

# An unusual case of prostate cancer with a solitary skin metastasis presenting as extramammary Paget's disease

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## Introduction

Prostate cancer is the second most commonly occurring cancer in men worldwide.<sup>1</sup> Common sites of distant metastases include the bone, lung and liver. Skin metastasis is extremely rare and can mimic other skin conditions resulting in poor recognition. We describe a case who presented with a cutaneous lesion of the anterior abdominal wall that was initially diagnosed as Extramammary Paget's Disease (EMPD), that was subsequently found to be metastatic from an underlying histologically confirmed carcinoma of the prostate. To our knowledge, this is a rare occurrence which has not been clearly illustrated in available literature.

## Case report

An 85-year-old Chinese man presented with a painless right lower abdominal superficial erythematous plaque with an exophytic nodular component arising from within (Figure 1). No other cutaneous lesions were seen. An incisional biopsy of the lesion revealed skin with intraepidermal nests and dispersed cells with large, irregular eccentric nuclei and moderate to large amounts of vacuolated cytoplasm; these cells are also seen infiltrating the dermis, suggestive of EMPD with invasive carcinoma (Figure 2 to 3). Immunohistochemical staining (Figure 4 to 6) showed the tumour cells to be positive for NKX3.1, with focal positivity for prostate-specific antigen (PSA), and rare cells expressing prostate acid phosphatase (PSAP). This immunoprofile raised the possibility of a prostatic primary.



Figure 1: Cutaneous lesion over right lower abdomen

Digital rectal examination (DRE) revealed a hard nodule in the right lobe of the prostate and serum PSA was raised at 15.57 ng/ml. Transrectal ultrasound guided prostate biopsy confirmed Gleason score 4+5 (grade group 5) mixed acinar and ductal prostatic adenocarcinoma. The tumour seen on the prostate biopsy morphologically resembled that seen in the skin lesion (Figure 7). A computed tomography (CT) of the thorax, abdomen and pelvis and bone scan was performed which showed no evidence of metastases. Further work up including endoscopy of the gastrointestinal tract and cysto-urethroscopy did not show any tumour.

He underwent wide excision of the cutaneous lesion. Gallium-68 PSMA (prostate-specific membrane antigen) positron emission tomography (PET) CT performed after wide excision did not show any other metastatic lesion. He was commenced on androgen deprivation therapy and radiotherapy to the prostate.

## Discussion

Cutaneous spread of prostate cancer is rare, and when it occurs, usually appear as solitary or multiple nodules on the abdominal skin, suprapubic area or anterior thigh.<sup>2</sup> The exact mechanism of cutaneous spread for prostate cancer is uncertain. Direct infiltration, hematogenous and lymphatic spread, or a combination of these have all been proposed.<sup>3</sup> In a review of 78 cases of prostate cancer metastases to the skin, the most frequent site of involvement was the inguinal region and penis (28%), followed by the abdomen (23%). Other areas such as face and chest have also been described in literature.<sup>4,5</sup>

The morphology of skin manifestations for prostate cancer are varied<sup>6</sup> and may pose a diagnostic challenge to clinicians. It may not have the typical nodular appearance, and may mimic other inflammatory conditions such as cellulitis or, in our case, Extramammary Paget's disease.

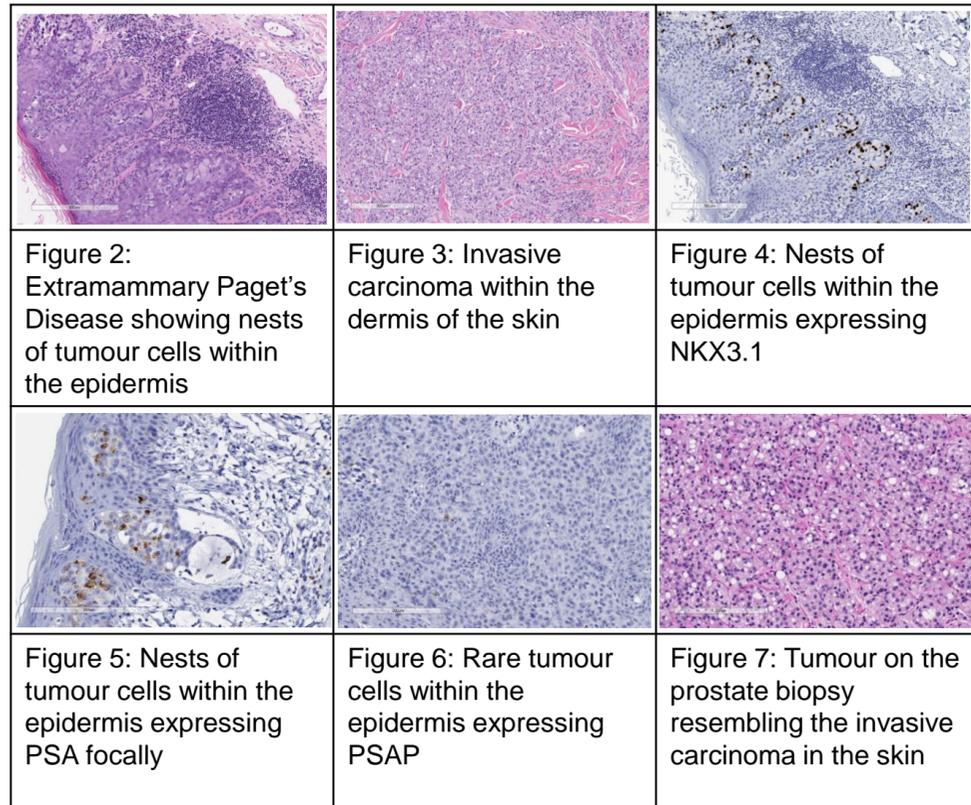


Figure 2: Extramammary Paget's Disease showing nests of tumour cells within the epidermis

Figure 3: Invasive carcinoma within the dermis of the skin

Figure 4: Nests of tumour cells within the epidermis expressing NKX3.1

Figure 5: Nests of tumour cells within the epidermis expressing PSA focally

Figure 6: Rare tumour cells within the epidermis expressing PSAP

Figure 7: Tumour on the prostate biopsy resembling the invasive carcinoma in the skin

Extramammary Paget's Disease is usually seen as erythematous lesions in areas rich in apocrine glands, such as the axilla or perineum. Up to 40% of EMPD have been found to associated with underlying internal malignancy, and most reported EMPD cases tend to be in close proximity to the primary lesion.<sup>7</sup> Cancer screening practices in the setting of EMPD vary widely.<sup>8</sup> In our institution, all patients with EMPD are routinely evaluated with thorough history taking and clinical examination, CT of the thorax, abdomen and pelvis, gastroscopy, colonoscopy, and cystoscopy. Prostate biopsy will be considered if PSA is raised or if DRE is abnormal. With a reported pagetoid pattern in a site not prone to the development of EMPD, there should be a high index of suspicion for cutaneous metastasis as a differential diagnosis.

Detailed histological examination with immunohistochemistry was crucial in differentiating a primary cutaneous malignancy versus a cutaneous metastasis from an occult primary malignancy in this case. In our case, immunohistochemistry staining against PSA, PSAP and NKX3.1 was used. Positive staining for PSA is regarded as a strong indicator of underlying prostate cancer. However, on rare occasions, PSA staining has been found to be positive in tumours of the salivary glands, pancreas, breast and ovaries, and its use in isolation for detecting secondary EMPD has also been questioned as it can also stain positive in apocrine sweat glands.<sup>9</sup> NKX3.1 is a transcription factor protein that is expressed specifically in the prostate gland which plays an important role in prostate development and carcinogenesis. Its highly restricted expression in prostate epithelial cells makes it useful as a diagnostic biomarker in prostate cancer, and has been shown to be highly sensitive and specific for identifying metastatic prostate adenocarcinoma. We believe that the use of a panel of immunohistochemical stains helps to increase the diagnostic accuracy.

The presence of cutaneous metastasis is usually an indicator of poorer prognosis, with mean survival time estimated to be seven months.<sup>10</sup> However, in our patient, there was complete excision of the solitary skin lesion with clear margins and no other sites of metastases seen on PSMA PET-CT following excision. Thus, he was treated with radiotherapy and androgen deprivation therapy for low volume metastatic disease. We expected his prognosis to be better than those currently described in literature.

## References

1. Bray F, Ferlay J, Soerjomataram I, et al. Prostate cancer statistics | World Cancer Research Fund. *CA: A Cancer Journal for Clinicians*.
2. Duran EP, Paradelo A, Fariña MC, et al. Cutaneous metastases from prostatic carcinoma. *J Surg Oncol*. Epub ahead of print 1996. DOI: 10.1002/(SICI)1096-9098(199606)62:2<144::AID-JSO12>3.0.CO;2-8.
3. Mueller TJ, Wu H, Greenberg RE, et al. Cutaneous metastases from genitourinary malignancies. *Urology*. Epub ahead of print 2004. DOI: 10.1016/j.urology.2004.01.014.
4. Esquivel-Pinto IA, Torres-Alvarez B, Gómez-Villa RJ, et al. A Case of Prostatic Carcinoma Manifesting as Cutaneous Facial Nodule. *Case Rep Urol* 2018; 2018: 1-6.
5. Mak G, Chin M, Nahar N, et al. Cutaneous metastasis of prostate carcinoma treated with radiotherapy: A case presentation. *BMC Res Notes* 2014; 7: 2-5.
6. Petcu EB, Gonzalez-Serva A, Wright RG, et al. Prostate carcinoma metastatic to the skin as an extramammary Paget's disease. *Diagn Pathol* 2012; 7: 1-6.
7. Morris CR, Hurst EA. Extramammary Paget Disease: A Review of the Literature-Part I: History, Epidemiology, Pathogenesis, Presentation, Histopathology, and Diagnostic Work-up. *Dermatol Surg* 2020; 46: 151-158.
8. Schmitt AR, Long BJ, Weaver AL, et al. Evidence-Based Screening Recommendations for Occult Cancers in the Setting of Newly Diagnosed Extramammary Paget Disease. *Mayo Clin Proc* 2018; 93: 877-883.
9. Hammer A, Hager H, Steiniche T. Prostate-specific antigen-positive extramammary Paget's disease - Association with prostate cancer. *Apmis* 2008; 116: 81-88.
10. Wang SQ, Mecca PS, Myskowski PL, et al. 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. *Journal of Cutaneous Pathology*. Epub ahead of print 2008. DOI: 10.1111/j.1600-0560.2007.00873.x.