

Pathology of Anal Cancer



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KEYWORDS

- Anal cancer • Anal squamous intraepithelial neoplasia • Squamous cell carcinoma
- Human papilloma virus (HPV) • Molecular

KEY POINTS

- Anal cancer is an uncommon tumor, squamous cell carcinoma (SCC) being the most frequent histology corresponding to 80% of all cases.
- Human papilloma virus (HPV) infection plays a key role in anal cancer development, encoding at least three oncoproteins with stimulatory properties.
- SCC expresses CK5/6, CK 13/19, and p63. P16 is a surrogate marker for the presence of HPV genome in tumor cells.

INTRODUCTION

Anal cancer accounts for approximately 2.4% of gastrointestinal malignancies.¹ Although anal cancer is a rare tumor, its frequency is increasing, especially in high-risk groups.² Tumors in this location are generally classified as anal canal or anal margin.

Squamous cell carcinoma (SCC) is the predominant type of tumor and shares many features with cervical cancer. Oncogenic human papilloma virus (HPV) infection plays a major role in both tumors.³ HIV infection is associated with a higher frequency of HPV-associated premalignant lesions and invasive tumors.⁴

Normal Anatomy of the Anus

The anal canal is the terminal part of the large intestine and is slightly longer in male than in female patients. It measures approximately 4 cm and extends from the rectal ampulla (pelvic floor level) to the anal verge, which is defined as the outer opening of the gastrointestinal tract. The anal verge is at the level of the squamous-mucocutaneous junction with the perianal skin.^{5,6}

The authors have nothing to disclose.

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Surg Oncol Clin N Am 26 (2017) 57–71
<http://dx.doi.org/10.1016/j.soc.2016.07.013>

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The dentate line (also called pectinate) consists of the anal valves and bases of the anal columns. It represents the anatomic division of the rectum from the anal canal. The dentate line originates from the embryonic union of the ectoderm with the endoderm. The anal canal epithelium can be divided into three zones (Fig. 1). The upper part consists of colorectal mucosal type, followed by an anal transition zone (ATZ) that is composed of specialized epithelium that starts at the dentate line and extends from 0.5-1 cm. Finally, the distal anal canal consists of squamous epithelium, which may be partially keratinized.^{5,6} The anatomic distribution is clinically significant because it is related to lymphatic drainage and different types of precursor epithelium.

The tumor can be accessed for biopsy using anoscopy, rectoscopy, or direct examination of anal and perineal exophytic lesions.

Histology Classification

Tumors of the anal canal were classified by the World Health Organization (WHO) in three main groups: epithelial, mesenchymal, and secondary tumors. Epithelial tumors were subdivided into malignant and premalignant lesions (Box 1).⁵

Human Papilloma Virus Infection

Evidence indicates an association between oncogenic HPV infection with premalignant and malignant lesions of the genital tract, including the anus.⁷ The presence of HPV in anal cancer is variable and may be influenced by the methodology used for virus identification and by population characteristics. The HPV infection can be detected in tumor tissue using different techniques, including in situ hybridization (Fig. 2) and polymerase chain reaction (PCR).

Currently, 88% of anal SCC tumor samples are usually HPV positive, with different rates according to geographic location.⁸ HPV16 infection is the most common, present in 86% of cases. In some cases, coinfection was found with multiple HPV types.⁹

HPV is a nonenveloped virus with double-stranded DNA in circular form, containing a genome of around 8000 base pairs.⁷ HPV can remain housed in the nuclei of basal epithelial cells for decades after initial infection of the mucosa, which usually occurs through sexual contact.¹⁰ There are more than 240 types described and the alpha human papillomavirus is usually related to mucosal infection.¹¹ The high-risk HPV genotypes (16 and 18) encode at least 3 oncoproteins with stimulatory properties: E5, E6,

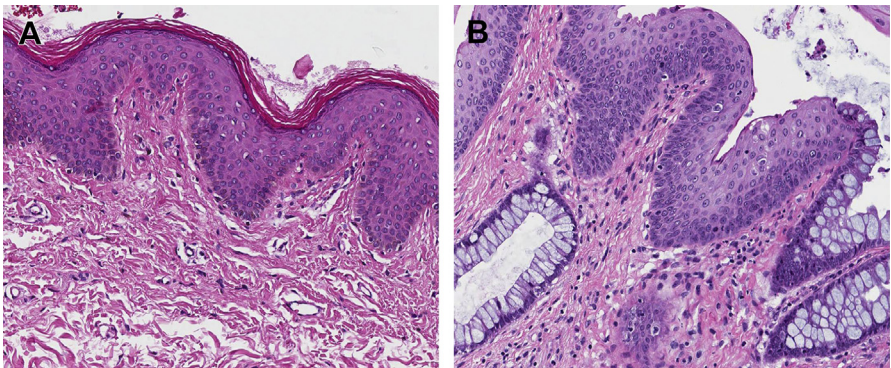


Fig. 1. Normal epithelium. (A) Squamous epithelium. (B) Anal transition zone epithelium showing in the left cuboidal or polygonal surface cells. In the right can be viewed colonic mucosa with an underlying crypt.

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