5 U/ml, respectively.

Transurethral resection of the bladder tumor (TURBT) and transrectal needle biopsies of the prostate and the rectal wall were performed for pathological diagnosis. High-grade urothelial carcinoma (UC) cells were detected in the bladder tumor, the prostate, and the smooth muscle of the rectal wall. We offered him and his family comprehensive information about his condition, including an estimate of the prognosis and various treatment options, including chemotherapies. They opted for supportive care and declined chemotherapy. Accordingly, total parenteral nutrition (TPN) via a peripherally inserted central catheter (PICC) and pain relief treatment using several drugs, including morphine, were administered.

The patient passed away five weeks after hospitalization. An autopsy was performed after obtaining informed consent from his family. The histopathological findings from the autopsy revealed high-grade UC with a micropapillary variant in the bladder, which had infiltrated into the rectal wall (Fig. 2 and 3A–C). The cancer cells had widely spread in the retroperitoneum through lymphatic dissemination, involving the superior mesenteric artery lymph nodes, duodenum, Virchow lymph node, and thyroid (Fig. 3D–F and 4A–C). Accumulation of ascites was caused by the peritoneal dissemination of UC (Fig. 4D–F). The patient

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Abbreviations

CT	computed tomography
DO	duodenum obstruction
PICC	peripherally inserted central catheter
RO	rectal obstruction
TPN	total parenteral nutrition
TURBT	transurethral resection of the bladder tumor
UC	urothelial carcinoma

retrogradely via the lateral pedicles to the rectum. Furthermore, several cases with RO caused by recurrent bladder cancer after radical cystectomy were reported, suggesting that the recurrent bladder cancer infiltrated into the rectum along the lateral pedicles.[2,3] The internal genitalia in females and Denonvilliers' fascia in males work as barriers to separate the bladder and the rectum and prevent bladder cancer cells from infiltrating directly into the rectum. Therefore, this infiltration of bladder cancer into the rectum is only possible in males who have lateral pedicles. As the cancer cells invade from the outside of the rectum, it is hard to detect their presence within the rectum through mucosal biopsy using colonoscopy. In such cases, a transrectal needle biopsy of the rectal wall was necessary for the diagnosis. Our present case aligns with

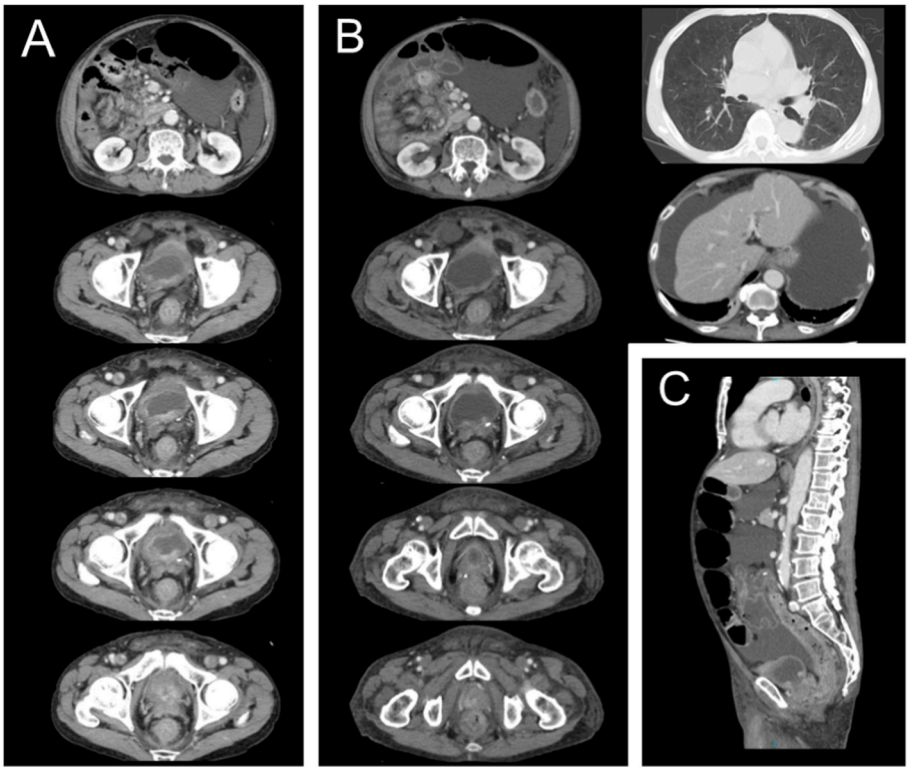

Fig. 1. Computed tomography (CT) scans
Horizontal views of an abdominal and pelvic enhanced CT scan during the patient's hospitalization (A). Horizontal views or sagittal views of an abdominal, pelvic, and chest-enhanced CT scan one week after transurethral resection and biopsies (B and C). Accumulation of ascites, gastrointestinal obstruction caused by circumferential rectal thickening, broad-based bladder tumor extending from the bladder trigone to the bladder neck, and bladder deformity with wall thickening were indicated (A). Distant metastasis was not indicated (A). A part of the bladder tumor extending from the trigone to the prostatic urethra was removed after resection (B). Signs of increased accumulation of ascites, small intestinal clumping, edematous intestinal tract, and attenuation of contrast effect of the intestinal tract and both kidneys, were indicated (B). Both CT scans showed no evidence of direct invasion by bladder cancer or distant metastases, including in the lungs, liver, and lymph nodes (B). The colon was dilated due to rectal obstruction (C).

had widespread systemic metastases due to lymphatic dissemination, although these metastases could not be detected on CT scans before his death.

3. Discussion

The underlying mechanism by which UC cells in the bladder reach the rectal wall remains unclear. Tanabe et al. reviewed several case reports of RO caused by bladder cancer.[2] The common features of those cases were "male," high-grade UC," "invasive cancer" and "poor prognosis." First, Kobayashi et al. hypothesized that invasive UC could infiltrate via the lateral pedicles to the rectum wall.[3] As the lateral pedicles are known as a lymphatic passageway from the lower rectum to inguinal lymph nodes, it was suggested that invasive UC cells located at the lateral bladder wall or near ureteral orifices could infiltrate the hypothesis described above, which includes factors such as "male gender," "high-grade UC," "invasive cancer," and "tumor location in the bladder."

In this case, high-grade UC with a micropapillary variant was widely metastasized. This variant is a very rare subtype of invasive UC and is known to have a poor prognosis. This variant exhibits adenocarcinoma-like characteristics, such as the elevation of serum levels of CEA and CA 19-9, as well as a similar pathological appearance. In this case, both urine cytology and ascites cytology would identify these variant cells as adenocarcinoma-like cancer cells and it was hard for us to diagnose the variant cells using fragmentary specimen samples obtained from the TURBT or needle core biopsies.

We previously reported an autopsy case involving RO and duodenal obstruction (DO) resulting from the recurrence of postoperative renal pelvic cancer in the bladder wall.[4] In both the previous case and this

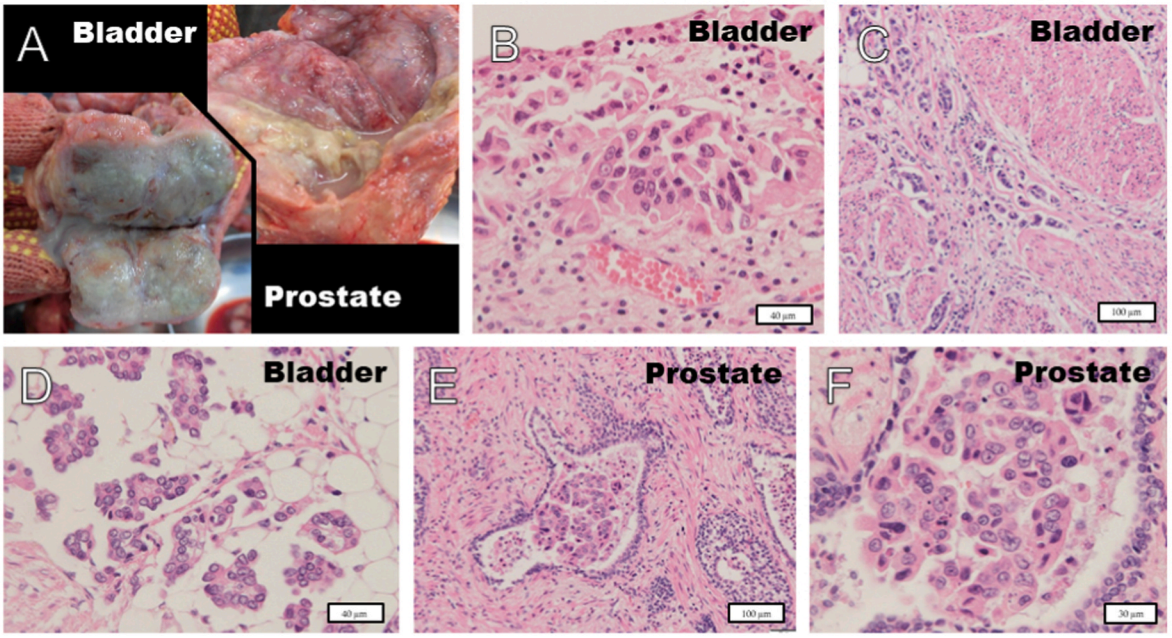

Fig. 2. Pathological findings of the bladder and prostate at the autopsy.
Pathological findings were obtained from the bladder (A–D) and prostate (A, E, and F). Macroscopic findings (A). Hematoxylin and eosin stain (B–F). The bladder wall showed thickening, and postoperative necrotic changes were evident; however, mass formation was not observed (A). Macroscopic changes were not seen in the prostate (A). The intramucosal cancer cells (B) and the invasive cancer cells in the bladder wall muscles (C). High-grade cancer cells invade the extravesical fat (D). The cancer cells invaded the glandular cavity of the prostate, and these cells were of the micropapillary variant (E and F).

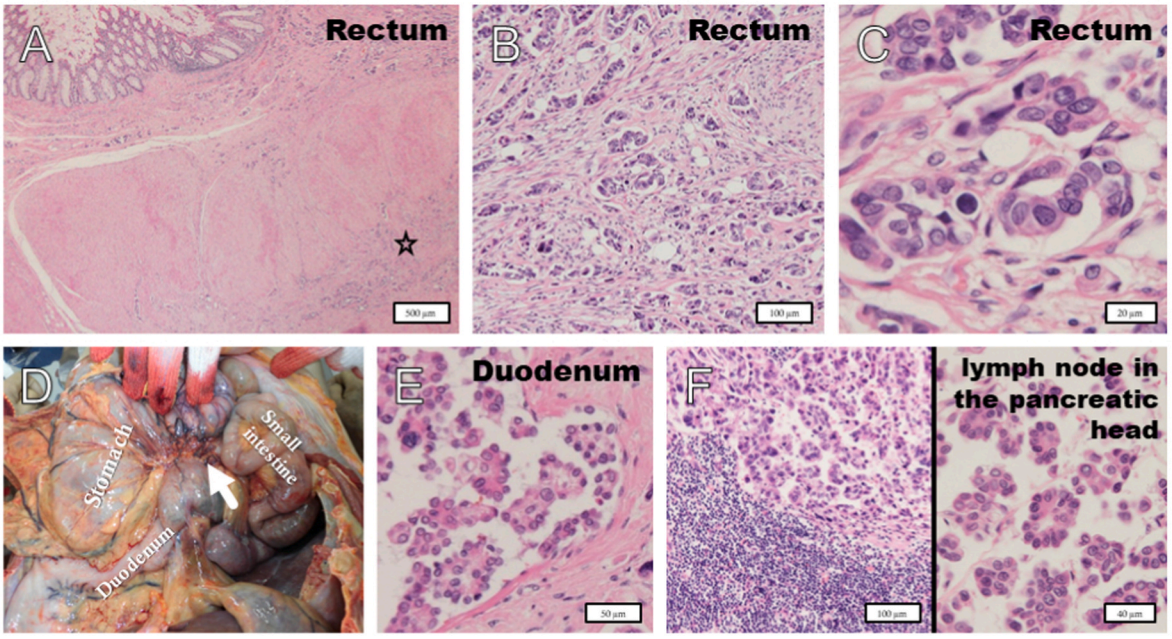

Fig. 3. Pathological findings of the rectum, duodenum, and lymph nodes at the autopsy.
Pathological findings were obtained from the rectum (A–C), superior mesenteric artery foot (D), duodenum (E), and lymph node in the pancreatic head (F). Hematoxylin and eosin stain (A–C, E, and C). Macroscopic findings (D). The star marks showed the orientation of invasive cancer cells (A). The cancer cells invaded the rectal wall muscles but not the mucosa (A). The cancer cells that invaded the rectal wall muscles were of the micropapillary variant (B and C). The superior mesenteric artery lymph node was swollen like a tumor, which was shown by an arrow, and it rolled a part of the duodenum and small intestine into a lump (D). The cancer cells with the micropapillary variant invaded lymphatic vessels in the duodenum (F) and lymph nodes in the pancreatic head (F).

present case, autopsy findings strongly indicated that cancer cells had spread to the upper body in the retroperitoneum via lymphatic dissemination. However, CT scans before their death did not reveal any lymph node swelling. Our experience strongly suggests that UC cells had already disseminated into the retroperitoneum without causing lymph node swelling when RO or DO was clinically diagnosed by imaging. Therefore, we should consider systemic therapies for a patient with RO caused by bladder cancer. If such a patient is physically strong during hospitalization, a colostomy may be performed, followed by neo-adjuvant chemotherapy before surgical resection. While there is no

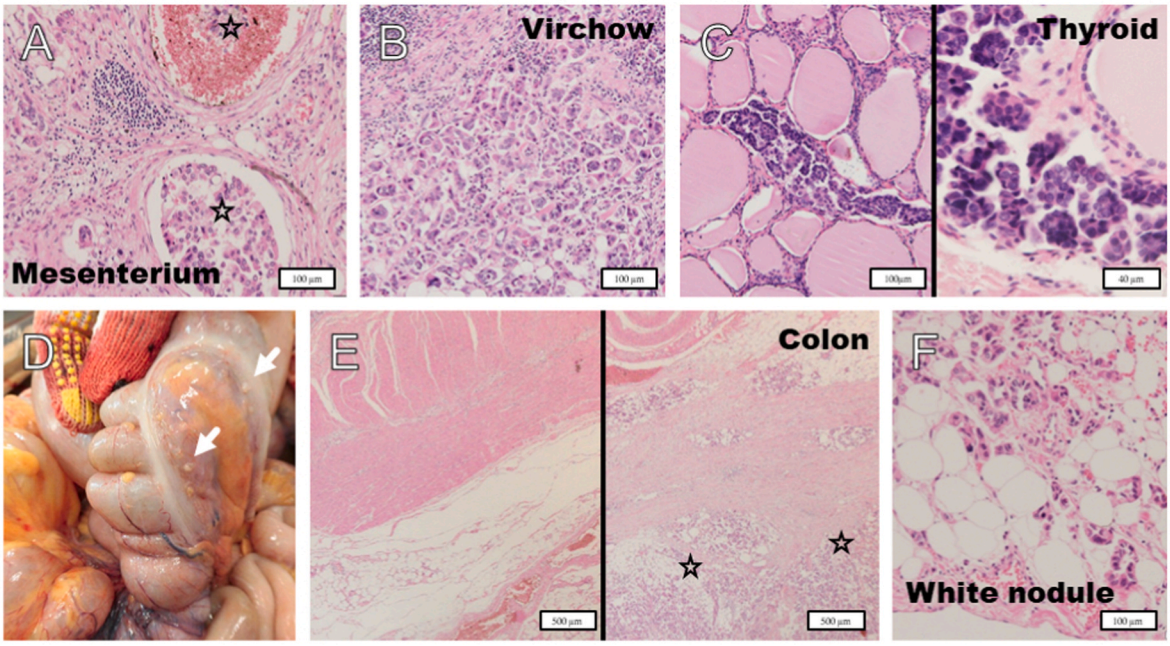

Fig. 4. Pathological findings of metastasis at the autopsy.
Pathological findings were obtained from the mesenterium (A), Virchow lymph node (B), thyroid (C), colon (D and E), and a white nodule on the serosa of the colon (F). Hematoxylin and eosin stain (A–C, E, and F). Macroscopic findings (D). The star marks showed the orientation of invasive cancer cells (A and E). The cancer cells invaded lymphatic vessels and veins in the mesenterium (A). The cancer cells with the micropapillary variant invaded the Virchow lymph node (B) and the thyroid (C). No macroscopic changes were observed in the colon, but several white nodules, indicated by arrows, were present on the colon's serosa (D). Cancer cells were not detected within the colon wall muscles but had invaded the colon's serosa (E). The cancer cells composed of the white nodules on the serosa of the colon resembled the micropapillary variant (F).

consensus on the optimal neoadjuvant chemotherapy regimen, the authors would have preferred gemcitabine-cisplatin therapy for this patient because of its high tolerability.

The main coordinator for RO or DO will be a gastroenterologist or a gastrointestinal surgeon.[5] Both DO or RO resulting from malignancies are managed with surgical approaches, such as surgical bypass, colostomy, or stent placement. The effectiveness of these treatments for restriction of obstruction was considered to be similar, with stent placement being a less invasive option. These treatments should be positively considered to improve a patient's general condition. However, in the present case, the surgeons determined that the patient might not be able to tolerate open surgery, which may be complicated by the accumulation of ascitic fluid. Stent placement for DO was deemed unsuitable because the small intestine appeared lumped together on CT scans. There are limited treatment options for patients with RO and/or DO; in such cases, supportive management using TPN is the main choice. Our patient also received TPN via PICC; had he been physically strong enough to receive chemotherapy, we would have used an implantable central venous access port instead of PICC for long-term intravenous fluid administration and chemotherapy. Unfortunately, the prognosis of patients with these obstructions is statistically poor.

4. Conclusion

Possible risk factors for RO caused due to bladder cancer include "male gender," "high-grade UC," "invasive cancer," and "tumor located on the lateral wall or near the bladder orifices." RO caused by bladder cancer is already a systemic disease due to lymphatic dissemination at the time of diagnosis. Hence, it is crucial to consider systemic treatment for the patient.

Consent

Written informed consent was obtained from the patient's family for the publication of this case report.

Declaration of generative AI in scientific writing

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CRediT authorship contribution statement

Takashi Ando: Conceptualization, Investigation, Resources, Writing – original draft. **Shinichi Morita:** Investigation, Resources. **Makoto Naito:** Investigation, Writing – review & editing.

Declarations of competing interest

None.

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