

Case Report

An Unusual Case of Invasive Carcinoma with Squamous and Low-Grade Glandular Features Arising in a Giant Condyloma Acuminatum

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We report an unusual case of invasive carcinoma with both squamous and glandular features arising in a giant anorectal condyloma acuminatum (GCA). The challenging part in rendering a definite diagnosis was the presence of a glandular component, its differentiation from other entities with similar histomorphology and low-grade human papilloma virus (HPV) expression in tumor cells. A 70-year-old woman presented with long standing symptoms of rectovaginal bleeding and recurrent perianal fistulas. She underwent an end-colostomy and later, an abdominoperineal resection. A large anorectal tumor was identified with associated invasive carcinoma showing both squamous and low-grade glandular features. The tumor recurred as pelvic mass within 6 months requiring chemoradiation therapy. The abdominoperineal resection specimen showed a large (> 5cm) verrucous mass at anorectal junction with an endophytic component invading vaginal fistulas and adjacent soft tissue. Histologically, the exophytic tumor had condylomatous proliferation with koilocytosis. The endophytic part showed invasive carcinoma with both squamous and low-grade glandular features. The glandular component was positive for CK7 and negative for CK20 and CDX-2, suggesting anal gland origin rather than a colorectal primary. High-risk HPV and p16 were both negative. In-situ hybridization (ISH) demonstrated low-grade HPV in tumor cells. GCA, also known as Buschke-Lowenstein tumor, occurs mostly in men and rarely transforms to invasive squamous cell carcinoma. Our female patient presented with recurring perianal fistulas and bleeding without detection of a condylomatous mass until after radical surgery. In addition, GCA associated with this particular pattern of squamous cell carcinoma (one with a glandular component) is exceedingly rare. The differential diagnoses included mucoepidermoid carcinoma, adenosquamous carcinoma and squamous cell carcinoma with mucinous microcystic pattern. The presence of low-risk HPV on ISH test, not only in the condyloma but also in the squamous and glandular cells of the invasive carcinoma, raises a question of its impact in tumor progression from condyloma to squamous as well as glandular invasive carcinoma. Besides being a diagnostic challenge, the clinical implication of this finding remains to be determined.

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INTRODUCTION

Giant condyloma acuminatum, also known as Buschke and Lowenstein tumor, is an uncommon, slow growing tumor with locally aggressive nature. It commonly involves the anogenital region and can form difficult to treat recurrences and cutaneous fistulas. Even more rare is an invasive squamous cell carcinoma, arising in the setting of giant condyloma, with a potential to metastasize.

We describe a rare case of anogenital giant condyloma acuminatum (GCA) in a woman who presents with multiple recurrences and formation of cutaneous fistulas, despite multiple surgeries and end colostomy. The tumor grew to a large verrucous mass (>5cm) in anorectum, involved vaginal fistula tracts and showed an unusual histomorphology of invasive carcinoma with both squamous and glandular differentiation.

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CASE PRESENTATION

A 70-year-old woman presented with history of perianal fistulas for years. She was status post end colostomy to promote healing but continued to have painful and purulent discharge from the fistulas. Later, she was subsequently diagnosed with rectovaginal fistulas and underwent an abdominoperineal resection.

Intraoperatively, the surgeons identified a large mass at the anorectal junction along with anovaginal and rectovaginal fistulas with pockets of pus. The tumor invaded fistula tracts and the adjacent fibroadipose tissue. The rectum and vagina were adherent with no real dissection plane. After careful dissection, the vaginal wall was freed, and the tumor was completely removed.



Figure 1. Large exophytic mass in anal canal.

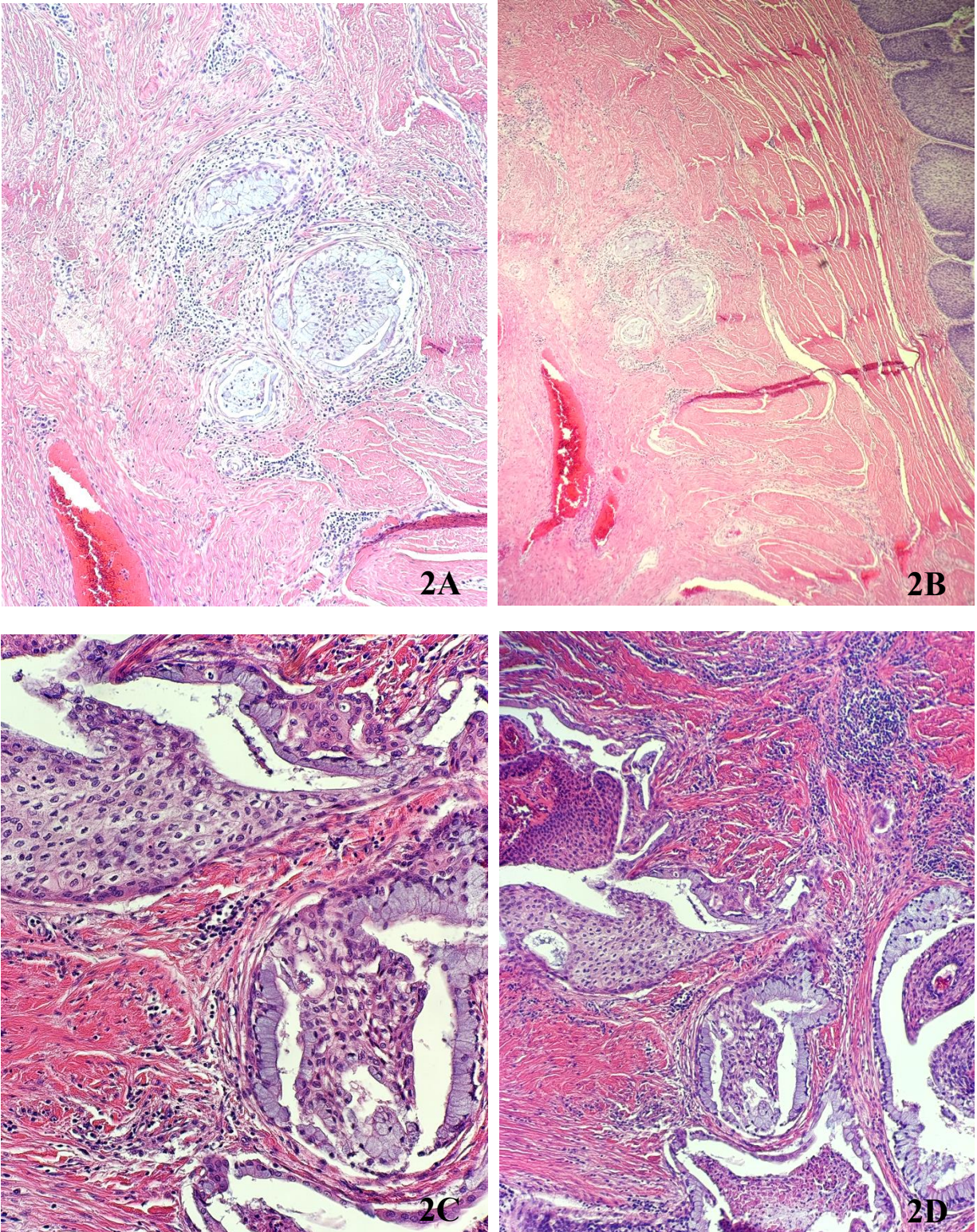


Figure 2. H&E stained sections show invasive carcinoma with squamous and glandular components in 100x magnification (2A, 2C) and 200x magnification (2B, 2D).

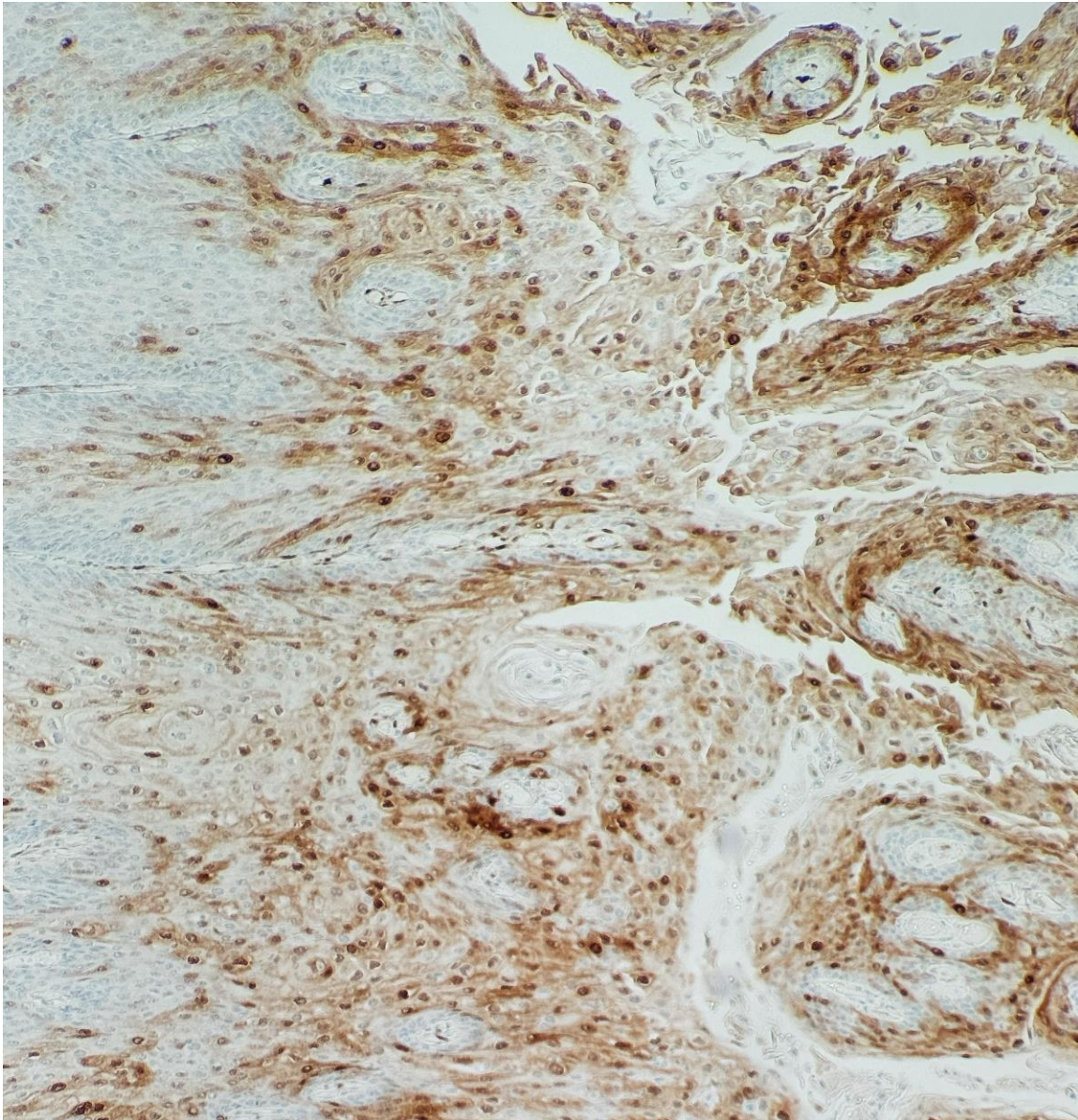


Figure 3. P16 immunohistochemistry shows patchy staining.

PATHOLOGIC AND ANCILLARY FINDINGS

The gross specimen showed a large (>5 cm), circumscribed and exophytic mass at the anorectal junction involving anorectal-vaginal fistulas. Representative tissue sections were submitted from the exophytic anorectal mass, the vaginal fistulas and deeper tissue penetrated by an endophytic tumor component.

Histologically, the exophytic mass showed papillary/verrucous architecture, koilocytosis and low grade squamous intraepithelial lesion, compatible with giant condyloma acuminatum. However, microscopic sections from deeper fistulous tissue showed endophytic and infiltrative tumor growth. Invasive carcinoma showed both squamous and

glandular differentiation.

The differential diagnoses included mucoepidermoid carcinoma, adenosquamous carcinoma, invasive squamous cell carcinoma with mucinous microcystic pattern metastatic carcinoma. Immunohistochemical stains and HPV in-situ hybridization (ISH) were performed. The glandular component of the invasive carcinoma is positive for CK7 and negative for CK20, CDX2, PAX8, and ER. Ki-67 only stained the squamous cell component with low to modest level and very minimal labeling in the glandular component. ISH revealed the presence of low-risk HPV, while high-risk HPV and p16 are both negative.

DISCUSSION

Giant condyloma acuminatum typically presents as a squamous lesion with no high-grade dysplasia and has a prominent fibrovascular core, forming an exophytic mass that is greater than 3 cm. GCA is often seen as a benign entity, but there have been previous reports of it transforming into a carcinoma.^{1, 4, 5} It is highly associated with low-risk human papillomaviruses (HPV), like HPV-6 and HPV-11. The HPV in-situ hybridization from our case is consistent with a GCA with the presence of low-risk HPV, while negative for high-risk HPV and p16. Our case presents in a similar manner with an exophytic mass with a low grade squamous intraepithelial lesion, but there was an endophytic component of invasive squamous carcinoma with glandular features.

Squamous cell carcinoma with glandular features is rare. We have considered other entities that are commonly associated with glandular architecture, but immunohistochemical stains of positive CK7 and negative CK20 and CDX2 suggest the invasive squamous cell carcinoma most likely originated from anal transitional cells or anal glands, rather than rectal type glandular epithelium.² The carcinoma is also negative for PAX8 and ER, which reveals that it does not have a gynecological origin. The tumor invades through the sphincter muscle into perianal soft tissue and arise in the background of a giant condyloma acuminatum.

The treatment of GCA is wide surgical excision, but GCA is known to have a high rate of recurrence. GCA recurrences are treated through radical surgery, with the addition of systemic chemotherapy of bleomycin, cisplatin, methotrexate and leucovorin for aggressive cases.³ In our case, the tumor was removed in July 2023 through an abdominoperineal resection. However, in December 2023, there was a retropubic hypermetabolic pelvic mass that was discovered through a CT guided biopsy. The mass was 2.6 cm and located behind the

right pubic symphysis. The biopsy was reported as fibroconnective tissue and scant clusters of atypical squamous epithelial cells that are positive for CK5/6 and p40. However, there was suspicion of a recurrence of GCA and invasive squamous carcinoma, so an excisional biopsy of the lesion was performed. Intraoperatively, the surgeons found a 4 cm firm, fixed submucosal vaginal mass over the right vaginal sidewall, approximately 2 cm proximally from the vulvovaginal introitus. The lesion revealed to be invasive carcinoma with squamous and glandular features, arising in the background of condyloma acuminata. As of June 2024, patient did undergo chemotherapy and radiation for pelvic cancer.

CONFLICTS OF INTEREST

None

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