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CASE REPORT

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Ectopic production of beta-hCG in anal cancer: A case report

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Key Clinical Message

Beta-hCG-producing anal cancer, though rare, poses significant diagnostic challenges and may resist standard therapies. Recognizing the potential for hormone production in anal cancer is important, as it underscores the need for more specialized diagnostic techniques and tailored treatments.

Abstract

This case report describes the second reported case of ectopic production of beta-hCG in anal cancer. A 53-year-old female presented with a new anal lesion. Biopsy showed a poorly differentiated squamous cell cancer (SCC) with undifferentiated sarcomatoid features, stage IIIA (cT2cN1cM0). Before starting concurrent chemotherapy and radiation, the patient had a positive urine pregnancy test. The beta-human chorionic gonadotropin (beta-hCG) production was attributed to the tumor, and upon completion of treatment, beta-hCG normalized. Six weeks from treatment completion, recurrence was noted along with a positive beta-hCG urine test. This case aims to highlight beta-hCG as an ectopic hormone that can indicate the presence of squamous cell anal cancer and discuss the potential implications it may have on management.

KEYWORDS

anal cancer, diagnostic techniques, ectopic hormones, multidisciplinary care

1 | INTRODUCTION

Beta-human chorionic gonadotropin (beta-hCG) is most commonly produced by the villous syncytiotrophoblast that forms during pregnancy. It has numerous functions but primarily promotes progesterone production and maintenance of the corpus luteum.[1] While the syncytiotrophoblast is the physiological origin of beta-hCG, it can be produced ectopically. Elevated beta-hCG levels are found in association with several tumors: seminomatous and nonseminomatous testicular tumors, ovarian germ cell tumors, and nontesticular teratomas.[2] Data from one study by Matzuk et al. (2003) examining beta-hCG in a mouse model suggest that it may result in a diminished response to radiotherapy and expedited metastasis.[3] Several other studies have also found ectopic production correlated with poorer prognosis.[4,5] This hormone, however, has rarely been associated with anal cancer.

In the one documented account of beta-hCG production in anal cancer by Pokharel et al. (2020), a 43-year-old female presented with p-16-positive squamous cell anal cancer.[6] During the patient's pre-treatment screening,

beta-hCG was positive. Treatment was held until it was determined that the tumor was producing the hormone. With treatment, the levels of beta-hCG eventually dropped to zero. It was postulated that this ectopic hormone production was likely due to the association between the development of precancerous anal and cervical lesions through human papillomavirus (HPV). The study concluded that beta-hCG expression might be the first sign of a primary malignancy.

An elevated beta-hCG has not been explored as a prognostic factor in anal cancer. Currently, the most important factors for prognosis in anal cancer are T and N stages, while grade and histology have no clear role.[7] This represents the second case report of a female patient who presented with squamous cell carcinoma of the anus with ectopic production of beta-hCG.

2 | CASE PRESENTATION

The patient is a 53-year-old postmenopausal G5P3023 female who presented with complaints of ongoing vulvar irritation and had a "hemorrhoid" at the posterior fourchette, which, on the exam, appeared suspicious for possible malignancy. The patient reported tenderness in the area but denied abdominal pain, dysuria, urinary frequency or urgency, weight loss, fevers, or recent injury or trauma. The patient's oncological history was significant for stage IB (pT1b, pN0(sn), cM0) grade 2 squamous cell carcinoma of the left labia majora s/p left radical hemivulvectomy and sentinel node biopsy in December 2021. The patient stated that menses occurred at the age of 12 and menopause at 45. Notably, the patient's grandmother had breast cancer, but there was no known family history of cervical, uterine, ovarian, colon, or prostate cancer. On physical exam, there was a 2.5 cm anal lesion suspicious of malignancy. It was partly obstructing the anus and was causing pain with defecation. There were no other palpable lesions noted on the digital rectal exam.

3 | METHODS

An anal mass biopsy was performed under anesthesia. According to the operative note, a large friable 3 cm wide × 4 cm long mass was noted in the anterior midline quadrant along the perianal skin. On digital rectal exam, the lesion did not extend into the anal canal. Additionally, there were no other palpable lesions noted on digital rectal exam. A biopsy of the area was taken. Biopsy results revealed a 3.2 cm sarcomatoid malignant neoplasm, most consistent with sarcomatoid squamous cell carcinoma (Figures 1 and 2). This lesion was staged as IIIA (cT2, cN0 vs. cN1, cM0) SCC of the anus (Figures 1 and 2). Immunohistochemistry stains were performed for further evaluation and demonstrated malignant spindle cells with patchy AE13, p40, and p63 expression lacking CK5/6 and K903 expression. Pretreatment testing demonstrated a positive urine pregnancy test and serum beta-HCG of 87.5 mIU/mL. The patient denied pregnancy and cited her menopausal status, which would make pregnancy unlikely. The ultrasound did not identify intrauterine pregnancy.

4 | CONCLUSION AND RESULTS

The immunohistochemistry from the biopsy was positive for beta-hCG (Figure 3). Given these results, the patient was treated with standard chemoradiation, receiving mitomycin/5FU with concurrent radiation. Beta-hCG was monitored via weekly urine pregnancy tests. The patient completed chemotherapy and radiation treatment in late August. Urine beta-hCG was negative. However, 6 weeks after completing treatment, testing of urine beta-hCG was found, once again, to be elevated. A positron emission tomography (PET) scan revealed a persistent hypermetabolic anal mass with SUV max of 17.6, not substantially changed, consistent with known anal cancer. Also, an unchanged mildly hypermetabolic left inguinal lymph node was also observed. There was no evidence of new or progressive disease. Given the persistent disease, robotic-assisted abdominoperineal resection with a colostomy was performed post-treatment. Imaging 7 months later demonstrated disease recurrence and progression. Subsequently, the patient started palliative pembrolizumab.

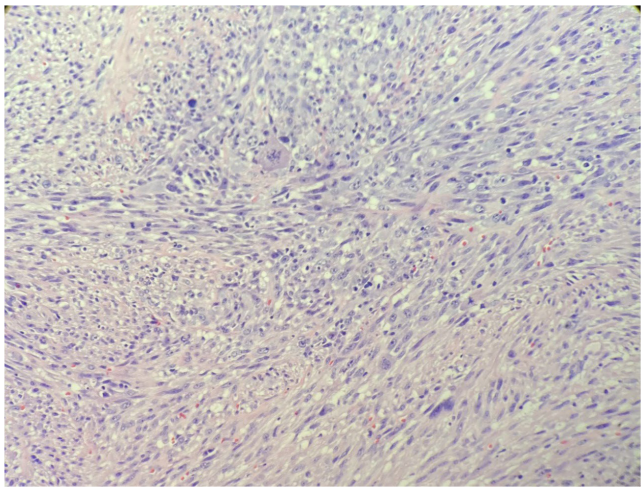

FIGURE 1 High-power micrograph showing fascicular growth pattern of malignant spindle cell sarcomatoid neoplasm with spindled nuclei, eosinophilic cytoplasm, scattered mitotic figures, and occasional marked pleomorphic nuclei.

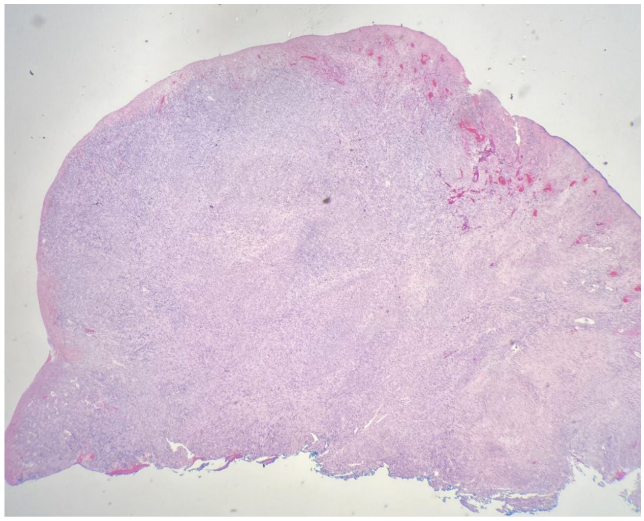

FIGURE 2 Low-power image of tumor.

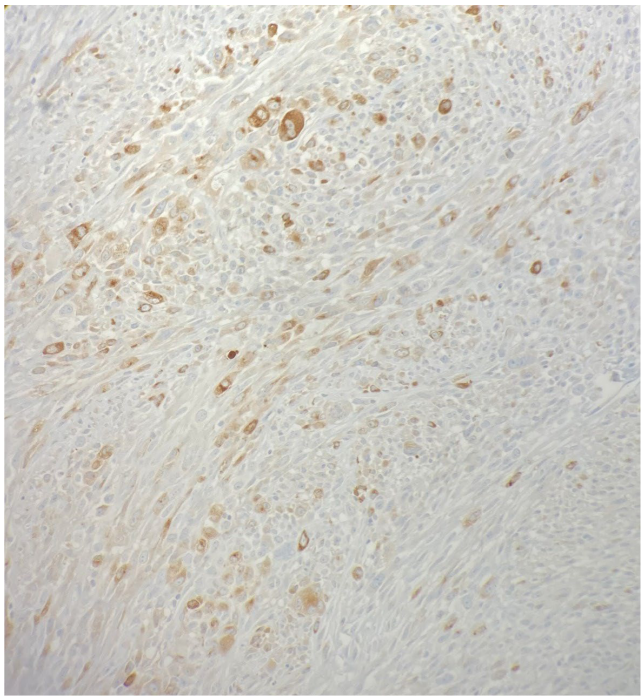

FIGURE 3 Beta-hCG stain demonstrating focal positivity in the neoplastic cells (cytoplasmic staining).

5 | DISCUSSION

The production of ectopic beta-hCG outside the usual placental location is concerning in several cancer types. This case report highlights the diagnostic challenges and potential clinical significance of this phenomenon. Previous research suggests that ectopic beta-hCG production may indicate a poor prognosis in breast cancer. However, the occurrence of ectopic beta-hCG production in the context of anal cancer is uncommon, with only two reported cases to date.[1,2,6] The absence of reported cases underscores the rarity of hormone-producing anal cancer and the need for more specialized diagnostic techniques to identify such tumors efficiently.

Currently, the diagnostic process for hormone-producing anal cancer can be challenging due to the rarity of the condition and the need for specialized testing.[6] Further research into new or improved diagnostic techniques, such as biomarker testing or imaging methods, may help to identify these tumors more accurately and efficiently. This research could lead to earlier diagnosis and treatment, potentially improving the prognosis for patients with hormone-producing anal cancer.

Additionally, research into hormone therapies targeting hormone-producing cells may offer these patients an effective treatment option.[8] Studies have shown that targeted therapies, such as aromatase inhibitors, have effectively treated hormone-producing breast and ovarian cancers.[9,10] Similar approaches may be effective in the treatment of hormone-producing anal cancer. Therefore, it is essential to explore these treatment options to improve outcomes for patients with this condition.

6 | CONCLUSION

In conclusion, hormone-producing anal cancer is a rare tumor that can be challenging to diagnose and may resist standard chemotherapy and radiation therapies. Therefore, coordinated multidisciplinary care is essential to optimize patient care and outcomes. This case lays the foundation for improving the care and prognosis for patients facing this unique challenge by highlighting the importance of considering the potential for hormone production in anal cancer.

AUTHOR CONTRIBUTIONS

Sierra Silverwood: Data curation; investigation; writing – original draft. **Peter Kohler:** Writing – review and editing. **Yelena Kier:** Conceptualization; investigation; supervision; writing – review and editing.

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None to declare.

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CONFLICT OF INTEREST STATEMENT

No conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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