Malignant melanoma scrotal metastasis: The importance of the genital examination

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INTRODUCTION

The total body skin examination is an essential component in the routine surveillance of patients with a history of melanoma. The appearance of distant cutaneous and subcutaneous melanoma metastasis represents disease that is high risk for recurrence in visceral sites, and these patients must be monitored closely.[1] Although primary malignant melanoma of the scrotum has been reported,[2-5] metastatic disease to the scrotum has not been described. Here we present the case of an elderly man with a history of stage IIIC melanoma who presented for a routine follow-up skin examination and was found to have metastatic disease involving the scrotum. This case reinforces the importance of the full body skin assessment, including examination of the genitals in patients with a known history of melanoma.

Abbreviations used:

CT: computerized tomography
PET: positron emission tomography

CASE REPORT

A 61-year-old man with a history of stage IIIC melanoma presented for routine follow-up and a total body skin examination. He denied any new or concerning skin lesions, including new or changing growths. Four years prior, he had an amelanotic superficial spreading melanoma of the left side of the upper back (4.58 mm Breslow depth, Clark level IV, with ulceration). Wide local excision with 3-cm surgical margins was performed because of the presence of macroscopic satellite lesions. Sentinel lymph node staging of the left axilla found 6 of 6 sentinel lymph nodes with microscopic implants of melanoma ranging in size from 0.1 to 10 mm. Seventeen additional lymph nodes were removed and all found to be normal. A brain magnetic resonance imaging, chest radiograph, and a computerized tomography (CT) scan of the abdomen and pelvis found no evidence of metastatic disease. His disease was characterized as stage IIIC (T4b, N3, M0) based on the American Joint Commission Cancer staging guidelines for melanoma. He was referred to the medical oncology department for possible interferon therapy, but the patient declined additional treatment. Three years later, local recurrence of his lesion was noted on the upper back. Radical excision was recommended at that time in addition to radiotherapy or immunotherapy, such as injectable oncolytic virus therapies. The patient elected for surgery alone, and the lesion was excised using 1-cm margins.

On examination, a benign-appearing, subcutaneous, 5-mm mobile, nontender, well-circumscribed, pink nodule of the scrotum was discovered during examination of the genitals. Given the benign appearance of the nodule, an excisional biopsy with 3-mm surgical margins was performed. Routine hematoxylin and eosin staining found a well-circumscribed, noninflammatory, dermal mass

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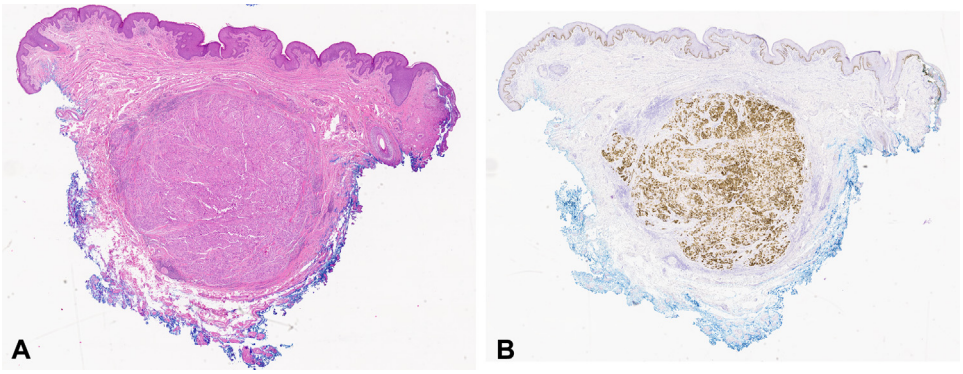

Fig 1. A, Routine hematoxylin-eosin staining. **B**, Melan-A immunohistochemical staining. (**A** and **B**, Original magnifications: ×13).

with atypical nested melanocytes, frequent mitotic figures, and no epidermal connection (Fig 1, *A*). The dermal mass was strongly positive for S-100 and melan-A (Fig 1, *B*) and demonstrated similar cytologic features as the patient's primary tumor. Taken together, the clinical and microscopic findings were most consistent with a diagnosis of metastatic melanoma to the scrotum. Repeat brain magnetic resonance imaging, chest radiograph, and CT scan of the abdomen and pelvis found no further evidence of metastatic disease. Systemic treatment was discussed, including interferon therapy or ipilimumab, but the patient declined systemic treatment. Six months later, he presented with seizures and was found to have multiple brain metastases.

DISCUSSION

Stage IIIC melanoma has a high risk of disease recurrence, with 5-year disease-free survival and overall survival rates of 11% and 30% to 45%, respectively.[6,7] The site-specific risk of first relapse in stage IIIC melanoma patients includes locoregional (skin/lymph nodes) disease and distant metastases in 33% and 51% of patients, respectively.[6] The skin is the most common organ-specific site for distant melanoma metastases and is classified as M1a disease according to the American Joint Commission Cancer staging guidelines. Although primary malignant melanoma of the scrotum has been reported, metastatic disease to the scrotum has not been described.[2-5] Possible mechanisms of cutaneous metastasis to this anatomic region in men (scrotum) and women (labia majora) include local extension of the tumor or lymphatic/hematogenous spread.[8]

Several histologic features are associated with metastatic disease, including the absence of inflammatory infiltrate, an epithelioid cytomorphology, cellular atypia representative of the primary tumor, a dermal mass with no epidermal connection, or prominent lateral dermal extension of malignant cells when an apparent epidermal connection is present (known as *epidermotropic metastatic melanoma*).[9,10] However, distinguishing between primary and metastatic melanoma based on histology alone is challenging and requires correlation with clinical data. No histologic stains can reliably differentiate primary melanoma from metastatic disease.

Current treatment options for distant dermal metastasis of melanoma are guided by whether the disease is limited and resectable or disseminated and unresectable. When resectable, excision until surgical margins are negative is recommended.[11] After resection, patients are observed or enrolled on a clinical trial. Treatment options for unresectable disease have expanded considerably over the last 5 years and include systemic immunotherapy (pembrolizumab, nivolumab, ipilimumab, or high-dose interleukin-2), targeted therapy with *BRAF* and *MEK* inhibitors for tumors expressing a *BRAF* mutation, or intratumoral injections with talimogene laherparepvec (T-VEC), a genetically engineered oncolytic strain of the herpes simplex virus type 1.[11]

This case highlights the importance of the total body skin examination, including the genitals, for routine surveillance of melanoma patients. Imaging with CT and positron emission tomography (PET) scans often misses a small dermal metastasis that can be detected on physical examination.[12] Palpation of the skin enables the detection of small dermal metastases that are often missed with CT and PET scans. Asymptomatic lesions of the genital region may go unnoticed by melanoma survivors or mimic benign growths, such as scrotal calcinosis or an epidermal cyst. A high index of suspicion for the pleomorphic clinical manifestations of metastatic melanoma should guide the physical examination and need for additional diagnostic testing.

Total body skin examination every 3 to 6 months for the first 2 years followed by an annual skin

examination is recommended for patients with a history of stage II to IV melanoma.[11] Imaging of the brain, chest, abdomen, and pelvis with chest radiograph, CT, or PET/CT scans every 4 to 12 months to screen for recurrent or metastatic disease should be considered in patients with a history of stage II to IV melanoma.[11] One recent study suggests that patients are more likely to agree to a total body skin examination when clinicians respect the patient's preferences for the physician's gender and degree of disrobement.[13] However, total body skin examination for skin cancer screening remains a controversial topic in the literature, and there is no national consensus for skin cancer screening in melanoma survivors.

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