0282 - HPV GENOTYPING IN 1,088 ANAL HSIL CASES: EXPECTED AND UNEXPECTED RESULTS

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INTRODUCTION

- High-grade squamous intraepithelial lesions (HSILs), the anal cancer precursors, are generally caused by oncogenic, high-risk Human Papillomavirus (hrHPV).
- HPV16-induced HSILs in particular have greater oncogenic potential than those induced by other types.
- HSILs with negative hrHPV co-testing are an unexpected finding and represent a clinical challenge.

OBJECTIVE

- To compare clinicopathological characteristics of anal HSIL patients harboring various hrHPV types.
- To identify causes of hrHPV-negative HSILs.

METHODS

- Anal swabs for anal cytology and hrHPV testing as well as high-resolution anoscopy-guided tissue biopsies were performed concurrently.
- Total of 1,088 swabs were collected from 742 individual patients with anal HSIL.
- Swabs were tested for hrHPV using the Cobas® 4800 HPV assay.
- Cobas® 4800 HPV assay (Roche) detects HPV16, 18, and gives pooled results for 12 additional hrHPV types: 31/33/35/39/45/51/52/56/58/59/66/68.
- For Cobas®-negative swabs, HSIL biopsy tissue was genotyped using real-time PCR.

RESULTS

Table 1. HrHPV DNA detected in anal swabs collected from HSIL patients by HIV status and gender

hrHPV DNA	Total (n=1,088)	HIV+ Men (n=966)	HIV- Men (n=40)	HIV+ Women (n=78)	HIV- Women (n=4)	*p*
Positive	1,045 (96%)	931 (96%)	36 (90%)	74 (95%)	4 (100%)	
HPV16*	476 (44%)	421 (44%)	16 (40%)	36 (46%)	3 (75%)	0.65
Non-16**	569 (52%)	510 (52%)	20 (50%)	38 (49%)	1 (25%)	
Negative	43 (4%)	35 (4%)	4 (10%)	4 (5%)	-	0.18

* HPV16 with or without HPV18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68
** HPV18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68

RESULTS

Table 2. Comparing clinicopathological characteristics of anal HSIL patients infected with HPV16, non-16 hrHPV, or negative for hrHPV

Characteristics \ hrHPV Types		HPV16 (n=321)	Non-16 hrHPV (n=378)	Negative (n=43)	P
Age (mean, range) in years		46 (21-76)	45 (20-75)	46 (23-72)	0.6
Gender	Male	292 (91)	347 (92)	39 (91)	0.4
	Female	29 (9)	31 (8)	4 (9)	
Race/Ethnicity	Total #	309	362	43	0.7
	Caucasian	120 (39)	137 (39)	15 (35)	
	African American	76 (24)	79 (21)	7 (16)	
	Hispanic	82 (27)	100 (28)	14 (33)	
	Other	31 (10)	46 (12)	7 (16)	
Anorectal Cytology	Unsatisfactory	13 (4)	21 (6)	5 (12)	<0.001
	Negative	28 (9)	58 (15)	7 (16)	
	ASCUS	98 (30)	147 (39)	21 (49)	
	LSIL	134 (42)	121 (32)	6 (14)	
	HSIL, ASC-H	48 (15)	31 (8)	4 (9)	
Number of HSIL	1 or 2	230 (72)	311 (82)	41 (95)	<0.001
	3 - 6	91(28)	67 (18)	2 (5)	
Smoking History	Total #	318	377	43	0.07
	Current	91 (29)	87 (23)	9 (21)	
	Former	81 (25)	90 (24)	12 (28)	
	Never	146 (46)	200 (53)	22 (51)	
HIV status	Total #	321	372	43	0.3
	Positive	303 (94)	353 (95)	39 (91)	
	Negative	18 (6)	19 (5)	4 (9)	
CD4+ T-cell, Cells/mm^3	Total #	291	347	38	0.6
	< 500	93 (32)	132 (38)	13 (34)	
	≥ 500	198 (68)	215 (62)	25 (66)	
HIV Viral Load, Copies/mL	Total #	300	353	39	0.1
	< 100	259 (86)	317 (90)	35 (90)	
	≥ 100	41 (14)	36 (10)	4 (10)	
History of Condylomata	Yes	169 (52)	182 (48)		0.09
	No	152 (47)	196 (52)		

Table 3. Tissue HPV genotyping of patients with Cobas® hrHPV-negative swabs (n=43)

HPV Types	Number of lesions
Negative	13
Low-risk HPV 6	2
High-risk HPV	13
16	3
18	2
45	2
31, 33, 35, 51, 52, 58, 59	6
Possibly carcinogenic HPV	15
53	2
67	6
69	1
73	3
82	3

HPV genotyping of Cobas®-negative HSILs revealed negative results (n=13), HPV6 (n=2), hrHPV (n=13), and possibly carcinogenic (IARC category 2B) types (n=15, HPV53, 67, 69, 73, 82).

CONCLUSIONS

- HPV16-positivity was associated with a greater number of concurrent HSILs presumably explaining the improved performance of anal cytology in these patients.
- A significant portion of “hrHPV-negative” HSILs are associated with “non-high-risk” HPV types that are not included in routine screening assays.

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Funding: NCI (K07CA180782)