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Cutaneous Metastasis of Prostate Adenocarcinoma: A Rare Presentation of a Common Disease

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Abstract

Prostate cancer is the most common cancer affecting men in the United States and the second greatest cause of cancer-related death. Metastases usually occur to bone followed by distant lymph nodes and then viscera. Cutaneous metastases are extremely rare. Their presence indicates advanced disease and a poor prognosis. As they are highly variable in appearance and may mimic a more benign process, biopsy is essential for identification. Serine proteases, particularly human tissue kallikreins, may play an important role in promoting metastasis and facilitate infiltration of the skin. Individual cancer genetics may predispose to more aggressive cancer and thus earlier and more distant metastases. In this article, we report our case of a 67-year-old man with a 4-year history of castrate-resistant prostate cancer with cutaneous metastases confirmed by histology. Despite multiple lines of systemic therapy, the patient suffered progressive disease with worsening performance status and was enrolled in hospice.

Keywords

oncology, prostate cancer, urologic cancer, cutaneous metastasis

Introduction

Prostate cancer is the most common malignancy in men, with an incidence of 106.5 per 100 000 in the United States, and the second most common cause of cancer-related death among American men after lung cancer.[1] Common sites of metastasis include bone (84%), lymph nodes (10.6%), liver (10.2%), lung, and pleura (9.1%); however, metastasis to the skin is quite rare (≤0.36%).[2-4] Cutaneous metastases tend to occur in the lower abdomen, thighs, and scrotum, but metastasis to chest, back, and face, or as a Sister Mary Joseph nodule have been reported.[3-9] When present, it is often late in the course of the disease and considered an ominous sign; patients usually die within a year of its appearance.[3-5]

Case Description

A 67-year-old man with metastatic castration-resistant prostate cancer presented for evaluation of worsening skin lesions on his lower abdomen and suprapubic area (Figure 1). The patient was initially diagnosed with prostate cancer (Gleason 4 + 5) metastatic to bone in an outside country in June 2016. Prostate-specific antigen (PSA) was 1310 ng/mL at diagnosis, BUN (blood urea nitrogen) was 96 mg/dL, and creatinine was 3.6 mg/dL; all other laboratory values were within normal limits. He was treated with goserelin injections every 3 months with good response for 2 years when his PSA started rising again. He refused systemic treatment at that time. In 2019, he underwent left orchiectomy for a localized seminoma.

In June 2019, he received a final dose of goserelin and moved to the United States to be with family and continue treatment. In July 2019, he was admitted for urinary retention and was found to have an acute kidney injury due to obstructive uropathy. Computed tomography of the abdomen and pelvis revealed bilateral hydronephrosis, hydroureter, and concentric bladder wall thickening despite a lack of urinary distention, suggesting neoplastic infiltration and obstruction of the ureteral outlets. There was significant retroperitoneal

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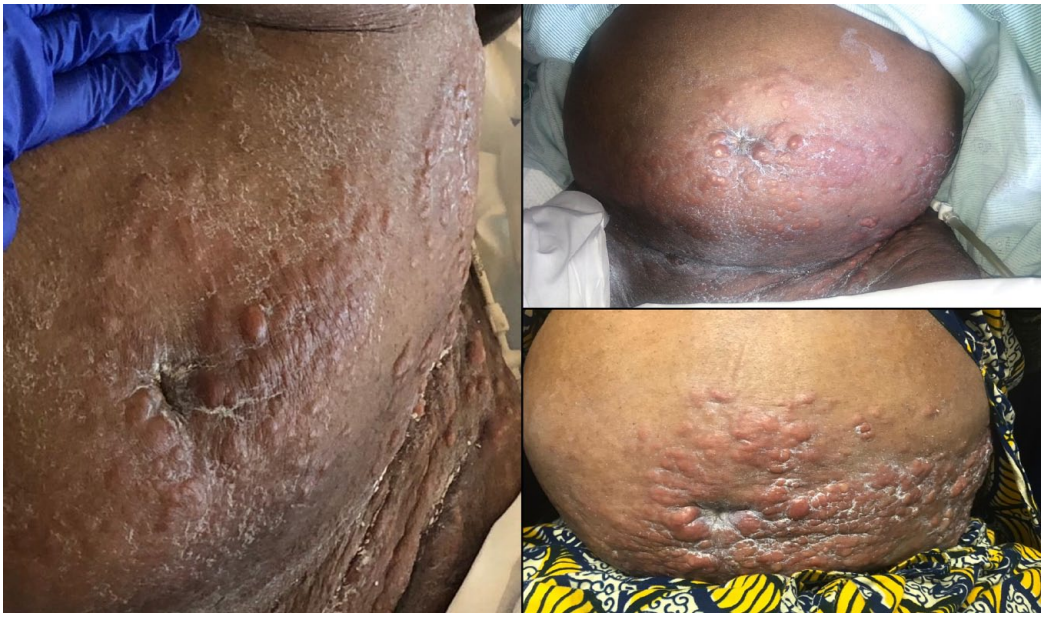

Figure 1. Metastasis of prostatic adenocarcinoma presenting as a confluence of reddish nodulopapular skin lesions over the bilateral lower abdomen with extension to the inguinal area and left flank. Left nephrostomy tube is visible.

lymphadenopathy that was biopsied confirming metastasis of the prostate cancer. He received bilateral nephrostomies and one injection of degarelix followed by maintenance leuprolide every 4 months. His PSA was 420 ng/mL at that time, but rose to 784 ng/mL over the ensuing 2 months. He also had recurrent urinary infections that delayed his systemic treatment. He was started on abiraterone with prednisone.

After 1 month of therapy, his PSA improved to 118 ng/mL but rose again 3 months later to 220 ng/mL when he presented with numerous grouped, flesh-colored, nodulopapular skin lesions on his left lower abdomen, mons pubis, and left flank. Biopsy of these lesions demonstrated poorly differentiated carcinoma with foamy cytoplasm and pyknotic nuclei, expressing PSA and prostate-specific acid phosphatase (PSAP), consistent with metastasis from a high-grade prostatic adenocarcinoma (Figure 2). His treatment was switched to docetaxel with prednisone. After 6 cycles of docetaxel, his skin lesions had regressed. His PSA initially improved but then sharply rose to 481 ng/mL in June 2020 and his chemotherapy was switched to cabazitaxel.

Despite 5 cycles of cabazitaxel, his PSA continued to rise to 600 mg/mL, and his cutaneous metastases reappeared. Computed tomography of the abdomen and pelvis demonstrated significant worsening of disease with increased size of liver and lymphatic metastases, along with numerous osteoblastic lesions in the vertebrae. Next-generation sequencing revealed Myc amplification, FGFR1 amplification, and BRCA2 inactivation. However, at that point he had been bed bound for 2 months with contractures, dependent activities of daily living, stage III chronic kidney disease, and recurrent pyelonephritis with extended spectrum β-lactamase positive organisms. He was referred and enrolled in hospice care.

Discussion

This case serves as an example of an unusual presentation of a relatively common disease. Cutaneous metastasis from genitourinary tract carcinomas are rare, most frequently arising from the kidney (66%), followed by the bladder (17%), prostate (12%), and testes (4%).[3] Prostate cancer usually first metastasizes to local lymph nodes and bone (hematogenously through Batson's plexus), followed by lung, liver, and adrenal glands.[2,9] If prostate cancer metastases to the skin it is almost always late in its course.[3-5] These metastases are usually localized to the abdominopelvic region per literature review, distributed to the inguinal region and penis (28%), abdomen (23%), head and neck (16%), chest (14%), extremities (10%), and back (9%).[10]

The gross appearance of cutaneous metastases from prostate cancer is highly variable. Skin lesions most often initially present as multiple rubbery nodules or plaques, less often as a single nodule, and uncommonly as edema or a nonspecific rash.[10,11] These may be asymptomatic or painful and ulcerated.[9,12] Their appearance may resemble zoster, basal cell carcinoma, angiosarcoma, cellulitis, pyoderma gangrenosum, mammary Paget's disease, telangiectasia, morphea, sebaceous cysts, or trichoepitheliomas.[11-13] Biopsy of these lesions is required for definitive diagnosis.

Histological examination of biopsy specimens typically demonstrates acinar adenocarcinoma, but rare variants including atrophic, ductal, xanthomatous, mucinous, signet

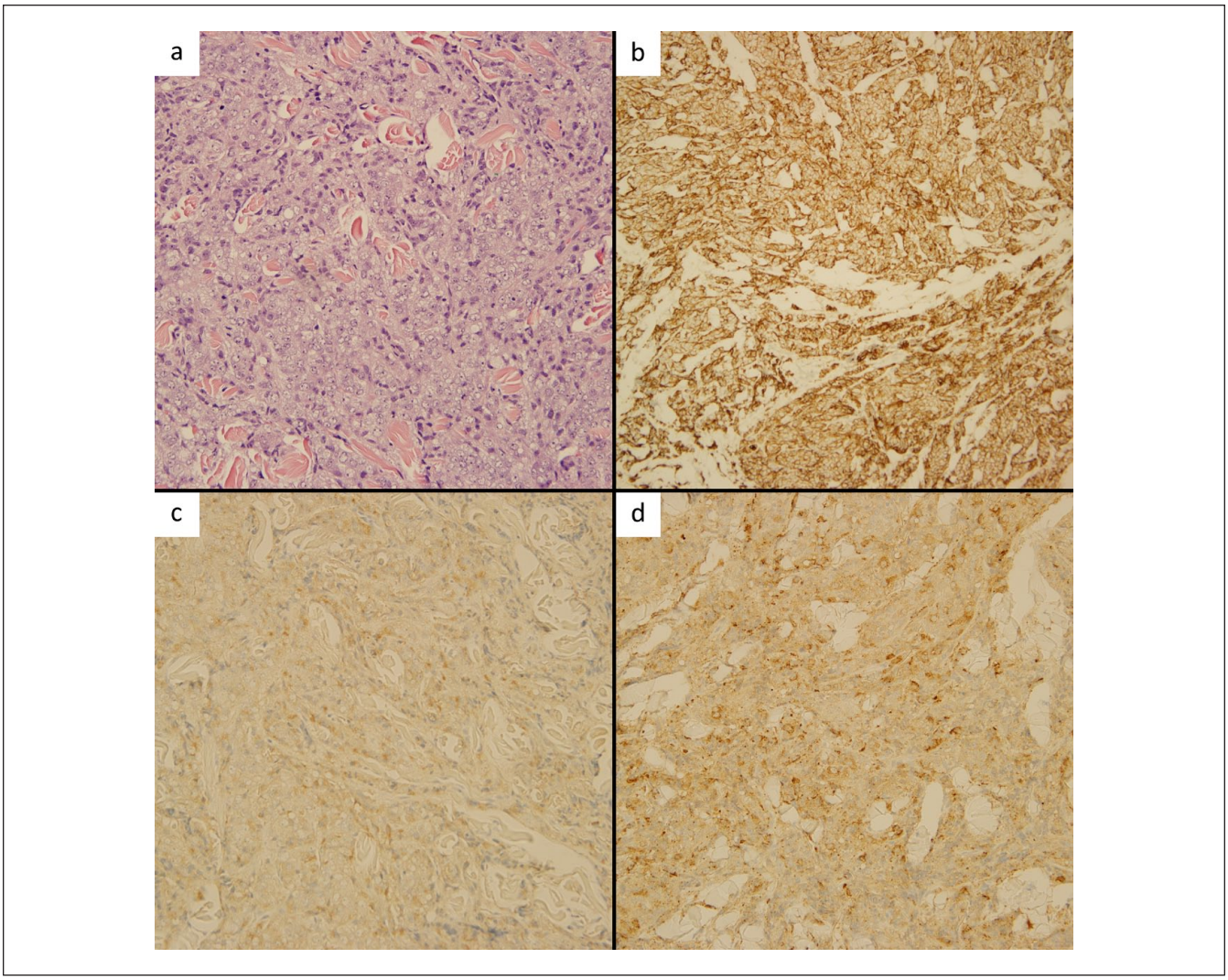

Figure 2. Histological slides obtained from a punch biopsy of a skin lesion demonstrating poorly differentiated carcinoma with sheets of malignant cells and focally microacinar formation on hematoxylin and eosin staining (a). Immunohistochemical staining was positive for AE1/3 (b), weakly positive for prostate-specific antigen (c), and strongly positive for prostate-specific acid phosphatase (d).

cell, squamous, urothelial, small cell, or mixed subtypes are possible.[14,15] PSA and PSAP are specific to benign or malignant epithelial cells of the prostate gland.[15-17] NKX3.1 and prostein (P501s) are highly sensitive and specific, but may also be present in sex cord stromal tumors.[17,18] GATA3, p63, 34βE12, thrombomodulin, and cytokeratins (CK) 7 and 20 are often positive in urothelial cancer and typically negative in adenocarcinoma of the prostate.[11,15,16] Very poorly differentiated cancers may be exceptional to the aforementioned immunohistochemical staining patterns (eg, PSA negative).[15,16] In our case, biopsy of the cutaneous lesions demonstrated strong reactivity for PSAP, minor reactivity for PSA, while both CK7 and CK20 were negative, confirming the nature of the lesions as being metastatic prostate adenocarcinoma.

The route of metastasis of prostate cancer to the skin is not precisely known but may occur through lymphatic or hematogenous spread from the primary tumor with extravasation and invasion of the dermis, direct extension from another site of metastasis, or seeding from a surgical instrument.[9,19] Serine proteases such as human tissue kallikreins may play a role in the ability of prostate cancer to infiltrate the skin by breaking down cell-cell adhesions in the epidermis.[20] Furthermore, they are involved in the epithelial-mesenchymal transition, a process by which epithelial cells lose their epithelial characteristics and take on those of mesenchymal tissue—a major step in the progression of cancer and a driving factor for metastasis.[20]

Cutaneous metastases may be treated locally or systemically. Electron radiation therapy has been employed as an effective palliative treatment for painful skin metastases.[21,22] Surgical excision and intralesional chemotherapy are also viable options for small and limited metastases.[9,10] Systemic chemotherapy has the advantage of potentially reducing the

primary malignancy as well as visceral and osseous metastases. According to one review, systemic treatment of the primary malignancy results in at least partial improvement in 65% of cases of cutaneous metastases within 4 to 8 weeks of initiating treatment.[9] Our patient's skin metastases demonstrated a similar response, initially regressing with systemic docetaxel and prednisone and completely disappearing by the second dose. The lesions did not recur until 9 months later when the cancer had stopped responding to taxanes and overall progressed leading to a decline in performance status and enrollment in hospice.

Conclusion

While prostate cancer is the most common cancer affecting men in the United States, metastasis to the skin is very rare and usually indicates advanced disease and a poor prognosis. Factors enabling or promoting cutaneous metastasis may include the human tissue kallikrein family of serine proteases and individual cancer genetics. Localized palliative therapy may be employed for symptomatic cutaneous metastases in select patients; however, systemic therapy is usually preferred. Although initially responsive to androgen deprivation therapy, prostate cancer inevitably becomes castrate resistant. As next-generation sequencing technologies become more widely available personalized therapy targeting specific mutations in an individual cancer is likely to become more commonplace, which may improve outcomes in cases like ours.

Teaching Points

1. Cutaneous metastasis of urologic cancers, including those of the prostate, are rare and associated with advanced disease and a poor prognosis.
2. Expression of tissue kallikreins may enhance cancer cell mobilization and facilitate metastatic infiltration of the skin.

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Ethics Approval

Our institution does not require ethical approval for reporting individual cases.

Informed Consent

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References

1. US Cancer Statistics Working Group. US Cancer Statistics Data Visualizations Tool, based on 2019 submission data (1999-2017): US Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute. Published 2020. Accessed October 12, 2020. https://www.cdc.gov/cancer/dataviz
2. Gandaglia G, Abdollah F, Schiffmann J, et al. Distribution of metastatic sites in patients with prostate cancer: a population-based analysis. *Prostate*. 2014;74:210-216. doi:10.1002/pros.22742
3. Mueller TJ, Wu H, Greenberg RE, et al. Cutaneous metastases from genitourinary malignancies. *Urology*. 2004;63:1021-1026. doi:10.1016/j.urology.2004.01.014
4. Brown GT, Patel V, Lee CCR. Cutaneous metastasis of prostate cancer: a case report and review of the literature with bioinformatics analysis of multiple healthcare delivery networks. *J Cutan Pathol*. 2014;41:524-528. doi:10.1111/cup.12296
5. Duran EP, Paradela A, Fariña MC, et al. Cutaneous metastases from prostatic carcinoma. *J Surg Oncol*. 1996;62:144-147. doi:10.1002/(SICI)1096-9098(199606)62:2<144::AID-JSO12>3.0.CO;2-8
6. Sharma R, Chandra M. Cutaneous metastases from carcinoma of the prostate: a case report. *Dermatol Online J*. 2005;11:24.
7. Brown G, Kurtzman D, Lian F, Sligh J. Eruptive nodules of the head and neck: a case report of metastatic prostate cancer. *Dermatol Online J*. 2014;20:doj_21544.
8. Mbaeri TU, Orakwe JC, Ezejiofor OI. Unsuspected skin metastasis of adenocarcinoma of the prostate in a patient on goserelin (Zoladex). *Niger J Surg*. 2018;24:138-141. doi:10.4103/njs.NJS_15_17
9. Esquivel-Pinto IA, Torres-Alvarez B, Gómez-Villa RJ, Castanedo-Cázares JP. A case of prostatic carcinoma manifesting as cutaneous facial nodule. *Case Rep Urol*. 2018;2018:5265909. doi:10.1155/2018/5265909
10. Wang SQ, Mecca PS, Myskowski PL, Slovin SF. Scrotal and penile papules and plaques as the initial manifestation of a cutaneous metastasis of adenocarcinoma of the prostate: case report and review of the literature. *J Cutan Pathol*. 2008;35:681-684. doi:10.1111/j.1600-0560.2007.00873.x
11. Habermehl G, Ko J. Cutaneous metastases: a review and diagnostic approach to tumors of unknown origin. *Arch Pathol Lab Med*. 2019;143:943-957. doi:10.5858/arpa.2018-0051-RA
12. Reddy S, Bang RH, Contreras ME. Telangiectatic cutaneous metastasis from carcinoma of the prostate. *Br J Dermatol*. 2007;156:598-600. doi:10.1111/j.1365-2133.2006.07696.x
13. Gupta S, Morgaonkar M, Jain SK. Cutaneous metastasis from prostate carcinoma. *Indian Dermatol Online J*. 2017;8:73-74. doi:10.4103/2229-5178.198763
14. Humphrey PA. Histopathology of prostate cancer. *Cold Spring Harb Perspect Med*. 2017;7:a030411. doi:10.1101/cshperspect.a030411

15. Li J, Wang Z. The pathology of unusual subtypes of prostate cancer. *Chin J Cancer Res*. 2016;28:130-143. doi:10.3978/j.issn.1000-9604.2016.01.06
16. Oh WJ, Chung AM, Kim JS, et al. Differential immunohistochemical profiles for distinguishing prostate carcinoma and urothelial carcinoma. *J Pathol Transl Med*. 2016;50:345-354. doi:10.4132/jptm.2016.06.14
17. Gurel B, Ali TZ, Montgomery EA, et al. NKX3.1 as a marker of prostatic origin in metastatic tumors. *Am J Surg Pathol*. 2010;34:1097-1105. doi:10.1097/PAS.0b013e3181e6cbf3
18. Arnesen C, Eich ML, Pena MR, et al. NKX3.1 and prostein expression in testicular tissue and sex cord-stromal tumors. *Am J Surg Pathol*. 2020;44:61-67. doi:10.1097/PAS.0000000000001367
19. Venable DD, Hastings D, Misra RP. Unusual metastatic patterns of prostate adenocarcinoma. *J Urol*. 1983;130:980-985. doi:10.1016/s0022-5347(17)51607-9
20. Mo L, Zhang J, Shi J, et al. Human kallikrein 7 induces epithelial-mesenchymal transition-like changes in prostate carcinoma cells: a role in prostate cancer invasion and progression. *Anticancer Res*. 2010;30:3413-3420.
21. Mak G, Chin M, Nahar N, De Souza P. Cutaneous metastasis of prostate carcinoma treated with radiotherapy: a case presentation. *BMC Res Notes*. 2014;7:505. doi:10.1186/1756-0500-7-505
22. Arase S, Sanuki N, Matsuura H. Cutaneous metastasis of prostate carcinoma treated with electron radiotherapy. *IJU Case Rep*. 2019;2:190-192. doi:10.1002/iju5.12078