Case Report

Triple combination therapy for clinically nonmetastatic super-high-risk prostate cancer

Koji Yoshimura, Kei Muraoka, Michiko Fukasawa, Mika Fukushima, Masatoshi Kumagai, Ryo Yabusaki, Masakatsu Ueda, Yusuke Shiraishi and Masaaki Imamura

[1]Department of Urology, Shizuoka General Hospital, Shizuoka City, Shizuoka, Japan

Abbreviations & Acronyms
CAB = combined androgen blockade
CT = computed tomography
PLND = pelvic lymph node dissection
PSA = prostate-specific antigen
RARP = robot-assisted laparoscopic radical prostatectomy
TCT = triple combination therapy
ISUP = International Society of Urological Pathology

Correspondence: Koji Yoshimura M.D., Ph.D., Department of Urology, Shizuoka General Hospital, 4-27-1, Kitaando, Aoi-ku, Shizuoka 420-8527, Japan. Email: ky7527@kuhp.kyoto-u.ac.jp

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Introduction: Patients with nonmetastatic but exceptionally high-risk prostate cancer are liable to have biochemical failure and may even die. Triple combination therapy, which consists of surgery, radiotherapy, and androgen-deprivation therapy, as first-line treatment, may control the disease for a long period.
Case presentation: We treated a patient with super-high-risk, nonmetastatic prostate cancer, with triple combination therapy. He was biochemical relapse free at 60 months after the initiation of treatment.
Conclusion: Triple combination therapy may be an option for super-high-risk, nonmetastatic prostate cancer.

Key words: androgen-deprivation therapy, prostate cancer, prostatectomy, radiation therapy.

Keynote message

Prostate cancer that is nonmetastatic but highly aggressive is liable for fatal recurrence, even after appropriate treatment. Here, we present a patient with super-high-risk, nonmetastatic prostate cancer who was successfully treated by a combination of prostatectomy with pelvic lymph node dissection, adjuvant radiotherapy, and continuous androgen deprivation. Triple combination therapy might be an option for super-high-risk prostate cancer.

Introduction

High-risk prostate cancer accounts for approximately one quarter of all cases.[1] A subset of patients have recurrent fatal prostate cancer, despite appropriate treatment. Thus, consensus regarding the optimal treatment for high-risk, nonmetastatic prostate cancer has not been established. Among patients with high-risk, nonmetastatic prostate cancer, some have highly aggressive disease, and they are susceptible to early fatal recurrence. In this report, we present a patient with super-high-risk, nonmetastatic prostate cancer who was successfully treated by TCT, which comprises prostatectomy with pelvic lymph node dissection, adjuvant radiotherapy, and continuous androgen deprivation.

Case presentation

A 73-year-old man was referred to our department for further treatment of prostate cancer. His initial serum PSA level was 7.212 ng/mL, but 13 of his 14 prostate biopsy cores were totally occupied by adenocarcinoma with a Gleason score of 10. CT and bone scintigraphy showed no metastatic findings, but magnetic resonance imaging revealed invasion of the right seminal vesicle (Fig. 1). Clinical stage was cT3bN0M0, and he had already received CAB therapy (bicalutamide plus leuprorelin acetate) before consultation at our department. The cancer had no obvious sign of metastasis but was highly aggressive. Therefore, we decided that trimodal therapy comprising prostatectomy and PLND, adjuvant radiotherapy regardless of pathology, and continuous CAB, would be applied as first-line treatment. Three months after the initiation of CAB, he underwent RARP with PLND. PLND included the lymph nodes

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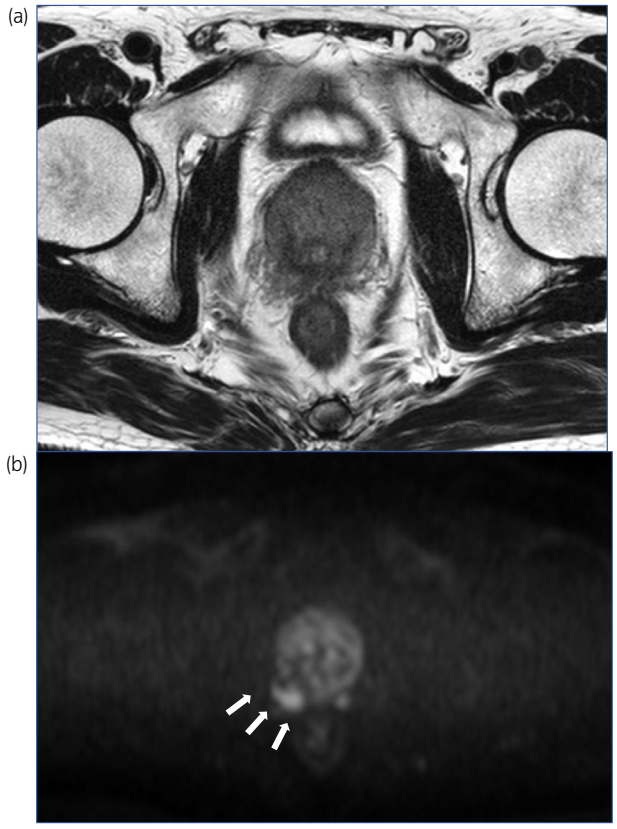

Fig. 1 Magnetic resonance imaging findings. (a) T2-weighted imaging demonstrated uniformly low intensity throughout the peripheral and transitional zones without a clear boundary between them. (b) Diffusion-weighted imaging suggested cancer invasion of the right seminal vesicle (arrows).

surrounding the external and internal iliac vessels, those occupying the obturator fossae, and those located in the triangles of Mercille. Pathologically, the tumor was stage pT3b or more, with a Gleason score of 10. The surgical margin was positive over a wide area of the specimen surface (Fig. 2), and one lymph node from the right obturator area was positive for cancer (Fig. 3). Therapeutic degeneration caused by CAB was minimal. Three months after RARP, the patient underwent adjuvant external beam irradiation therapy (60 Gy in 30 fractions) of the prostatic bed. CAB continued during and after RARP and irradiation. Sixty months after RARP, he had no evidence of disease by CT, with the PSA level <0.02 ng/mL.

Discussion

Our case had cT3b prostate cancer with ISUP group 5 carcinoma occupying almost the whole gland. Although the term super-high-risk prostate cancer is not officially accepted, it would be acceptable to use for this case. Super-high-risk prostate cancer would be likely to have micrometastases, which cannot be detected by conventional imaging modalities, such as CT and bone scintigraphy. Our case had lymph node metastases that were not detected preoperatively by conventional CT. More sophisticated imaging modalities, such as 68-Ga prostate-specific membrane antigen positron emission tomography, could partially resolve this problem.[2] However, even if micrometastasis, as far as classified as oligometastasis, is detected preoperatively, treatment of the local lesion could contribute to the outcome.[3] Extensive reduction of cancer volume achieved by prostatectomy with PNLD could

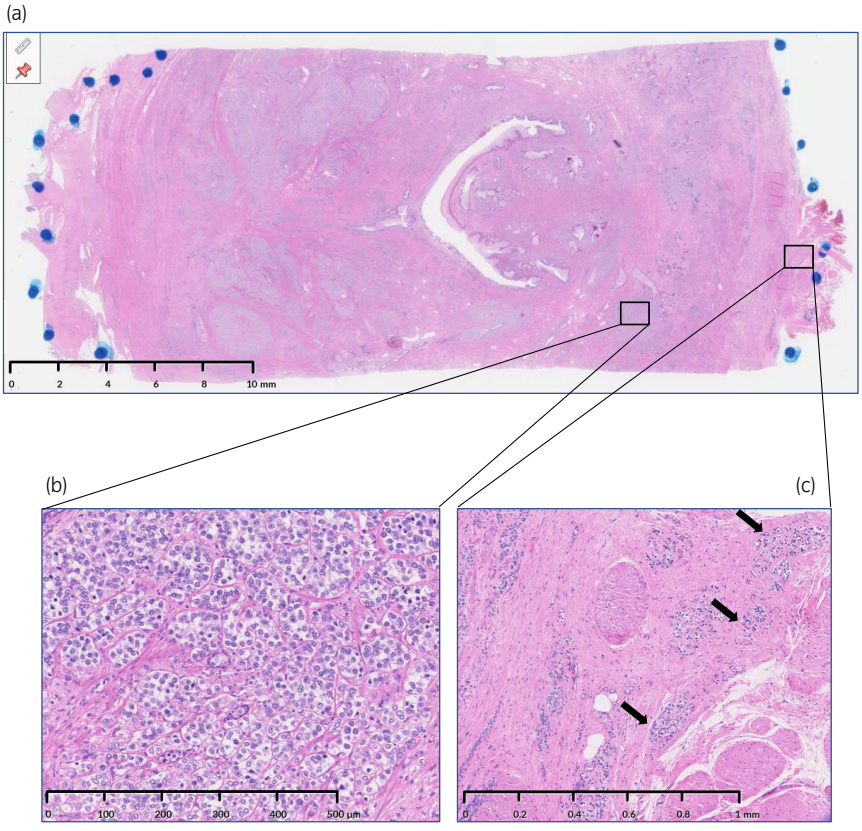

Fig. 2 Pathology of the prostate. (a) Cancer cells occupied nearly the whole sectioned area of the prostate with substantial positive margins (blue dots). (b) Cancer cells were viable and classified as International Society of Urological Pathology (ISUP) group 5. (c) Cancer cells invaded the rhabdosphincter tissue around the prostate (arrows).

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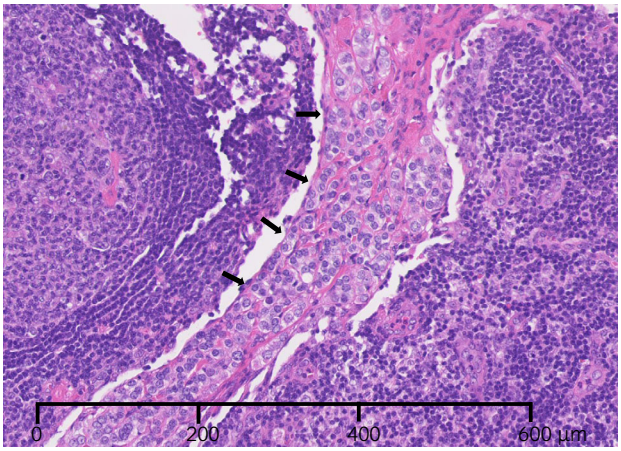

Fig. 3 Pathology of a lymph node. Metastasis was observed (arrows).

contribute to long-term control of the disease regardless of the presence of micrometastasis.

We determined preoperatively the procedure of adjuvant radiotherapy. There has been controversy regarding the superiority of adjuvant radiotherapy to salvage radiotherapy for high-risk prostate cancer.[4] Recently, Kneebone et al. reported that early salvage radiotherapy for high-risk prostate cancer achieved similar biochemical control to adjuvant radiotherapy.[5] Salvage radiotherapy had a similar oncological outcome to adjuvant radiotherapy, but it avoided unnecessary radiation in half of the patients, which was potentially harmful to the pelvis; therefore, they recommended salvage radiotherapy rather than adjuvant radiotherapy.[5] We generally apply salvage radiotherapy but not adjuvant radiotherapy for high-risk prostate cancer. However, it is not clear whether salvage radiotherapy has a similar anticancer effect compared with adjuvant radiotherapy for super-high-risk prostate cancer. Fortunately, our patient had no adverse reaction induced by radiotherapy.

Multimodal treatment strategies are more feasible than monotherapy for super-high-risk prostate cancer. Our TCT strategy comprises prostatectomy with PLND, salvage irradiation, and continuous CAB as first-line treatment. This conforms to the curative treatment for oligometastatic prostate cancer, namely, local consolidative therapy for the primary tumor, metastasis-directed therapy, and systemic chemohormonal therapy,[3] although our strategy did not include metastasis-directed therapy. In addition to the present case, we achieved 2-year-long cancer control using the same therapeutic strategy in another patient with super-high-risk prostate cancer. That patient had stage cT3aN0M0 cancer with ISUP group 5 and an initial PSA level of 328.7 ng/mL.

Any two of the treatment modalities, such as prostatectomy plus irradiation or irradiation plus androgen-deprivation therapy, might be sufficient and the combination of all three modalities might be redundant. These combinations of treatment modalities clearly aim for the eradication of prostate cancer. However, we did not aim for eradication but for a long-term control of the disease from the beginning, since super-high-risk prostate cancer would likely have micrometastases, which could not be eradicated. Even with the combination of all three therapeutic modalities, such an aggressive disease could not be eradicated. Despite the positive outcome of treatment of prostate cancer in these two cases, it might be probable that the disease is only controlled at present. Five- and 2-year follow-ups might be too short to judge the efficacy of TCT, and we should carefully observe these patients in the future.

As aforementioned, the clinical courses of our two patients alone are far from sufficient proof of the efficacy of the TCT; nevertheless, this treatment strategy might be one of the options in selected patients with super-high-risk prostate cancer.

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Author contributions

Koji Yoshimura: Conceptualization; writing – original draft. Kei Muraoka: Validation. Michiko Fukasawa: Validation. Mika Fukushima: Resources; validation. Masatoshi Kumagai: Validation. Ryo Yabusaki: Validation. Masakatsu Ueda: Supervision. Yusuke Shiraishi: Supervision. Masaaki Imamura: Supervision.

Conflict of interest

The authors declare no conflict of interest.

Approval of the research protocol by an Institutional Reviewer Board

Not applicable.

Informed consent

Informed consent was obtained from the patient.

Registry and the Registration No. of the study/trial

Not applicable.

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