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Prostate cancer featuring a unique progression pattern: A case of prominent direct perineal invasion without definite metastasis

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ABSTRACT

Locally advanced prostate cancer can extend into the pelvis, and can also invade the bladder and rectum. We encountered a patient with prostate cancer that exhibited severe local invasion, protruding into the perineum. Distant metastasis was absent, despite the large tumor size. The tumor bled and caused difficulty sitting and standing, compromising the patient's quality of life. Total pelvic exenteration and chemotherapy were considered, but the patient's general condition rendered these therapies inappropriate. However, of the limited treatment options available given the patient's condition, palliative irradiation of the protruding region proved effective.

Introduction

Locally invasive prostate cancer (PCa) of the rectum or bladder is often accompanied by distant metastasis. We encountered a patient with PCa exhibiting a unique progression pattern; the tumor protruded into the perineal region and was very large. This type of PCa pattern has not been described in previous reports. We report the clinical course and treatment, then review the literature.

Case presentation

An 82-year-old man was diagnosed with PCa by his former doctor. The initial prostate-specific antigen (PSA) level was 29.15 ng/mL, the Gleason score was 5 + 4 = 9, and the stage was T4 (rectum) N0M0. The patient had no relevant family history. He underwent external beam radiation therapy (EBRT; 66 Gy/33 fractions) of the prostate and the sites of rectal invasion, in combination with hormonal therapy including surgical castration and bicalutamide. A cystostomy was performed to treat dysuria. The patient discontinued treatment after 7 months. At 10 months after initial diagnosis, he was admitted to our hospital for the treatment of fever. The patient's PSA level was 4.37 ng/mL at admission. Digital rectal examination revealed that the rectal mucosa was intact. A protruding mass (approximately 4 cm in diameter) was observed in the perineum (Fig. 1a; Fig. 1a–d shows the time course of perineal tumor). Imaging examination showed that the prostate tumor protruded beyond the perineal skin; it had spread to the pelvis, seminal vesicles, bladder, rectum, and anal canal (Fig. 2a). No obvious distant metastasis was present on computed tomography and bone scan. Needle biopsy was performed to determine the differential diagnosis, which considered both anal canal and hemorrhoidal cancers. The pathological diagnosis was PCa (adenocarcinoma, Gleason score 5 + 5 = 10). Histologically, an atypical epithelium arranged in a sheet- or cord-like pattern, associated with infiltration of inflammatory cells was observed (Fig. 2b). Nuclear atypia associated with necrosis was evident. Immunohistochemical examination showed focally positive PSA (Fig. 2c), as well as expression of AMACR and NKX3.1 (Fig. 2d).

The tumor grew rapidly from 4 cm to 12 cm in diameter over 1 month (Fig. 1b). The patient required frequent blood transfusions and found it difficult to stand and sit. A colostomy was performed to alleviate defecation difficulty. To control the patient's symptoms, EBRT was delivered to the region of perineal invasion (39 Gy/13 fractions), with care being taken not to overlap the earlier irradiation fields. The tumor shrank rapidly (Fig. 1c), bleeding was reduced, and the patient was able to briefly stand and walk. The only treatment-related side-effect was

Abbreviations: EBRT, external beam radiation therapy; LDH, lactate dehydrogenase; PCa, prostate cancer; PSA, prostate-specific antigen; QOL, quality-of-life.

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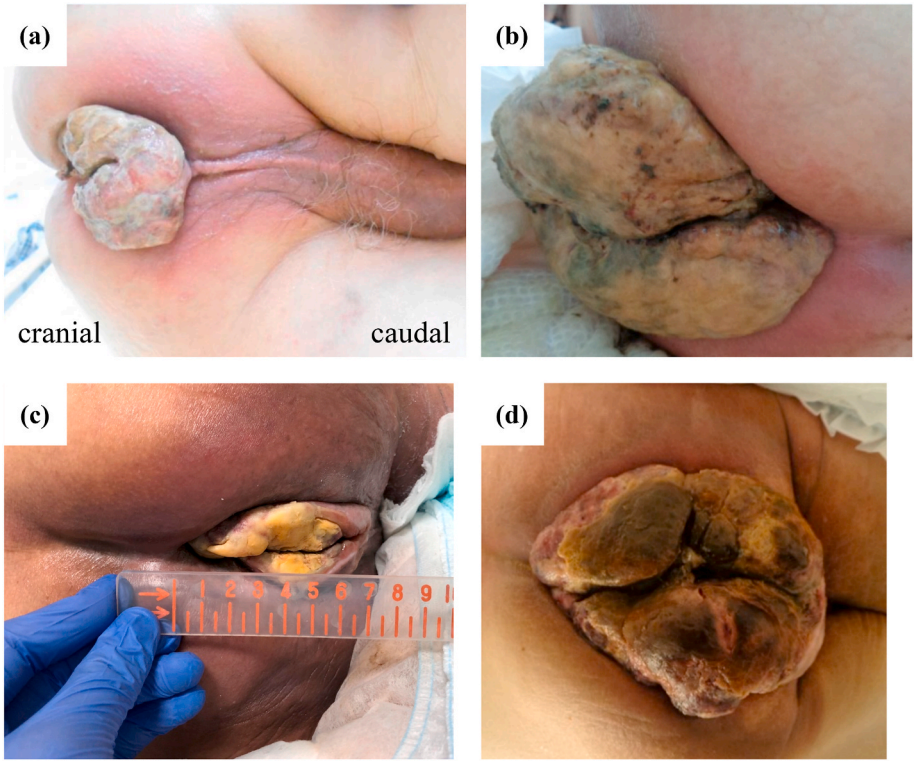

Fig. 1. Perineal tumor. a. The tumor was 4 cm in diameter at admission. b. The tumor grew to 12 cm in diameter over 1 month and exhibited bleeding. c. After radiation therapy, the tumor shrank and the patient was able to sit and stand. d. Image acquired at 5 months after irradiation: the tumor shrank for 3 months, but then grew again.

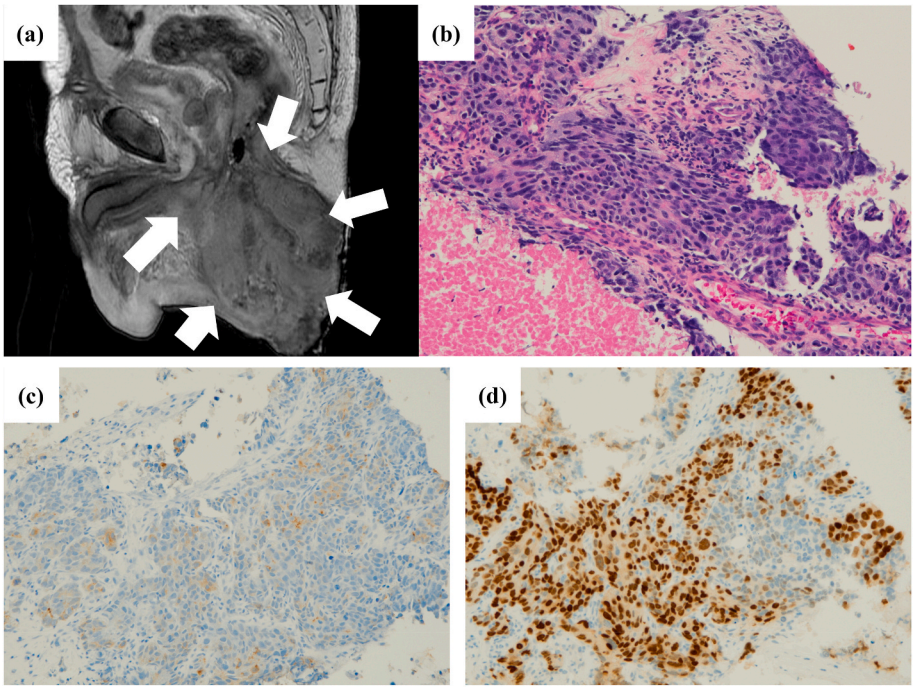

Fig. 2. Magnetic resonance imaging and pathological images. a. Magnetic resonance imaging revealed that the tumor had invaded the perineal skin, left seminal vesicle, bladder, corpus spongiosum urethrae, anal canal, and rectum. b. Histological examination revealed an atypical epithelium arranged in a sheet- or cord-like pattern, associated with infiltration of inflammatory cells (× 4, hematoxylin and eosin staining). Nuclear atypia associated with necrosis was evident. c, d. Immunohistochemical examination showed focally positive PSA (c) and expression of NKX3.1 (d).

radiation dermatitis (Common Terminology Criteria for Adverse Events Grade 2). In addition to the radiotherapy, we administered the androgen receptor-axis-targeted agents abiraterone or enzalutamide. Although the tumor-shrinkage effects of radiation were sustained, the PSA level did not markedly decrease and the response to androgen receptor-axis-targeted agents was limited (Fig. 3). At 3 months after radiation therapy, the perineal tumor showed recurrent growth (Fig. 1d). Although the perineal tumor had recurred rapidly, only swelling of pararectal lymph nodes was detected, with no distant metastasis. Further treatments such as chemotherapy were considered, but the patient's general condition was poor and only palliative treatment was administered. The patient experienced repeated episodes of sepsis

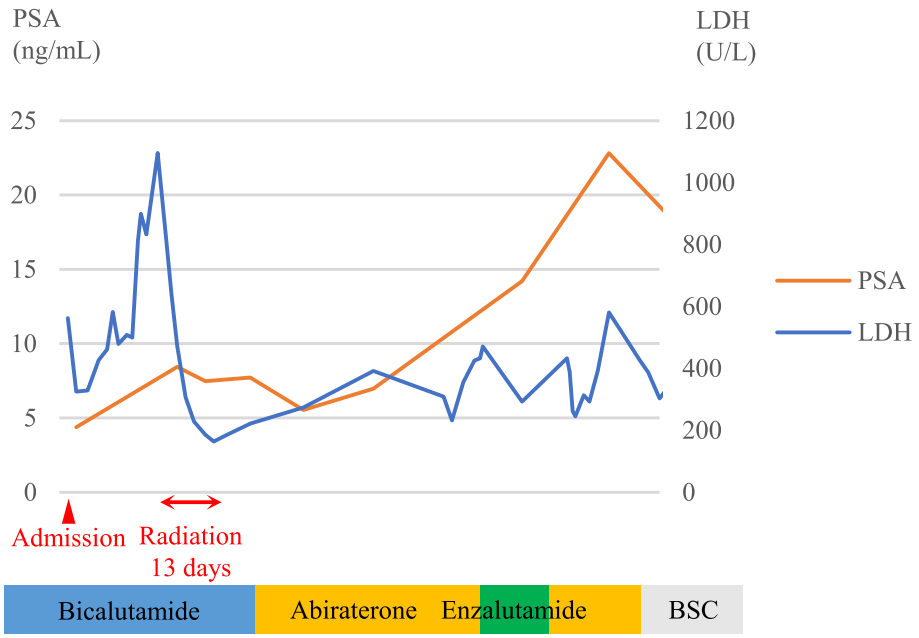

Fig. 3. Changes in PSA and lactate dehydrogenase (LDH) levels. Before radiation therapy, LDH level more closely reflected the extent of tumor activity, compared with the PSA level, which did not change substantially after initial diagnosis and did not decrease after prescription of androgen receptor-axis-targeted agents. The PSA level tended to increase after 3 months of irradiation, when the tumor became enlarged again.

resulting from tumor infection. The patient died 18 months after initial diagnosis.

Discussion

We encountered a patient with castration-resistant PCa exhibiting a unique clinical course. Although some cases of PCa skin metastasis have been reported,[1] no paper to date has described a prostate tumor that directly invaded the perineum, as observed in our present case. While transperineal procedures may trigger tumor migration,[2] the initial prostate biopsy was performed transrectally and EBRT was prescribed rather than seed brachytherapy.

Urological tumors that invade the skin are rare. The perineal tumor rendered the patient unable to sit or stand, resulting in substantial quality-of-life (QOL) reduction. Frequent blood transfusions were required. The tumor was advanced and radical treatment was difficult, but palliative surgery was considered. Total pelvic exenteration was suggested, in combination with excision of the perineal tumors and perineal skin reconstruction. Three cases featuring perineal invasion of rectal cancer in patients aged between 38 and 52 years have been reported; total pelvic exenteration was performed after chemotherapy and radiation therapy.[3] In some patients with PCa rectal invasions, total pelvic exenteration was performed to relieve pain.[4] This surgery was effective in 78.6% of patients, but all were younger than 80 years of age. Our patient was older than 80 years of age at the time of diagnosis; he also exhibited poor performance status, despite the absence of any co-existing disease. Chemotherapy may be another option for poorly differentiated PCa as in this case. While platinum-based chemotherapy is reportedly effective when encountering undifferentiated or aggressive cancers,[5] it was not implemented because of the patient's age and poor performance status.

After careful discussion with radiologists, palliative radiotherapy was performed to reduce the size of the perineal tumor and control bleeding. This treatment seemed to be very effective considering the limited treatment options due to the patient's poor condition and advanced age.

In this case, it was interesting not only for the pattern of local invasion but also for the absence of distant metastasis despite the prominent local progression. On the other hand, we consider that advanced imaging techniques such as prostate-specific membrane antigen positron emission tomography/computed tomography could have detected occult distant metastasis.

In the case of tumor with prominent invasion and rapid growth, even in a situation with poor performance status, the possibility of palliative treatment with careful irradiation planning was suggested. It may be useful for perineal invasion of other carcinomas such as hemorrhoidal cancer or rectal cancer.

Conclusion

We encountered a patient with PCa exhibiting a unique form of invasion. To our knowledge, no similar PCa has been reported. The tumor substantially impaired the patient's QOL. Although intensive curative treatment was impossible considering the patient's age and general condition, palliative EBRT of the protruding tumor region was very effective, improved the patient's QOL, and controlled the tumor for several months.

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