

HPV-Associated Cancers: Histopathology Insight

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Introduction

Human papillomavirus (HPV) is a well-established oncogenic driver, contributing to a significant proportion of cervical, oropharyngeal, and anogenital cancers. Histopathological examination remains crucial for understanding the progression, morphological features, and molecular alterations in HPV-associated malignancies. This poster highlights key histological characteristics, diagnostic markers, and tissue-based biomarkers that enhance our comprehension of HPV-driven carcinogenesis. By integrating microscopic findings with clinical correlations, we aim to provide valuable insights for improved diagnosis and therapeutic strategies.

Epidemiology of HPV Associated Cancer

HPV causes ~5% of all UK cancers (~3,200 cases yearly). Although the HPV vaccine has been given in schools since 2008 to girls and in 2019 to boys, leading to big drops in HPV infections and fall in the rate of cervical cancer.

Throat cancer on the other hand is rising especially in men. Throat cancer has doubled since 1990s and it is becoming more common than cervical cancer in the UK. (BJC, 2023). HPV now accounts for 51% of oropharyngeal SCC in the UK, of these 85-96% are caused HPV-16 infection (Lechner et al 2022).

Methods

Cervical and oropharyngeal tissue analysis on samples 2025, H&E staining, P16 HPV genotype.

UK HPV Cancer Cases (Annual Estimates)

Cancer Type	Cases Caused by HPV (Yearly)	Percentage Linked to HPV
Oropharyngeal (Throat)	~2,500 (mostly men)	~75%
Cervical	~850	~9%
Anal	~1,300	~99%
Vaginal	~300	~50%
Vulvar	~100	~75%
Penile	~100	~50%

Histological Features of HPV Associated Cancer

Types	Characteristics
Cervical Cancer	Squamous Cell Carcinoma (SCC) <ul style="list-style-type: none"> Koilocytosis Dysplastic changes (CIN 1-3)
	Adenocarcinoma HPV-related (Mucinous, Endocervical Type) <ul style="list-style-type: none"> Glandular structures with nuclear atypia Stratified, elongated nuclei ("picket fence" appearance) Mitotic figures and apoptotic bodies May show intracytoplasmic mucin
Oropharyngeal Squamous Cell Carcinoma	<ul style="list-style-type: none"> Non-keratinising or basaloid morphology Sheets or nests of immature basaloid cells High nuclear-to-cytoplasmic ratio Focal keratinisation (less common than in smoking-related SCC) Strong p16 Immunostaining
Anal Squamous Cell Carcinoma	Like cervical SCC <ul style="list-style-type: none"> Koilocytosis in precursor lesions (AIN - Anal Intraepithelial Neoplasia) Invasive SCC with variable keratinisation
Penile, Vulvar, and Vaginal Cancers	<ul style="list-style-type: none"> Basaloid or warty features Koilocytosis in adjacent epithelium

Immunohistochemical (IHC) Features

p16 Overexpression, hence it is a reliable surrogate marker in oropharyngeal and cervical cancers. HPV genotype.

Diagnostic Insight from Search

Koilocytosis: nuclear enlargement and chromatin clearing in cervical samples p16 shows a diffused cytoplasmic / nuclear staining and this correlates with HPV integration.

Morphological Features of Oropharyngeal Cancers

- Tumour location for oropharyngeal cancer be in various parts of the oropharynx, including the base of the tongue, tonsils, soft palate, and the walls of the pharynx (Lechner et al 2022).

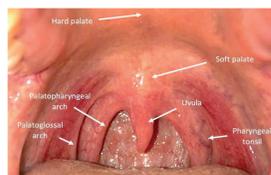


Figure 1. Shows various structures in the Oropharynx. Image adopted from Simple OSCE

- HPV-positive oropharyngeal cancers tend to have distinct morphological features compared to HPV-negative ones. HPV-positive cancers often have a basaloid appearance, with cells showing less keratinisation and more uniform nuclei.

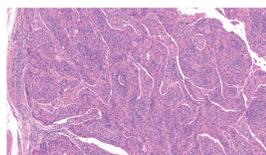


Figure 2. Digital image of left tongue base resection T2 GTS/tongue base SCC. H&E, X40. Source HSL Histopathology lab

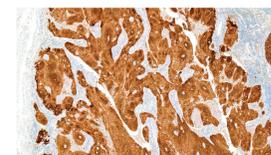


Figure 3. Digital image of left tongue base resection T2 GTS/tongue base SCC. p16, X40. Source HSL Histopathology lab

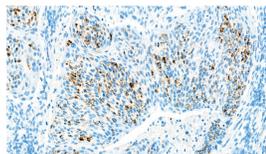


Figure 4. Digital image left tongue base resection T2 GTS/tongue base SCC. nuclear positive HPV 16 /18 X40. Source HSL Histopathology lab

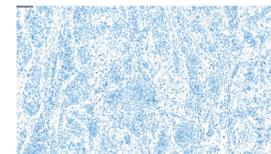


Figure 5. Digital image left tongue base resection T2 GTS/tongue base SCC. Negative HPV 6 / 11 X40. Source HSL Histopathology lab

Non HPV associated SCC morphology for comparison:

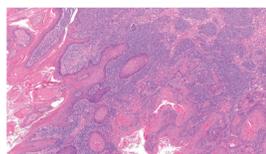


Figure 6. Digital image Left maxilla with bone SCC. H&E, X40. Source HSL Histopathology lab



Figure 6. Digital image left maxilla with bone SCC. Negative p16. X40 Source HSL Histopathology lab

Morphological Features of Cervical HPV



Figure 8. Shows the structures in the cervix. Image adopted from Cleveland Clinic's Health Library, 2025

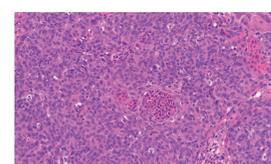


Figure 9. Digital image of LLETZ. Invasive characteristic features of HPV epithelial. Source HSL Histopathology lab

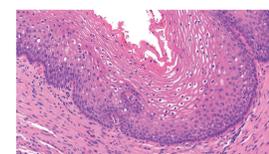


Figure 10. Digital image of LLETZ. CIN3 Characteristic features of severe dysplasia. Source HSL Histopathology lab

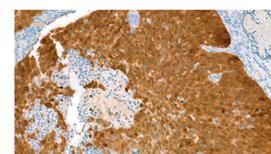


Figure 11. Digital image of LLETZ. P16, High nuclear-to-cytoplasmic ratio. Source HSL Histopathology lab

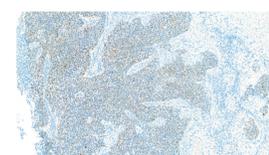


Figure 12. Digital image of LLETZ. nuclear positive HPV 16/18 X40. Source HSL Histopathology lab

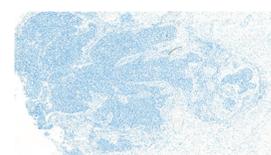


Figure 13. Digital image of LLETZ. Negative HPV 6/11 X40. Source HSL Histopathology lab

Discussion

HPV infection has been well established as a cause of cervical, oropharyngeal, anal and genital tract cancers (Lerman et al 2017). However more recently, it has been established that HPV-16 is the most common high-risk type identified in oropharyngeal cancers. HPV-16 has been identified in over 90% of oropharyngeal SCC and 50% of Cervical SCC. HPV18, 33, and 52 are less frequently identified oropharyngeal SCC.

HPV-Positive SCCs morphology are predominantly non-keratinising or basaloid patterns, characterised by sheets of immature basaloid cells with high nuclear to cytoplasmic ratios, minimal keratinisation, and frequent lymphoid stroma infiltration. Hybrid variants may show abrupt keratinisation or comedo-type necrosis within non-maturing tumour islands.

HPV- Negative SCCs morphology is typically keratinising, with well differentiated squamous pearls, intercellular bridges, and stromal desmoplasia. Variants include verrucous, spindle cell, and adeno-squamous subtypes. Histopathological evaluation remains pivotal in distinguishing HPV-driven SCCs, which demand tailored therapeutic approaches. Understanding these differences enhances prognostic accuracy of oropharyngeal and laryngeal cancers.

Conclusion

Histology remains pivotal in diagnosing HPV - associated cancers. P16 block staining and non-keratinising morphology are key indicators.

References

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6. British journal of cancer (2023): Trends in HPV related cancers

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