A Case Report of Synchronous Prostate Cancer and Rectal Gastrointestinal Stromal Tumor and its Management

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A 72-year-old Japanese man presented to the hospital with complaints of gross hematuria. Contrast enhanced computed tomography revealed a broad-based, approximately 3-cm bladder tumor near the right ureteral orifice and a 5-cm mass located between the prostate and rectum. The patient underwent transurethral resection of the bladder tumor and a transrectal biopsy of the lesion. Histological examination of the specimens suggested that the patient had a muscle invasive adenocarcinoma from transurethral resection and a rectal gastrointestinal stromal tumor in TRUS biopsy. Patient underwent total pelvic exenteration and ileal and colonic stomas to divert urine and faeces. Final pathology report of the resected specimen revealed a rectal gastrointestinal stromal tumor and prostatic adenocarcinoma, which had invaded the urinary bladder and seminal vesicles. Synchronous gastrointestinal stromal tumor in rectum and prostate cancer treated with total pelvic exenteration has not been reported before in literature.

Keywords: prostate cancer; gastrointestinal stromal tumor (GIST); Synchronous cancer; total pelvic exenteration (TPE)

INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are common gastrointestinal mesenchymal tumors commonly found in the stomach and small intestine. However, GISTs of the rectum represent less than 2% of all GISTs in the adult population[(1)]. Furthermore, GISTs display a wide variety of histopathological features and are thus difficult to confirm with a definite diagnosis. Here we report the diagnostic difficulties and treatment of a simultaneous case of advanced prostate cancer and GIST of the rectum using total pelvic exenteration (TPE), along with some literature review.

CASE REPORT

A 72-year-old Japanese man presented to our hospital, Matsuyama Shimin Hospital, with complaints of painless gross hematuria. He was a farmer and he had observed macrohematuria after crop work. He was 167 centimeters

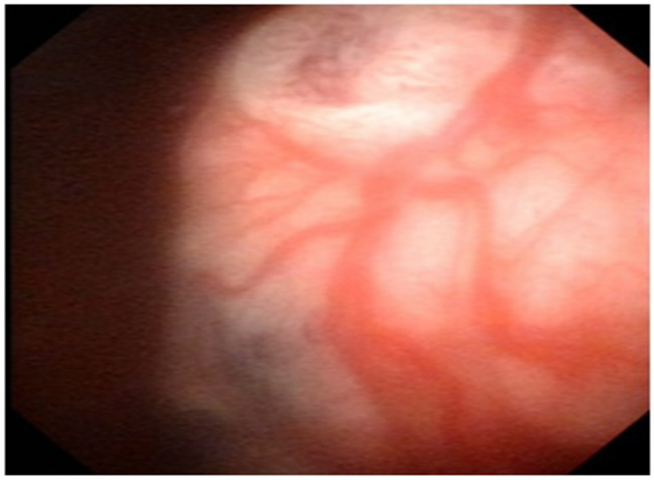

Figure 1. Cystoscopy demonstrated a non-papillary, broad-based, bladder tumor near the right ureteral orifice

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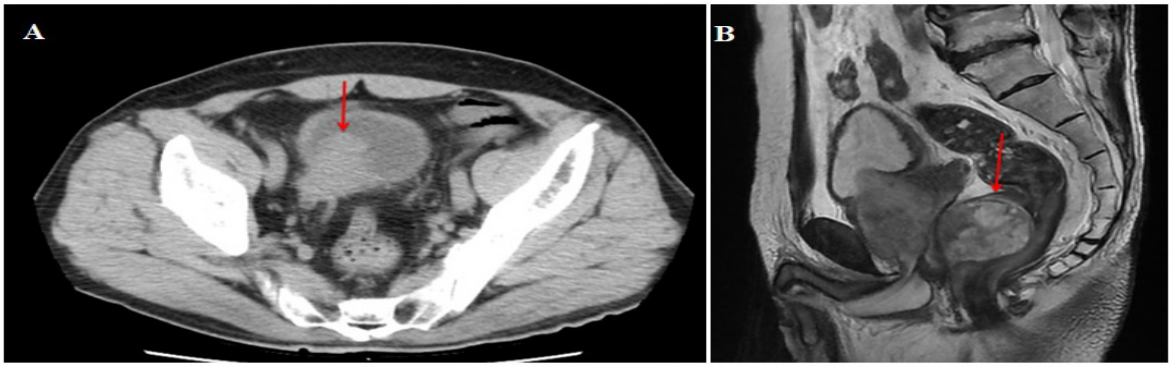

Figure 2. A: Computed tomography showed that the bladder tumor extended to the right orifice, causing hydronephrosis. **B:** Magnetic resonance image revealed a mass of approximately 5 cm in diameter that was located between the prostate and rectum.

in height and weighed 57 kilograms. He had no particular physical and family history. Primary scanning with ultrasonography (US) revealed a tumor lesion in the bladder, and cystoscopy demonstrated an approximately 3-cm, non-papillary, broad-based bladder tumor near the right ureteral orifice (**Figure 1**). Computed tomography (CT) showed a bladder tumor extended to the right ureteric orifice, causing hydronephrosis of the right kidney (Figure 2a), whereas magnetic resonance imaging (MRI) showed a mass of approximately 5 cm in diameter that was located between the prostate and rectum **(Figure 2b**). Bone scintigraphy, chest and abdominal CT scan demonstrated no sign of metastasis. The radiological diagnosis in conclusion was advanced bladder cancer (T3b) and GIST of the rectum. Urine cytology was negative for malignant cells and total prostate-specific antigen (PSA) was 5.01 ng/ml. A few days later, transurethral resection of the bladder tumor (TURBT) and transrectal prostatic biopsy was performed. Histological examination of the bladder tumor tissue suggested an adenocarcinoma, whereas examination of the prostatic biopsy tissue revealed a GIST with spindle cells, and prostatic tissue. Because of the diagnosis of synchronous invasive bladder adenocarcinoma and GIST at the recto-prostatic shelf, we performed open cysto-prostatectomy with ileal conduit and Miles' operation in a few weeks after the TURBT. Intraoperative analysis of ureteric margins was negative for cancer. We dissected lateral and internal iliac lymph nodes and obturator lymph node according to the protocol of total cystectomy. Histopathological examination of the resected specimen revealed GIST of the rectum (**Figures 3a, 3b**) and prostatic adenocarcinoma, which had invaded the urinary bladder and seminal vesicles (pT4). The cystoprostatectomy specimen had a Gleason score of 4+5, a positive extraprostatic extension (EPE), and a positive resection margin (RM) (**Figures 4a, 4b, 4c**). There was no connection between prostate cancer and GIST. There was no sign of metastasis in the resected lymph nodes. Because the postoperative course was uneventful besides slight fever due to pyelonephritis, the patient was discharged from our hospital on Day 36 postoperatively. Plain CT and the blood collection for PSA level were taken every 3 months after operation. Although the serum PSA level dropped to 0.001 ng/ml, it rose to 0.304 ng/ml 6 months postoperatively. The CT revealed no sign of recurrence or metastasis even when the PSA level elevated. The patient is currently undergoing maximal androgen blockade (MAB), and a serum PSA level of 0.001 ng/ml is being currently maintained. Now the patient has no clinical condition such as macrohematuria, lower abdominal discomfort or fever. Based on follow-up imaging examinations there is no sign of recurrence or metastasis, and is not any complications associated with urinary tract or bowel function 25 months after the operation.

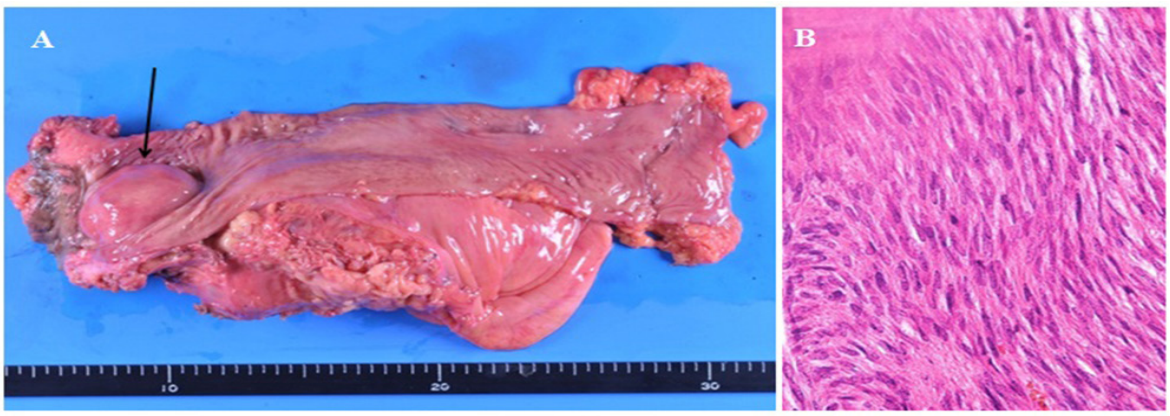

Figure 3. A: The gastrointestinal stromal tumor protruded to the inner side of the rectum, as concluded from macroscopic analysis. **B:** Histopathological examination of the resected gastrointestinal stromal tumor of the rectum specimen showed a spindle cell tumor that originated from muscularis propria.

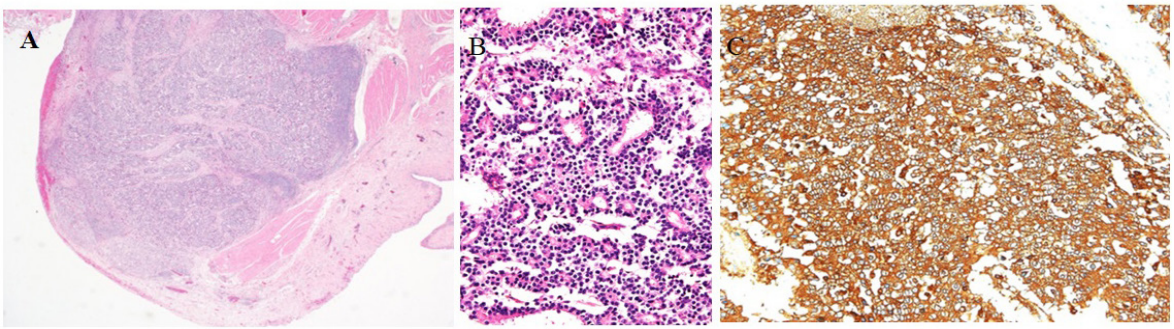

Figure 4. A: Histopathological examination of the resected specimen revealed prostatic adenocarcinoma, which invaded the urinary bladder and seminal vesicles (pT4). **B:** Example of prostatic carcinoma cells, demonstrating the glandular cavity structure (Gleason score of 5+4). **C:** Example of tumor cells, demonstrating diffuse, cytoplasmic, prostate-specific antigen-positive immunostaining

DISCUSSION

The term GIST was defined in 1983[2], and it includes tumors of the gastrointestinal tract that cannot be classified as either smooth muscle or neurogenic in origin. Among gastrointestinal mesenchymal tumors, GISTs are the most common. By definition, GIST is a mesenchymal neoplasm expressing the KIT protein, and it is driven by mutations in KIT or platelet-derived growth factor receptor-alpha (PDGFR-α). GISTs are derived from the interstitial cells of Cajal (ICC), which are KIT-positive, pacemaker cells that regulate peristalsis and have varying immunophenotypic and ultrastructural features of both smooth muscle and neural differentiation. Activation of KIT by mutations leads to ICC proliferation and GIST[3]. In the present case report, tumor cells demonstrated diffuse, cytoplasmic, c-kit-positive immunostaining.

GIST is a rare disease whose annual incidence is approximately 10 cases per million. The reported incidence rate of GIST of the rectum is approximately 1 case per 1000 GISTs[4]. Primary prostate and rectal carcinoma are the leading malignancies, but the incidence of synchronous was 0.2%, between 2006 and 2011[5]. Thinking of the GIST's rarity, the synchronous prostate and GIST is rarer. The improvement of diagnostic accuracy of MRI have led to detect more synchronous prostate and rectal adenocarcinoma. Pre-treatment MRI for rectal disease plays a very important role for detecting synchronous diseases[6].

Large GISTs may result in altered intestinal function, rectal bleeding (in the case of ulceration), abdominal pain, and urinary symptoms attributed to bladder compression. Surgery is the standard treatment for non-metastatic GISTs. The tumor should be removed en bloc with its pseudocapsule to yield an adequate resection margin. In some cases, preoperative treatment with imatinib may be considered[7], although there are currently no studies to support this practice.

In the present case, we performed TPE, including open total cystectomy and prostatectomy with ileal conduit and Miles' operation, based on the preoperative diagnosis of invasive bladder tumor and GIST of the rectum. As a matter of course, prostate cancer is sensitive for radiotherapy. And recently there are techniques which have both higher curability and less side effect such as brachytherapy, IMRT or VMAT (volumetric arc therapy)[8-12]. But in the present case we did not reach the precise diagnosis preoperatively. Furthermore, there is no evidence that GIST is radio-sensitive. Therefore, we did not select radiation therapy for the first-line therapy. However, histopathological examination of the resected specimen demonstrated GIST of the rectum and prostatic adenocarcinoma, which had invaded the urinary bladder and seminal vesicles. Rectal GISTs are rare tumors, whereas prostatic adenocarcinoma is the most common neoplasia in elderly men. Because of weak evidence that the prostate cancer was invasive, a lack of continuity between the bladder tumor and prostate based on cystoscopy, and relatively low serum PSA levels, a precise preoperative diagnosis was extremely difficult. In addition, there are only a few cases of invasive prostate carcinoma with low serum PSA levels. A transperineal prostate biopsy might be effective; however, our transrectal prostatic biopsy included no prostatic tissue. Therefore, we had made wrong diagnosis. We maybe should have undertaken transperineal prostatic biopsy and diagnosed properly before operation. If we could have fortunately diagnosed this case as advanced prostatic adenocarcinoma preoperatively, it might be possible that we could cure prostatic cancer with hormonal therapy or radiotherapy instead of total cystectomy with ileal conduit.

Similarly, in the case of synchronous prostate and rectal adenocarcinoma the diagnosis is also difficult due to the possibility that rectal and prostatic carcinomas can arise simultaneously[13]. Because the diagnosis may change the treatment selection, cooperation with pathologist is also necessary.

On the other hand, when the PSA elevated postoperatively, radiation therapy was the expected option. We strongly proposed the patient radiotherapy after biological PSA progression, but the patient firmly refused it due to misleading fear for radiation exposure. Fortunately, in the present time there has been no sign of recurrence since then, but the hormone resistance may appear in the near future.

Before and after the operation, we discussed the neoadjuvant and adjuvant imatinib therapy for the GIST with digestive surgeons. The effectiveness of adjuvant imatinib is proven by RCTs[14-15]. Joensuu[16] et. al reported that particularly with a high risk of GIST recurrence, compared with 12 month of adjuvant imatinib, 36 months of imatinib improved overall survival of GIST patients. In the present case, because the GIST was totally resected with negative margin and the histopathol-

ogy examination revealed the moderate risk GIST, we did not administrate adjuvant imatinib. We will consider imatinib use in case GIST recurs.
On the other hand, if we had preoperatively known the bladder tumor were prostate adenocarcinoma, we would be able to administrate imatinib first before operation in anticipation of the tumor size reduction and then might be able to undertake less minimally invasive anal preserving operation.
Thus, although the preoperative diagnosis is difficult, the synchronous case of prostate cancer and GIST of the rectum is a rare occurrence.

CONCLUSIONS

We report a case of simultaneous double cancer of advanced prostate cancer and GIST of rectum with diagnostic difficulties which we treated by TPE as a report of rare occurrence.

CONFLICT OF INTEREST

The authors report no conflicts of interest.

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