

MEETING ABSTRACTS

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HPV genotype and EGFR activation in conjunctival carcinoma among HIV patients in East Africa

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Purpose

There is a substantial growth in the number of HIV patients with conjunctival squamous cell carcinoma in East Africa. However, the etiologic mechanism is unclear and therapeutic options are very limited. We hypothesized that this unique AIDS-associated malignancy would harbor human papillomavirus and involve activation of the EGFR signaling pathway. Positive findings would identify etiologic causes and provide clinical guidance to improve treatment.

Experimental design

Expression of p-MAPK/MAPK, p-Akt/Akt, and p-EGFR/EGFR in cell nucleus and cytoplasm of 38 FFPE specimens was assessed by immunohistochemistry; HPV genotype was detected by qPCR; EGFR mutation was assessed by DNA sequencing; and EGFR mRNA expression was measured using relative qPCR. Statistical analyses included two-sided Fisher exact test or chi-square test, Spearman correlation coefficient, and ANOVA.

Results

HPV 18 was found in 23 of 38 (61%) samples, with HPV 16 double-genotype in 6 patients. Immunohistochemistry and qPCR data suggest that activation and expression of the EGFR signaling pathway are related to disease progression of conjunctival cancer. The associations of cytoplasmic p-MAPK and cytoplasmic p-Akt

with tumor invasiveness were significant ($p = 0.05$ and 0.028 , respectively). Nuclear p-EGFR appeared only in invasive tumors. A significant positive association between EGFR expression and disease invasiveness was observed ($p=0.01$). A SNP in 10 patients and one missense mutation were found within EGFR tyrosine kinase domain. Statistical analysis indicates that patients with measurable EGFR expression more likely harbor EGFR mutations, compared to those with negative EGFR expression (35.3% vs. 0%).

Conclusions

Our data indicate a relationship between HPV infection and EGFR signaling in patients with AIDS-associated squamous cell carcinoma of the conjunctiva. HPV infection and EGFR activation/alteration may contribute to and sustain the high prevalence of the cancer in East Africa. Our findings support clinical trials that involve HPV vaccination, with application of therapeutic agents that target the EGFR pathway. These clinical strategies may reduce the incidence of conjunctival carcinoma among HIV patients in equatorial Africa.

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