

Ectopic Production of Beta-hCG in Anal Cancer: A Case Report

Sierra Silverwood¹, Peter Kohler², and Yelena Kier²

¹Michigan State University College of Human Medicine

²Munson Medical Center

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Sierra Silverwood¹, Peter Kohler, MD², and Yelena Kier, DO²

¹ Michigan State University College of Human Medicine, Traverse City, MI, USA

² Cowell Cancer Center, Munson Healthcare Foundation, Traverse City, MI, USA

Corresponding Author: Sierra Silverwood, silverwo@msu.edu

Consent Statement: 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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Case: 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 (+) beta-hCG urine testing.

Conclusion: 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 implication it may have on management.

Keywords: Anal Cancer, Ectopic Hormones, Multidisciplinary Care, Diagnostic Techniques

Introduction

Beta-human chorionic gonadotropin (beta-hCG) is 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 non-testicular teratomas.² Data from one study by Burcynska et al. (2013) examining beta-hCG in a mouse model suggest it may result in a diminished response to radiotherapy and expedited metastasis. Several other studies have also found ectopic production correlated with poorer prognosis.^{3,4} 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., a 43-year-old female presented with p-16 positive squamous cell anal cancer.⁵ 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.⁶ 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.

Case Presentation

In 2017, a 53-year-old female presented with a calcified mass in the left upper lobe of the lung, diagnosed as a carcinoid tumor. She underwent a video-assisted thoracoscopic surgery (VATS) upper lobectomy in 2018 with a final pathological staging of pT2aN0, stage II. Four years later, she was diagnosed with stage 1B HPV-negative squamous cell carcinoma of the left labia majora and underwent a left radical hemivulvectomy and sentinel lymph node biopsy.

The patient presented with a new anal lesion in June 2022. Biopsy revealed a poorly differentiated squamous cell cancer undifferentiated with sarcomatoid features (Images 1 and 2). This lesion was staged as IIIA (cT2, cN0 vs. cN1, cM0) SCC of the anus (Images 1 and 2). Pre-treatment testing demonstrated a positive urine pregnancy test and serum beta-HCG of 87.5 mIU/mL. The patient was postmenopausal by history and had a prior uterine ablation. The ultrasound did not identify intrauterine pregnancy. Given these results, the patient was treated with standard chemo-radiation.

The immunohistochemistry from the biopsy was positive for beta-hCG (Image 3). Beta-hCG was monitored via weekly urine pregnancy tests. The patient completed chemotherapy and radiation treatment in late August. Urine beta-hCG was negative. Six weeks after completing treatment, testing of urine beta-hCG was found, once again, to be elevated. A positron emission tomography (PET) scan in October 2022 revealed a persistent hypermetabolic mass with a maximum standardized uptake value (SUVmax) of 17.6 (not felt to be substantially changed from the previous scan). There was no evidence of metastatic disease. Given the persistent disease, robotic-assisted abdominoperineal resection with a colostomy was performed post-treatment. Imaging seven months later demonstrated disease recurrence and progression. Subsequently, the patient started palliative pembrolizumab.

Discussion

The production of ectopic beta-hCG outside the usual placental location is concerning in several cancer types.² Previous research suggests that ectopic beta-hCG production may indicate a poor prognosis in breast cancer.^{1,2} However, the occurrence of ectopic beta-hCG production in the context of anal cancer is rare, with only two reported cases to date.⁵

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.⁵ 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.¹³ Studies have shown that targeted therapies, such as aromatase inhibitors, have effectively treated hormone-producing breast and ovarian cancers.^{14,15} 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.

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. The case presented highlights the importance of considering the potential for hormone production in anal cancer and the need for specialized testing and management.

Disclosures

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References

1. Cole LA. Biological functions of hCG and hCG-related molecules. *Reproductive Biology and Endocrinology*. 2010;8. doi:10.1186/1477-7827-8-102
2. Beta-Human Chorionic Gonadotropin, Quantitative, Serum - Mayo Clinic Laboratories | Neurology Catalog. Accessed January 1, 2023. <https://neurology.testcatalog.org/show/BHCG>
3. Iles RK. Ectopic hCG β expression by epithelial cancer: Malignant behaviour, metastasis and inhibition of tumor cell apoptosis. *Mol Cell Endocrinol*. 2007;260-262. doi:10.1016/j.mce.2006.02.019
4. Inoue N, Watanabe H, Takehara H, Hamazaki M, Kagami S. Refractory pediatric nonrhabdomyosarcoma soft tissue sarcoma associated with ectopic production of beta hCG and hypercalcemia induced by PTHrP. *Pediatr Blood Cancer*. 2011;57(7). doi:10.1002/pbc.23271
5. Pokharel K, Gilbar PJ, Mansfield SK, Nair LM, So A. Elevated beta human chorionic gonadotropin in a non-pregnant female diagnosed with anal squamous cell carcinoma. *Journal of Oncology Pharmacy Practice*. 2020;26(5). doi:10.1177/1078155219893428
6. Das P, Crane CH, Eng C, Ajani JA. Prognostic factors for squamous cell cancer of the anal canal. *Gastrointest Cancer Res*. 2008;2(1).
7. Key Statistics for Anal Cancer. Accessed January 1, 2023. <https://www.cancer.org/cancer/anal-cancer/about/what-is-key-statistics.html>
8. Yao JN, Zhang XX, Zhou HN, et al. Human papillomavirus related anal squamous cell carcinoma survival: A systematic review and meta-analysis. *Transl Cancer Res*. 2017;6(3). doi:10.21037/tcr.2017.06.13
9. Types of anal cancer | Cancer Research UK. Accessed January 1, 2023. <https://www.cancerresearchuk.org/about-cancer/anal-cancer/stages-types/types>
10. Anal Cancer Screening for People at High Risk | OncoLink. Accessed January 1, 2023. <https://www.oncolink.org/risk-and-prevention/prevention-screening/anal-cancer-screening>
11. Anal Cancer Survival Rates. Accessed January 1, 2023. <https://www.cancer.org/cancer/anal-cancer/detection-diagnosis-staging/survival-rates.html>
12. Schüler-Toprak S, Treeck O, Ortmann O. Human chorionic gonadotropin and breast cancer. *Int J Mol Sci*. 2017;18(7). doi:10.3390/ijms18071587
13. Ferreira AR, di Meglio A, Pistilli B, et al. Differential impact of endocrine therapy and chemotherapy on quality of life of breast cancer survivors: a prospective patient-reported outcomes analysis. *Annals of Oncology*. 2019;30(11). doi:10.1093/annonc/mdz298
14. Chumsri S, Howes T, Bao T, Sabnis G, Brodie A. Aromatase, aromatase inhibitors, and breast cancer. *Journal of Steroid Biochemistry and Molecular Biology*. 2011;125(1-2). doi:10.1016/j.jsbmb.2011.02.001
15. Simpkins F, Garcia-Soto A, Slingerland J. New insights on the role of hormonal therapy in ovarian cancer. In: *Steroids*. Vol 78. ; 2013. doi:10.1016/j.steroids.2013.01.008
16. Taberna M, Gil Moncayo F, Jané-Salas E, et al. The Multidisciplinary Team (MDT) Approach and Quality of Care. *Front Oncol*. 2020;10. doi:10.3389/fonc.2020.00085

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