

# A rare case of anal squamous cell carcinoma metastasizing to the scrotum



Josiah Williams, BS, Steven Feldman, MD, PhD, and Daniel J. Teague, MD  
Winston-Salem, North Carolina

**Key words:** anal carcinoma; case report; general dermatology; medical dermatology; metastasis; oncology.

## INTRODUCTION

Skin metastases are found in up to 10% of metastatic cancers.<sup>1</sup> Breast cancer is the most common cause of cutaneous metastases in women, and lung cancer is the most common cause in men.<sup>2</sup> Here we describe recurrent anal carcinoma with metastases to the scrotum.<sup>3</sup>

## CASE REPORT

A 60-year-old black man was referred by his oncologist to the dermatology clinic in June 2019 with a presumptive diagnosis of genital warts. Eighteen months before, he had received a diagnosis of TNM stage IIIb human papillomavirus 16+ squamous cell carcinoma of the anal canal. He originally presented in April 2017 with an anal mass and several months of bleeding, and a biopsy of the mass confirmed the diagnosis of anal squamous carcinoma with a positive p16 stain result (Fig 1). Subsequent computed tomographic scan displayed enlarged right-sided inguinal lymph nodes, and superficial inguinal lymph node biopsy confirmed squamous cell carcinoma. Human papillomavirus polymerase chain reaction was not run because it is an expensive test and would not have affected staging or treatment because the cancer had already spread to the lymph nodes and because p16 staining result was positive. The patient was treated with a combination of surgery, chemotherapy, and radiation therapy. Two months before presenting to the dermatology clinic, he appeared to be in remission; neither radiographic studies nor serial biopsies around the anal verge showed any evidence of residual disease.

At the dermatology clinic, multiple 4- to 10-mm, dome-shaped, firm, nontender nodules were present on his scrotum (Fig 2). The color of the nodules varied from pink to dark brown and was generally uniform across each lesion. A slightly eroded top was evident on some of the lesions. Biopsies revealed poorly differentiated carcinoma (Figs 3 and 4). Additional staining identified the tissue as metastatic anal carcinoma with notable epidermotropism, and p16 staining result was again positive (Fig 5).

When the scrotal biopsies showed metastatic spread of the anal carcinoma, he was referred to oncology for further treatment. The patient is currently receiving treatment as of 9 months after his scrotal metastases were identified. Treatment during the course of his disease has involved surgery and chemoradiotherapy, including mitomycin and 5-fluorouracil infusions.

The patient's history was not positive for typical risk factors for anal carcinoma. He had no history of HIV or malignancy before his diagnosis of anal carcinoma, and his medications did not include any immunosuppressive agents. Furthermore, his social history included being married in a heterosexual relationship for greater than 23 years and no high risk sexual behavior. He had no history of smoking cigarettes but occasionally smoked a cigar and had a distant history of marijuana use. He had not received a diagnosis of human papillomavirus before his anal carcinoma diagnosis.

## DISCUSSION

Anal squamous cell carcinoma is uncommon, constituting only 2% of all gastrointestinal cancers and 0.4% of newly diagnosed cancers each year in

From the Department of Dermatology, Wake Forest School of Medicine, Winston-Salem.

Funding sources: None.

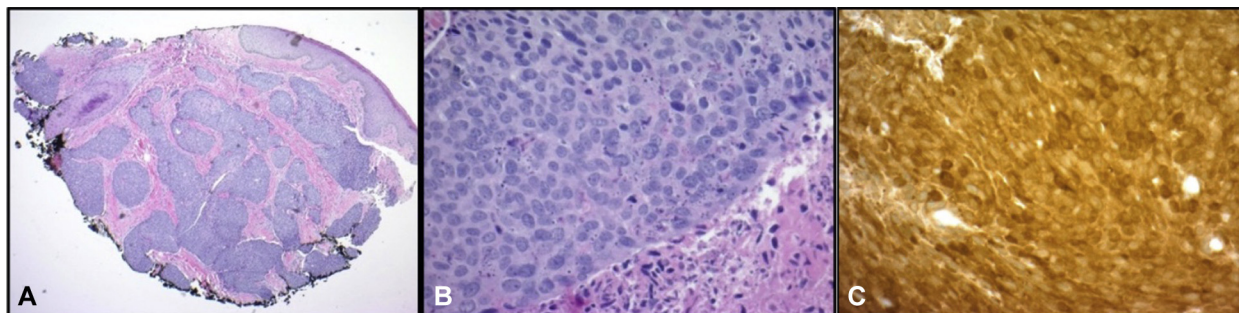
Conflicts of interest: None disclosed.

Correspondence to: Steven Feldman, MD, PhD, Department of Dermatology, Wake Forest School of Medicine, 4618 Country Club Rd, Winston-Salem, NC 27104. E-mail: [sfeldman@wakehealth.edu](mailto:sfeldman@wakehealth.edu).

JAAD Case Reports 2020;6:743-6.  
2352-5126

© 2020 by the American Academy of Dermatology, Inc. Published by Elsevier, Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

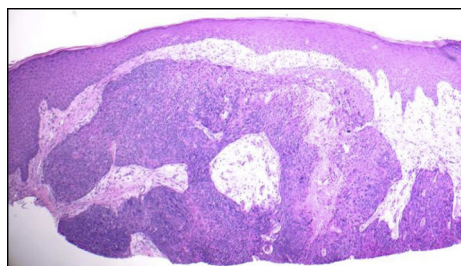
<https://doi.org/10.1016/j.jidcr.2020.06.012>



**Fig 1.** Histopathology of the primary tumor at diagnosis. Biopsies at the original diagnosis display islands of atypical epithelial cells in a background of dermal fibrosis, most evident at  $\times 40$  (A). Higher magnification demonstrates nuclear atypia and mitotic figures at  $\times 400$  (B). Result for p16 staining was positive, indicative of human papillomavirus infection (C).



**Fig 2.** Scrotal lesions at dermatology referral. Multiple dome-shaped, firm, nontender, 4- to 10-mm metastatic lesions were present on the entire scrotum. Several biopsies were taken, as marked in the image.



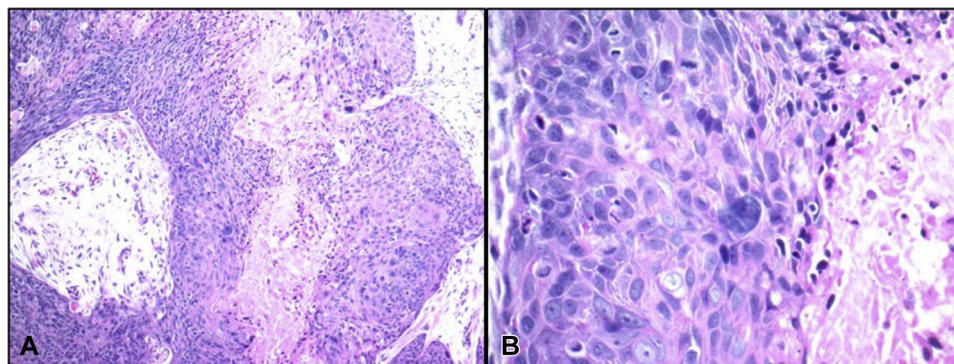
**Fig 3.** Histopathology of a metastatic lesion at dermatology presentation. The tissue architecture is evident, showing atypical cells on a background of dermal fibrosis underlying a slightly nodular and focally crusted epidermis. (Hematoxylin-eosin stain; original magnification:  $\times 40$ .)

the United States.<sup>4</sup> Few to no data are available on anal carcinoma metastasizing to the scrotum; however, a similar case was reported wherein rectal adenocarcinoma in a woman metastasized to the vulva.<sup>5</sup> Cancers that have been observed to metastasize to the scrotum include colorectal cancer, prostate cancer, lung cancer, and gastric adenocarcinoma.<sup>3,6</sup>

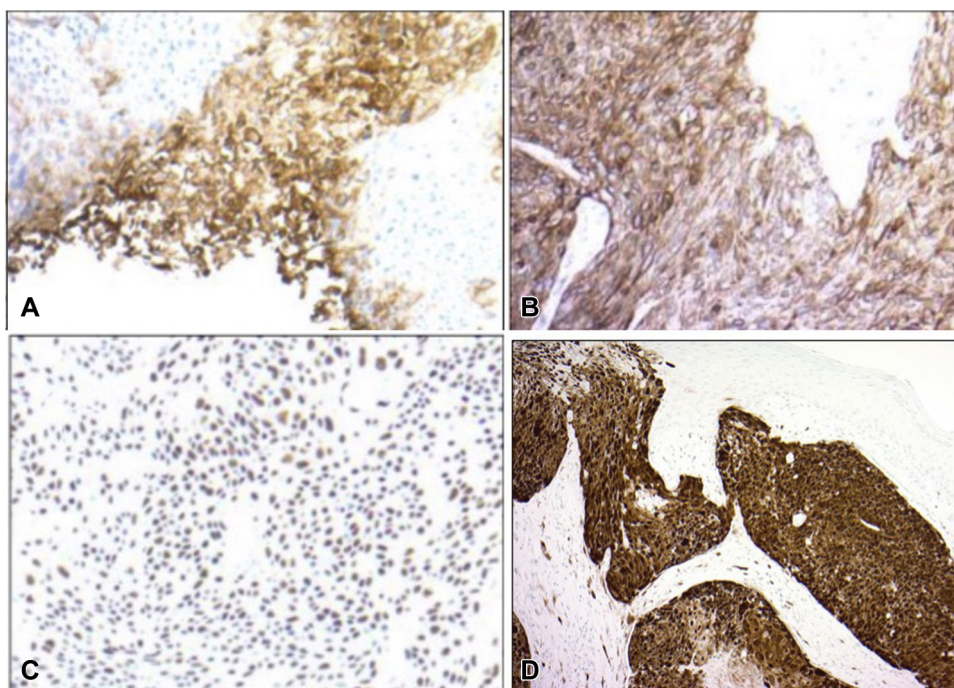
The most important risk factor for anal carcinoma is human papillomavirus 16 or 18 infection, with 90% of cases being attributable to human papillomavirus. Other risk factors include HIV, smoking, men who have sex with men, and chronic immunosuppression such as in transplantation.<sup>7</sup> The most common presenting symptom of anal squamous carcinoma is bleeding, as observed in this patient, but other presenting symptoms include pain, discomfort, pruritus, constipation, or diarrhea. The diagnosis is made with physical examination and biopsy.<sup>8</sup> Unlike most gastrointestinal malignancies, which are staged according to depth of invasion, tumor size is used to stage anal carcinoma.<sup>4</sup> If the anal

sphincter is not involved, patients with stage 1 disease may be treated with excision.<sup>8</sup> However, surgery does not have a significant role in metastatic disease and is typically used only for palliative care or persistent or recurrent disease. Instead, the standard treatment for anal carcinoma is chemoradiation.<sup>4</sup>

Our proposed mechanism of metastasis from the anal canal to the scrotum is via lymphatics because both the scrotum and lower anal canal drain to the superficial inguinal lymph nodes and because most carcinomas typically spread via lymphatics.<sup>9,10</sup> This patient's superficial inguinal lymph node biopsy result was positive for squamous cell carcinoma, which further supports retrograde lymphatic spread to the scrotum as the mechanism of metastasis. Lymphatic spread is often preceded by tumor-derived cytokines and growth factors draining to regional lymph nodes, which prime the microenvironment for metastasis by forming what is called a premetastatic niche.<sup>11</sup> It has been shown in colon cancer that premetastatic niche formation can be mediated by vascular



**Fig 4.** Histopathology of metastatic lesions at dermatology presentation. Atypical epithelial cells with areas of necrosis and degenerative change are visible at  $\times 100$  (A), whereas nuclear pleomorphism and atypical mitoses are more clearly seen at  $\times 400$  (B).



**Fig 5.** Additional staining of the metastatic lesions at dermatology presentation. Carcinoembryonic antigen polyclonal staining (A) showed positive staining results within areas of lesional cells that show at least focal glandular differentiation. Cytokeratin 7 staining (B) showed significant staining of lesional cells but the result was negative within the background epidermis. Likewise, p63 (C) showed positive staining of lesional cells, as did p16 (D).

endothelial growth factor A, which causes tumor-associated macrophages to release C-X-C motif chemokine ligand 1, which helps create a premetastatic niche by recruiting C-X-C motif chemokine receptor 2-positive myeloid-derived suppressor cells.<sup>12</sup> Because squamous cell carcinomas are also known to produce significant levels of vascular endothelial growth factor A, we suggest a similar mechanism may have been involved in metastatic spread in this case.<sup>13</sup>

## CONCLUSIONS

Metastases to the scrotum are uncommon.<sup>3</sup> Anal carcinoma metastasizing to the scrotum is a rare phenomenon that was observed in our patient. Metastatic spread could be included in the differential diagnosis for atypical scrotal lesions if the history is suggestive, and examination of the scrotum could be considered for patients with anal cancer because the lower anal canal and scrotum both drain to superficial inguinal lymph nodes.

## REFERENCES

1. Alcaraz I, Cerroni L, Rütten A, Kutzner H, Requena L. Cutaneous metastases from internal malignancies: a clinicopathologic and immunohistochemical review. *Am J Dermatopathol*. 2012;34(4):347-393.
2. Hussein MRA. Skin metastasis: a pathologist's perspective. *J Cutan Pathol*. 2010;37(9):e1-e20.
3. Leung ST, Chu CY, Lai BMH, Cheung FMF, Khoo JLS. Scrotal wall metastasis as the first manifestation of primary gastric adenocarcinoma. *Hong Kong Med J*. 2014;20:70-73.
4. Osborne MC, Maykel J, Johnson EK, Steele SR. Anal squamous cell carcinoma: an evolution in disease and management. *World J Gastroenterol*. 2014;20(36):13052-13059.
5. Akpak YK, Dandin Ö, Gün I, Atay V, Haholu A. A rare case of vulvar skin metastasis of rectal cancer after surgery. *Int J Dermatol*. 2014;53(6):e337-e338.
6. Hoyt BS, Cohen PR. Cutaneous scrotal metastasis: origins and clinical characteristics of visceral malignancies that metastasize to the scrotum. *Int J Dermatol*. 2013;52(4):398-403.
7. López LS, La Rosa L. Human papilloma virus infection and anal squamous intraepithelial lesions. *Clin Colon Rectal Surg*. 2019;32(5):347-357.
8. Morton M, Melnitchouk N, Bleday R. Squamous cell carcinoma of the anal canal. *Curr Probl Cancer*. 2018;42(5):486-492.
9. Leonard D, Beddy D, Dozois EJ. Neoplasms of anal canal and perianal skin. *Clin Colon Rectal Surg*. 2011;24(1):54-63.
10. Wong SY, Hynes RO. Lymphatic or hematogenous dissemination: how does a metastatic tumor cell decide? *Cell Cycle*. 2016;5(8):812-827.
11. Sleeman JP. The lymph node pre-metastatic niche. *J Mol Med*. 2015;93(11):1173-1184.
12. Wang D, Sun H, Wei J, Cen B, DuBois RN. CXCL1 is critical for premetastatic niche formation and metastasis in colorectal cancer. *Cancer Res*. 2017;77:3655-3665.
13. Wu FL, Nolan K, Strait AA, et al. Macrophages promote growth of squamous cancer independent of T cells. *J Dent Res*. 2019;98(8):896-903.