

The Versicolour Gyre-Squamous Cell Carcinoma-Anal Canal: A Mini Review

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ABSTRACT

Squamous Cell Carcinoma (SCC) of anal canal is a frequently discerned malignant neoplasm confined to the anal tract. Thus denominated by World Health Organization (WHO), the neoplasm exemplifies primary squamous cell carcinoma of anus. Basaloid variant of squamous cell carcinoma is additionally designated as cloacogenic or transitional cell carcinoma of anal canal. Besides, mucoepidermoid carcinoma of anal canal denominates neoplasms delineating prominent features of mucinous transition.

Keywords

Squamous Cell Carcinoma (SCC), Anal canal, Cancer cells, Tumour

Introduction

Squamous cell carcinoma of anal canal is a frequently discerned malignant neoplasm confined to the anal tract. Thus denominated by World Health Organization (WHO), the neoplasm exemplifies primary squamous cell carcinoma of anus.

Basaloid variant of squamous cell carcinoma is additionally designated as cloacogenic or transitional cell carcinoma of anal canal. Besides, mucoepidermoid carcinoma of anal canal denominates neoplasms delineating prominent features of mucinous transition.

Squamous cell carcinoma of anal canal arising superior to dentate line are generally discerned within sixth decade and depict a female preponderance. Squamous cell carcinoma of anal canal subjacent to dentate line are commonly exemplified within third decade and demonstrate a male predominance [1,2].

Squamous cell carcinoma of anal canal emerging subjacent to dentate line is commonly associated with definitive conditions as a condyloma, anal fistula or exposure to radiation. The neoplasm may be engendered on account of exposure to high risk subtypes of Human Papilloma Virus (HPV) as 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 or 68. Frequently, tumefaction exhibits overexpression of Epidermal Growth Factor Receptor (EGFR) [2,3].

Squamous cell carcinoma of anal canal may represent with cogent clinical symptoms as rectal bleeding, pain or mass within anal region.

Upon gross examination, squamous cell carcinoma of anal canal manifests as a nodular, ulcerated neoplasm with magnitude varying from ≥ 3 centimetres to 4 centimetres. Tumefaction is associated with deep seated infiltration into anal canal wall with proximal and distal tumour extension into submucosa of distal rectum and proximal anus [3,4].

Grading of squamous cell carcinoma is contingent to actors such as nuclear pleomorphism, nucleolar magnitude, mitotic activity and tumour associated necrosis. Squamous cell carcinoma is

graded as:

- Well differentiated tumour comprised of squamous cell nests of variable outline and magnitude. Enlarged squamous cells appear incorporated with abundant eosinophilic cytoplasm and well configured intercellular bridges. Abundant keratin pearls and occasional mitotic figures with focal necrosis is encountered.
- Moderately differentiated tumour constituted of spherical to irregular nests, cords and sheets of squamous cells of variable magnitude. Enlarged to intermediate, uniform squamous cells demonstrate indistinct cellular margins. Focal keratinization and mitotic figures may be identified.
- Poorly differentiated tumour is composed of miniature nests, cords and sheets or singularly dispersed squamous epithelial cells. Miniature squamous cells pervaded with scant cytoplasm, hyperchromatic nuclei and active mitoses are encountered. Focal keratinization is absent or exceptional. Tumour grading is non concordant to prognostic outcomes. Upon microscopy, squamous cell carcinoma of anal canal simulates squamous cell carcinoma encountered within diverse body sites [3,4].

Squamous cell carcinoma of anal canal exemplifies cogent morphologic variants denominated as:

- Keratinizing variant comprised of neoplastic squamous cells incorporated with enlarged, hyperchromatic nuclei, coarse nuclear chromatin and inconspicuous nucleoli. Keratin pearls, abundant keratohyaline granules and intercellular bridges are frequently discerned. Generally, keratinizing squamous cell carcinoma appears beneath the dentate line.
- Non keratinizing variant is constituted of polygonal squamous epithelial cells with intercellular bridges configuring sheets or nests. Keratin pearls appear absent. Neoplastic squamous cells are pervaded with enlarged nuclei, irregular, coarse, granular nuclear chromatin and singular or multiple nucleoli. Mitotic activity is significant. Commonly, non keratinizing squamous cell carcinoma emerges superior to the dentate line.
- Basaloid variant of squamous cell carcinoma enunciates well defined nests of immature basaloid cells permeated with scanty cytoplasm and peripheral palisading of pleomorphic, hyperchromatic nuclei. Mitotic activity

is significant. Geographic or comedo-like necrosis is encountered. Focal keratinization is delineated although keratin pearls are absent [3,4].

Basaloid subtype demonstrates a plexiform pattern of tumour configuration with palisading of miniature undifferentiated cells circumscribing tumour cell nests or nodules with foci of centric necrosis. Mitotic figures are frequent. Encompassing stroma appears desmoplastic. Tumour invasion into circumscribing soft tissue is commonly discerned. The variant enunciates an aggressive biological behaviour. Nodules of neoplastic squamous epithelial cells may exemplify significant infiltration of eosinophils, foci of mucoepidermoid carcinoma with configuration of mucinous micro-cysts or appear as a poorly differentiated tumefaction [3,4]. Squamous cell carcinoma of

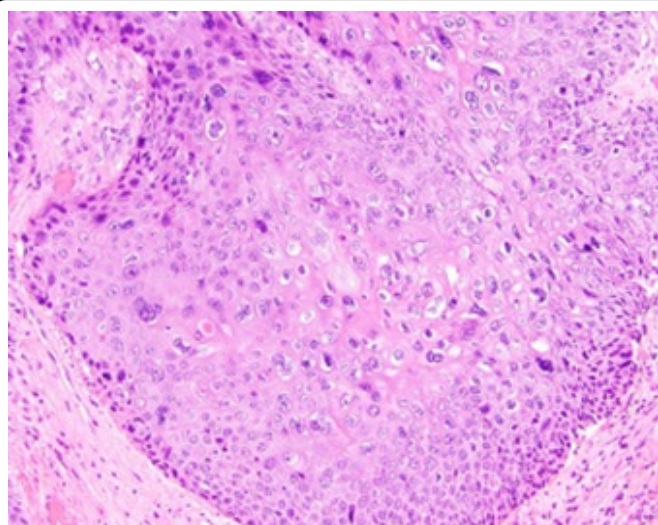


Figure 1: Squamous cell carcinoma of anal canal demonstrating enlarged squamous cells with abundant eosinophilic cytoplasm, coarse nuclear chromatin and prominent nucleoli. Intercellular bridges and mitotic figures are discernible. Keratin pearls are absent [7].

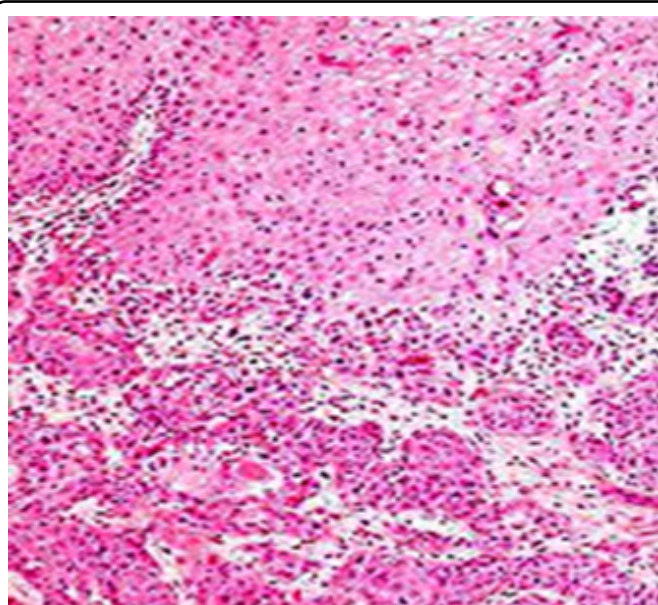


Figure 2: Squamous cell carcinoma of anal canal delineating enlarged squamous cells imbued with abundant eosinophilic cytoplasm, vesicular nuclei with conspicuous nucleoli and intercellular bridges. Focal necrosis and reactive inflammatory infiltrate within circumscribing desmoplastic stroma is encountered [8].

anal canal may enunciate 'small cell' morphology with definitive features of anaplasia. However, foci of neuroendocrine differentiation are absent. Frequently, foci of squamous cell carcinoma of anal canal replace crypts confined within adjacent rectal mucosa. The neoplasm may delineate dysplastic alterations within superimposed or adjacent stratified squamous epithelium, thereby articulating anal intraepithelial neoplasia [3,4].

TNM classification of squamous cell carcinoma of anal canal is designated as:

Primary tumour

- TX: Primary tumour cannot be assessed
- T0: Absence of primary tumour
- Tis: Carcinoma in situ as encountered with Bowen's disease, High-Grade Squamous Intraepithelial Lesion (HSIL) or anal intraepithelial neoplasia II or III (AIN II, AIN III)
- T1: Tumour is <2 centimetres
- T2: Tumour is between 2 centimetres and 5 centimetres
- T3: Tumour is >5 centimetres
- T4: Tumour of variable magnitude infiltrates adjacent organs as urethra, urinary bladder or vagina

Direct tumour invasion of rectal wall, perirectal cutaneous surface, subcutaneous tissue or sphincter muscles does not classify as T4. Tumour magnitude may be evaluated upon diverse planes wherein longest tumour diameter requires assessment.

Regional lymph nodes

- NX: Regional lymph nodes cannot be assessed
- N0: Regional lymph node metastasis absent
- N1: Regional lymph node metastasis into inguinal, perirectal, internal iliac or external iliac lymph nodes categorized as
- ~N1a: Regional lymph node metastasis into inguinal, meso-rectal, perirectal or internal iliac lymph nodes upon ipsilateral tumour site
- ~N1b: Regional lymph node metastasis into external iliac lymph nodes
- ~N1c: Regional lymph node metastasis into inguinal, meso-rectal, perirectal or internal iliac lymph nodes and into external iliac lymph nodes

Distant Metastasis

- MX: Distant metastasis cannot be assessed
- M0: Distant metastasis absent
- M1: Distant metastasis present [3,4]
- Squamous cell carcinoma of anal canal is graded as
- GX: Tumour grade cannot be assessed
- G1: Tumour is well differentiated and tumour cells simulate normal squamous epithelial cells
- G2: Tumour is moderately differentiated
- G3: Tumour is poorly differentiated and tumour cells do not simulate normal squamous epithelial cells
- G4: Tumour is undifferentiated and tumour cells barely simulate normal squamous epithelial cells [4,5]

Staging of squamous cell carcinoma of anal canal is designated as

- Stage 0: Carcinoma *in situ* (Tis, N0, M0)
- Stage 1: Tumour is <2 centimetre with absent regional lymph node or distant metastasis (T1, N0, M0)
- Stage II: Tumour is >2 centimetres with absent regional lymph node or distant metastasis (T2 or T3, N0, M0)
- Stage IIIA: Tumour of variable magnitude with regional lymph node metastasis or dissemination into adjacent pelvic organs as urethra, urinary bladder or vagina (T1 or T2, N1, M0) or (T4, N0, M0)
- Stage IIIB: Tumour infiltration into adjacent organs with regional or perirectal lymph node metastasis and absent distant metastasis OR tumour of variable magnitude with regional or distant lymph node metastasis with absence of distant metastasis (T4, N1, M0) or (any T, N2 or N3, M0) [4,5]
- Stage IV: Tumour of variable magnitude with regional lymph node and distant metastasis (any T, any N, M1).
- Recurrent carcinoma: squamous cell carcinoma which reappears following therapy and necessitates additional evaluation in order to assess extent of tumour recurrence [4,5]

Discussion and Conclusion

Squamous cell carcinoma of the anal canal requires segregation from neoplasms such as basal cell carcinoma, small cell carcinoma, verrucous carcinoma or conditions such as anal fissure, anal fistula, haemorrhoids, psoriasis or condylomata acuminatum. Squamous cell carcinoma of anal canal can be appropriately treated with cogent surgical eradication of neoplasm followed by adjuvant chemotherapy and radiation therapy [5,6].

Prognostic outcomes of squamous cell carcinoma of anal canal are contingent to tumour stage as assessed with American Joint

Committee of Cancer (AJCC) guidelines.

Neoplasms situated upon distal sites appear amenable to preliminary detection, demonstrate gradual tumour progression and superior prognostic outcomes. Prognosis is favourable in neoplasms treated with enhanced dose of radiation therapy administered continually or with minimal interruptions. Prognosis is unfavourable in neoplasms incriminating elderly male subjects or individuals infected with Human Immunodeficiency Virus (HIV) [5,6].

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7. Image 1 Courtesy: Pathology outlines
8. Image 2 Courtesy: Oncoclex.com