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Atypical Skin Metastases of Mucinous Adenocarcinoma of the Prostate With Signet Ring Cells

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To the Editor:

Skin metastases from carcinoma of the prostate are extremely rare. When they occur, they usually appear as multiple nodules in the suprapubic area or on the anterior aspect of the thighs. The appearance of distant lesions, outside the typical areas, is uncommon, with only 14 reports in the past 25 years. We report a case with an atypical presentation of skin metastases from adenocarcinoma of the prostate, also highlighting the utility of prostate specific antigen (PSA) as an immunohistochemical marker in skin metastases of unknown origin in elderly men.

The patient was a 62-year-old man who developed multiple nodular lesions on the thorax, axillas, and face; the lesions had developed over the previous 3 months. They were particularly numerous on the face, especially on the right side, extending towards the scalp (Figure 1). Associated symptoms included a 4-month history of dyspnea on exertion and costal pain on deep inspiration,



Figure 1. Multiple nodular lesions on the face.

together with difficulty urinating over the past 2 years. With a clinical suspicion of skin metastases, biopsy was performed of 1 of the lesions on the thorax. Histological study revealed a well-defined, dermal tumor nodule that did not reach the epidermis. It was formed of undifferentiated epithelioid cells, arranged in cords, and with signet ring morphology (Figures 2A and 2B). These cells were surrounded by a mucinous stroma (Figure 2C). Immunohistochemical analysis was intensely positive for cellular adhesion molecule 5.2 and PSA (Figure 2D). In view of the results obtained up to that time, additional tests were performed that focused particularly on the prostate; these tests had the following main findings: normocytic anemia, PSA of 3901 ng/mL, bilateral basal interstitial-alveolar infiltrates on the chest x-ray, and a thoracoabdominopelvic computed tomography showing thickened, irregular walls of the bladder; right paratracheal, subcarinal, para-aortic, and interaortocaval lymph nodes; and blastic bone changes, compatible with a metastatic pattern. On rectal examination, the prostate was found to be increased in size with no sulcus; it was poorly defined, fixed, and had palpable, stony-hard nodules in both lobes. Prostatic biopsy revealed adenocarcinoma affecting 90% of each lobe (Gleason score, 8). It was particularly noticeable that the histology of the primary tumor was similar to that of the skin metastases, with signet ring cells surrounded by a mucinous stroma. In view of the advanced stage of the disease, it was decided to administer palliative treatment with the gonadotropin releasing hormone analogue, goserelin, 10.8 mg subcutaneously every 3 months. The patient presented a progressive reduction in the number of skin lesions over the following months.

Skin metastases from internal tumors are uncommon in clinical practice. In women, the most common origin of skin metastases is adenocarcinoma of the breast, whilst squamous cell carcinoma of the lung is the most common

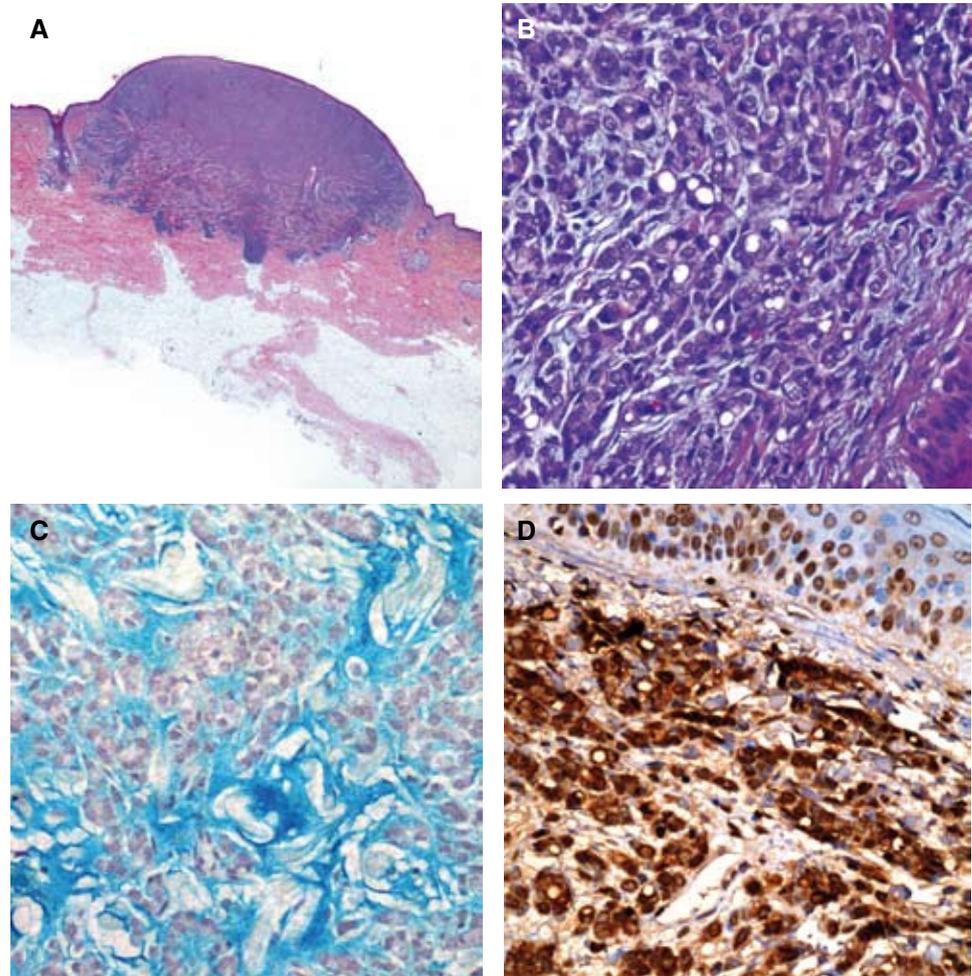


Figure 2. A, Well-defined tumor nodule in the dermis (hematoxylin-eosin, $\times 10$). B, Proliferation of atypical cells with signet ring morphology, arranged in layers and with a glandular pattern (hematoxylin-eosin, $\times 200$). C, Abundant mucinous stroma (alcian blue). D, Intense positivity for prostate specific antigen.

in men. The appearance of skin metastases in patients with cancer of the prostate is extremely rare: they represent only 1% of all skin metastases.¹ The largest series of patients with skin metastases came from a study by Lookingbill et al,² with a total of 4020 patients. In that series, despite the high frequency of carcinoma of the prostate, it was notable that there were no cases of skin metastases of prostatic origin. Current information about skin metastases from cancer of the prostate comes from the publication of small series or case reports; there are approximately 91 publications.

Based on those publications, we know that the typical clinical presentation is as multiple nodules in the suprapubic region and on the anterior aspect of the thighs or abdomen.³ Metastases outside these typical areas are very rare, with only 16 cases reported in the past 25 years (Table).³⁻¹⁶ When they appear, they are a sign of poor prognosis, indicating dissemination of the tumor. It is therefore common to find involvement of other body areas, particularly the pelvic bones and lymph nodes, in the study of tumor extension.⁷⁻¹⁰

Exceptionally, skin metastases can be the first sign of prostatic disease. In these cases, it is essential to perform a detailed clinical study to look for associated systemic symptoms, as it is otherwise difficult to orientate the diagnosis towards skin metastases, and, more so, towards a prostatic origin. We draw particular attention to the utility of measuring the serum PSA in cases of suspected skin metastases.¹⁶

From a dermatopathological point of view, metastases from carcinoma of the prostate are identified as nodules or sheets of tumor cells arranged between the dermal collagen fibers, showing glandular differentiation. Cells with a round nucleus and 1 or more eosinophilic nucleoli are typically observed on cytology.³⁻⁷ In our case, both the primary tumor and the metastases were of a mucinous adenocarcinoma with signet ring cells. This histological type of adenocarcinoma of the prostate is rare, but it is usually one of the most aggressive.¹⁷ The finding of signet ring cells in a mucinous stroma means that a primary tumor of the lung, stomach, or colon must be excluded^{1,2,17}; it is in these cases that the PSA becomes particularly important

Table. Metastases at Atypical Sites

Reference	Presentation	Site	Clinical Appearance
Venable 1983 ³	Tumor mass	Supraclavicular	Metastasis
Whitmore 1986 ⁴	Indurated plaques	Thorax	Morphea
Pieslor 1986 ⁵	Umbilical nodule	Umbilicus	Sister Mary Joseph nodule
Rossetti 1991 ⁶	Tumor nodule	Thorax	Basal cell carcinoma
Azaña 1993 ⁷	Nodular lesions	Neck	Metastasis
Cox 1994 ⁸	Nodular lesions	Head and neck	Cellulitis
Pique 1996 ⁹	Indurated erythematous plaque	Thorax	Morphea
	Multiple skin nodules	Abdomen	
Offidani 1997 ¹⁰	Nodules	Scalp, thorax	Metastasis
Marcoval 1998 ¹¹	Papulonodular lesions	Areola and nipple	Paget disease
Ng 2000 ¹²	Inflammatory plaque	Thigh	Cellulitis
Boswell 2005 ¹³	Irregular violaceous plaque	Forehead	Angiosarcoma
Sharma 2005 ¹⁴	Papules and nodules	Face, neck, and thorax	Trichoepitheliomas
Fukuda 2006 ¹⁵	Firm, elastic nodule	Umbilicus	Sister Mary Joseph nodule
Wu 2006 ¹⁶	Multiple erythematous nodules	Left anterior region of thorax	Metastasis
Present case	Multiple nodules	Scalp, face, and thorax	Metastasis

as an immunohistochemical marker, being an unequivocal sign of the prostatic origin of the skin tumors.

In summary, we present a case of atypical skin metastases of prostatic origin. We would like to highlight the atypical characteristics of this case—it developed in a relatively young individual for this type of tumor, the presentation was with multiple nodules at an uncommon site, the histological subtype was of signet ring cells in a mucinous stroma, and it was a highly aggressive—and the utility of PSA as an immunohistochemical marker in these cases.

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Conflicts of interest

The authors declare no conflicts of interest.

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Morphea Distributed Along Narrow Blaschko Lines

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To the Editor:

A 4-year-old girl, with no personal or family history of interest, presented pigmented lesions on the arms and trunk that had appeared approximately 1 year earlier. The initial lesions were papules of normal skin color that progressed to hyperpigmented, slightly raised lesions with a smooth, shiny surface and that were indurated and sclerotic. On examination, the lesions were observed along the length of the left upper limb, following 2 narrow lines from the wrist to the shoulder (Figure 1); this line continued across the left shoulder to the midline of the back. Another similar, linear lesion was found on the left side of the abdomen, following an S-shaped path.

There were no associated cutaneous or systemic symptoms. The complete blood count and biochemistry were normal. Antinuclear antibodies were positive at a titer of 1/160 and the results for perinuclear antineutrophil cytoplasmic antibodies, cytoplasmic antineutrophil cytoplasmic antibodies, and anti-Ro, anti-La, anti-Smith, anti-ribonucleoprotein, anti-Scleroderma DNA Topoisomerase I, and anti-Jo1 antibodies were negative. Histopathological

examination revealed a normal epidermis with thickening of the dermis due to the presence of wide, sclerotic bands of collagen, mainly in the middle and deep dermis. In addition, there was a moderate inflammatory infiltrate formed of lymphocytes and a few plasma cells, with a superficial, deep, and perivascular distribution (Figure 2). The skin adnexa appeared atrophic, with no peripheral adipose tissue, and staining with orcein demonstrated preservation of the elastic fibers.

The lesions had been stable since their onset and it was therefore decided to maintain the patient under observation with no treatment.

Linear morphea is a rare disorder that usually occurs in childhood and can affect any area of the body surface. It includes what are considered to be special forms, such as morphea en coup de sabre and progressive facial hemiatrophy. A number of cases of morphea following the Blaschko lines on the trunk and limbs have been reported previously.¹⁻³ However, frontoparietal morphea en coup de sabre is more clearly limited to the Blaschko lines described.⁴ In the case of linear morphea of the



Figure 1. Indurated papules grouped along the left upper limb and on the left hemiabdomen.

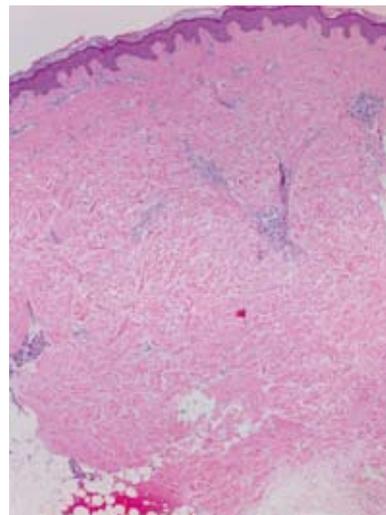


Figure 2. Thickening and sclerosis of the dermal collagen bundles, with a moderate perivascular inflammatory infiltrate formed of lymphocytes and a few plasma cells. Hematoxylin-eosin, $\times 10$.