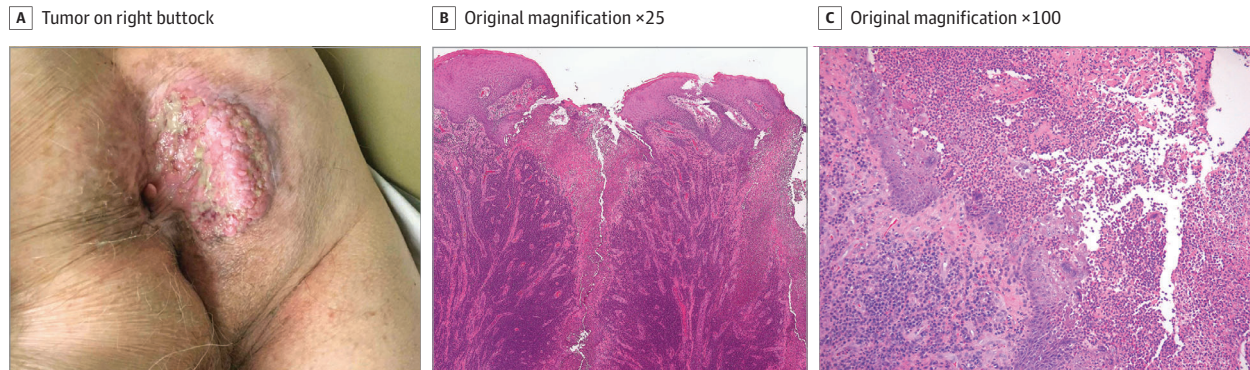


## JAMA Dermatology Clinicopathological Challenge

## A Treatment-Refractory, Perianal Tumor Arising in an Otherwise Healthy Older Adult Woman

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**Figure 1.** A, Clinical image of 5 × 7-cm verrucous, exophytic tumor with scant yellow drainage on the right medial buttock extending to the perianal skin. B, Hematoxylin-eosin stain image from the incisional biopsy featuring a hyperplastic epidermis with ulceration, necrosis, and a very dense inflammatory infiltrate. C, Hematoxylin-eosin stain demonstrating plasma cells composing the infiltrate while the epithelium shows focal multinucleated keratinocytes, some with gray-blue cytoplasm.

**A woman in her 80s** presented with an 8-month history of a growing, painful tumor on her right buttock. The patient felt well otherwise and denied experiencing fevers, chills, sweats, weight loss, or malaise. Her medical history was notable for chronic kidney disease and genital herpes simplex virus (HSV). She reported no history of genital warts, HIV, or inflammatory bowel disease. A biopsy was performed, and results were consistent with a noninfectious, granulomatous ulcer. Based on the clinical appearance and prior pathologic findings, the patient received treatment of oral antibiotics, intralesional steroids, topical steroids, and immunomodulators, without improvement. Findings from colorectal surgical evaluation of the internal anal mucosa were negative for malignant neoplasm.

At referral, physical examination findings revealed a 5 × 7-cm verrucous, exophytic tumor with scant yellow drainage on the right medial buttock extending to the perianal skin (Figure 1A). Findings from the remaining skin examination were normal. Superficial bacterial cultures were obtained from the lesion and grew methicillin-resistant *Staphylococcus aureus*. An incisional biopsy was performed for diagnostic clarification (Figure 1B and C).

## WHAT IS YOUR DIAGNOSIS?

- A. Squamous cell carcinoma
- B. CD30-positive primary cutaneous anaplastic large cell lymphoma
- C. Herpes vegetans
- D. Giant condyloma acuminatum (Buschke-Löwenstein tumor)

## Diagnosis

C. Herpes vegetans

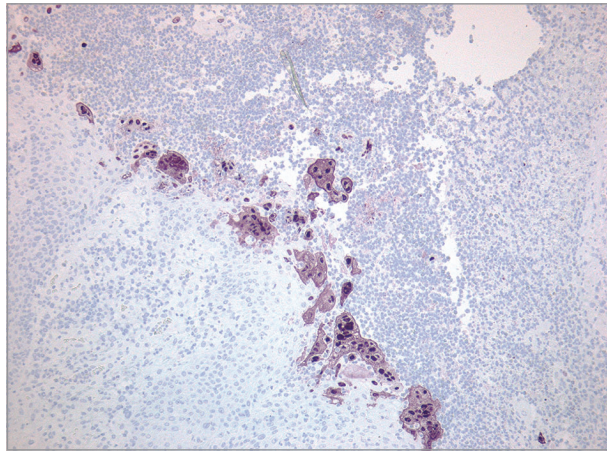
## Discussion

Histologic results showed epithelial hyperplasia, ulceration, and focal multinucleated keratinocytes (Figure 1B and C). Immunostaining was positive for HSV (Figure 2) but negative for varicella-zoster virus. Microbial cultures were negative for deep fungal infection and acid-fast bacteria but positive for HSV type 2. Given the clinicopathologic findings, herpes vegetans was diagnosed.

Herpes vegetans is a verrucous presentation of HSV in immunocompromised patients, including those with HIV, congenital immunodeficiency disorders, malignant neoplasm, and organ

transplants.<sup>1</sup> The condition is exceedingly uncommon in immunocompetent patients.<sup>2</sup> Coinfections of HSV with other cutaneous infections, such as fungal and human papillomavirus (HPV) infections, have also presented as verrucous plaques, which can complicate the diagnosis.<sup>3</sup> Herpes vegetans is frequently reported to be recalcitrant to oral antiviral therapy,<sup>4</sup> and although, to our knowledge, precise rates of drug resistance have not been elucidated, antinucleoside resistance has been associated with several characteristics of the disease, including prolonged symptom duration, recurrent outbreaks, and prior failed therapy attempts.<sup>5</sup>

Squamous cell carcinoma (SCC) can present as a nonhealing ulcer, fissure, nodule, or plaque in the anogenital region. Infections with HPV types 16 and 18 are associated with SCC in younger adults,



**Figure 2.** Immunohistochemical staining positive for herpes simplex virus types 1 and 2 within epithelial cells, including multinucleated keratinocytes (original magnification  $\times 100$ ).

whereas chronic inflammatory conditions, such as lichen sclerosus, are associated with SCC in older adults.<sup>6</sup> Histologic characteristics of anogenital SCC resemble those of SCC in other parts of the body, but basaloid and warty carcinomas have been associated with HPV infection, whereas keratinizing SCCs have not.<sup>6</sup> Sentinel lymph node biopsy or inguinofemoral lymphadenectomy may be required depending on the extent of disease.<sup>7</sup>

Another verruciform tumor of the perianal region believed to be related to HPV infection is giant condyloma acuminatum, or Buschke-Löwenstein tumor. Giant condyloma acuminatum can be considered as being on the verrucous carcinoma spectrum, which includes epithelioma cuniculatum of the foot and oral florid papillomatosis.<sup>8</sup> Unlike SCC, giant condyloma acuminatum is associated with low-risk HPV types 6 and 11. Although generally considered benign and slow growing, it can invade local subcutis, fascia,

and bone and tends to recur if not completely excised.<sup>9</sup> Histopathologic findings of giant condyloma acuminatum resemble those of a condyloma with endophytic expansion into the underlying tissue.<sup>9</sup> Treatment options include radical surgical excision, intralesional interferon, and topical cidofovir.<sup>9</sup>

CD30-positive primary cutaneous anaplastic large cell lymphoma is an indolent form of cutaneous lymphoma that can display pseudocarcinomatous hyperplasia, mimicking SCC and herpes vegetans. CD30-positive lymphoproliferative disorders are the second most common group of cutaneous T-cell lymphomas; however, pseudocarcinomatous hyperplasia is rare, with fewer than 50 cases reported.<sup>10</sup> It typically presents as a solitary nodule or plaque with a hyperkeratotic and ulcerated surface on a person's trunk or face. Histologic characteristics include a dense inflammatory infiltrate of medium to large atypical lymphocytes, prominent hyperkeratosis, and irregular acanthosis with occasional keratinocyte atypia. Immunostaining with CD30 is positive in the large atypical lymphocytes. Treatment with excision and radiotherapy portends a good prognosis with a 10-year disease-related survival rate of greater than 90%.<sup>10</sup>

This patient was initially treated with vinegar soaks and oral valacyclovir for 3 weeks without improvement. Thus, infectious disease and colorectal surgery consultations were sought for management options. Following shared decision-making with the patient, debulking was performed, followed by treatment with topical 1% cidofovir cream daily for 8 weeks, then 5% imiquimod cream 3 times weekly for 8 weeks. After 4 months, the patient had complete resolution of the lesion. As demonstrated in this case, it is important to consider herpes vegetans in the differential diagnosis of anogenital lesions given the wide array of clinical mimicry and to prevent invasive and inappropriate treatment. Despite limited randomized clinical trial data regarding treatment for herpes vegetans, a combination of medical and surgical treatments may be an effective and patient-centered approach.

#### ARTICLE INFORMATION

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