Characterization of HPV-induced vaginal and vulvar carcinoma

av

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Abstract

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Vaginal and vulvar carcinomas are rare gynaecological malignancies, partly caused by the human papilloma virus (HPV). HPV-16 is the most frequent genotype found and HPV as a prognostic factor for these women has not been fully investigated. A persistent HPV-infection may lead to cancer development and viral attributes such as load, integration and methylation of the E2-binding sites (E2BS) in the viral control region may affect the viral oncogene expression.

The aim of this thesis was to evaluate the HPV-prevalence in two cohorts of vaginal and vulvar carcinomas and to elude the impact of HPV on prognosis. Also, the different variants of HPV-16, HPV-16 viral load, integration and E2BS3 and 4 methylation were investigated. In addition, four different genotyping assays for use in formalin fixed paraffin embedded (FFPE) material was compared in paper IV.

The results from this thesis show that vaginal and vulvar carcinomas constitute two biologically different carcinomas in terms of HPV-prevalence, prognostic impact of HPV and HPV-16 viral characteristics. HPV-prevalence was higher in the vaginal series compared to the vulvar series and HPV was a prognostic factor in the vaginal series where prognosis also depended on actual genotype. Clinical impact of the HPV-16 parameters such as variant, viral load and methylation of E2BS3 and 4 could only be found in the vulvar series. Results from paper IV show that all tested assays were compatible with FFPE and when using broader assays, additional genotypes were found. This may secure a more conclusive genotyping for screening and follow-up diagnostics in the post vaccination era.

Keywords: vaginal carcinoma, vulvar carcinoma, HPV, integration, methylation, genotyping.

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