

Interobserver Differences In Diagnosis Of Anal Cytological Samples With HPV Infection In Men Who Have Sex With Men and Transgender Women.

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Introduction

Anorectal cytology has been increasingly used as a screening method for early anal squamous lesions detection. In men who have sex with men (MSM) and transgender women (TGW) anal cancer is particularly high, with an additional increase among those infected with Human Immunodeficiency Virus (HIV) and HPV co-infections. There is no agreement in the diagnostic criteria of anal cytopathologies. The objective of this study was to compare interobserver diagnostic differences and similarities of anal samples with HPV infections confirmed by molecular techniques.

Methods

From a previous study on anal cytology in MSM and TGW populations. We analysed fifteen cases in which the results were obtained from a senior pathologist. All samples were consistent with HPV-related modifications. Four residents of pathology, who did not know the final diagnosis, independently evaluated these samples. To assess the interobserver variability in identifying intraepithelial lesions and the presence of HPV infection and other viruses (including herpes virus). Together with those samples an available anal biopsy results with immunohistochemistry and clinical information of an HIV positive patient who had an intraepithelial HPV anal modification anal was included for evaluation. For each of these 15 samples each resident analysed whether this cytological sample showed morphological signs of infection with HPV, and to make specific recommendations for follow-up analysis, and if it is required HPV molecular tests. Data was analysed using STATA 12.0 to measure variability with a Venn diagram and Kappa.

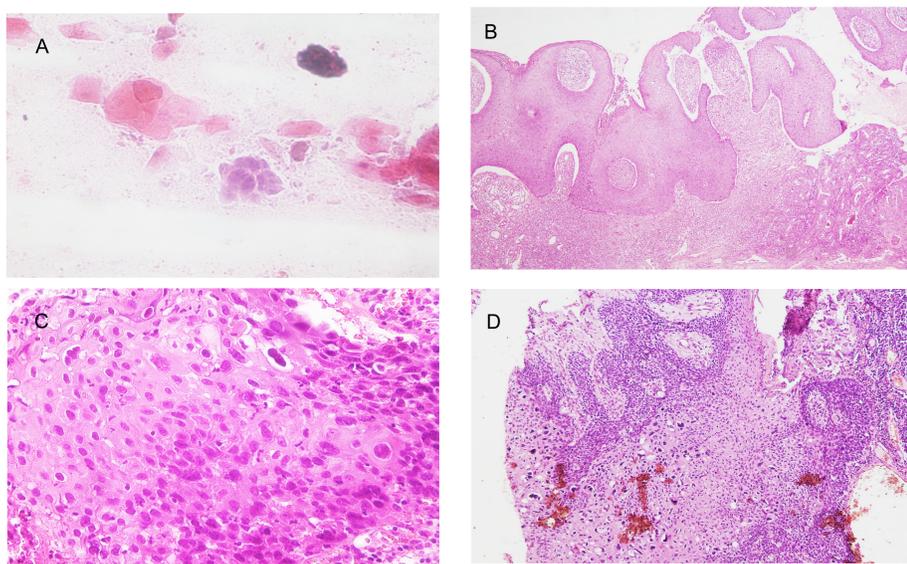


FIGURE 1. (A) 10X, traditional cytology, limited sampling, hyperchromatic nuclei, and cytoplasmic/nuclei anomalies; (B) 4X, Biopsy, Condilomatous lesion, necrosis; (C) 10X, Epithelial atypia, atypical mitosis and stromal infiltrates; (D) Stromal invasion within lesion's atypical cells

Kappa for diagnosis of premalignant lesions.			
	Kappa	P	Matching power
All observer	0.4185	0.0000	Moderate
Observer 1 and 2	0.5482	0.0000	Moderate
Observer 3 and 4	0.3296	0.0021	Moderate
Observer 1 and 3	0.4828	0.0000	Weak
Observer 1 and 4	0.3258	0.0025	Weak
Observer 2 and 3	0.5427	0.0000	Moderate
Observer 2 and 4	0.3824	0.0017	Weak

Table 1. Kappa for diagnosis of HPV-induced premalignant lesions.

Results

Four observers evaluated a total of 15 cases. Of these four cases were found to be unsatisfactory for evaluation and discarded for interim analysis. The assessment of the quality of the samples presented an 86.67% agreement between all observers' kappa value of 0.7458 (p 0.0001). Correlation analysis between observers was 71% for observers 1 and 2 while 3 and 4 was only 53%. The interobserver variability in the diagnosis of the samples was measured by Kappa (Table 1).

Assessment of interobserver variability for presence of morphological changes suggestive of HPV infection is summarized on Table 2.

Kappa for detection of HPV infection			
	Kappa	P	Matching power
All observer	0.2007	0.0040	Weak
Observer 1 and 2	0.7000	0.0000	Good
Observer 3 and 4	0.1304	0.1024	Weak

Table 2. Kappa for detection of HPV infections

Observation of a biopsied anal sample in an HIV (+) individual was consistent with an interpretation as a high-grade lesion and recommended for biopsy analysis in all interobserver. The biopsy of this lesion reported squamous cell carcinoma in the posterior layer of a giant condyloma, and positivity for cytokeratin AE1 / AE2, CK7 and P63.

Conclusions

Evaluation of anorectal cytology specimens' characteristics varies within interobservers from a good identification of quality of samples. Site of diagnosis sampling has a weak overall agreement for all observers, while it is better (moderate) (k 0.5482) between observers 1 and 2, which are older residents (2nd and 3rd years respectively). Detection of HPV induced modifications by interobserver agreement is weak, while among the residents with more years is good (kappa 0.70 vs 0.20), which supports the hypothesis that experience improves the agreement.

Agreement for the detection of high-grade lesions is very good, although only one case was available in this category. It is required an standardised manual for morphological anal modifications to better instruct pathologists in recognition of HPV-induced anomalies, this will reduce the amount of false negative reports in early screening of anal malignancies

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