Liquid biopsy analysis of the serum exosomal micro-rna signature in vulvar carcinoma may benefit the diagnosis, prognosis of survival and predict hpv-positivity

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Abstract

Background & Objectives

Vulvar carcinoma is a rare gynaecological disease, mainly affecting postmenopausal women. Increasing incidence in younger women is mostly driven by persistent HPV infection. There are no diagnostic biomarkers.

Recently, circulating exosomal Micro-RNAs (miRNA) emerged as promising liquid biopsy tool for none-invasive cancer diagnosis, since different tumour entities present unique expression profiles.

Methods

The purpose of this study was to identify a panel of plasma-derived exosomal miRNAs as specific biomarkers for vulvar carcinoma.

Five plasma samples of healthy donors and ten of vulvar carcinoma patients were screened for exosomal miRNAs with Next Generation Sequencing. The top seven most dysregulated miRNAs and four potential stably expressed housekeeping genes were selected for qRT-PCR analysis in 84 vulvar carcinoma samples, of these 78 Vulvar squamous cell carcinomas, and 60 healthy female control samples. Differential expression was determined with the 2-ΔΔCT method. A binary regression was used to construct a miRNA-panel. The HPV status of 44 tumour tissues was assessed using mass spectrometry-based analysis.

Results

Of the candidate housekeeping genes, miR-378a-3p showed the most stable expression (p=0.903) and was selected as an endogenous control for normalization. Six out of seven of the target miRNAs showed a statistically significant dysregulation (p<0.005): miR-143-3p, miR-223-3p, miR-451a, miR-4516, miR-151a-5p, miR-16-5p. The combination of all six miRNAs resulted in a panel with superior diagnostic ability (p<0.001; AUC=0.805). 38/44 tumour samples were positive for HPV. MiR-143-3p and miR-223-3p could discriminate between HPV-positive and HPV-negative subgroups and miR-16-5p dysregulation was significantly associated with lymph node positivity (p=0.044). Cox-regression showed that downregulation of miR-16-5p and upregulation of miR-451a was associated with poorer survival (p=0.012, HR=0.19, 95%CI:0.05–0.69; p=0.036, HR=3.54, 95%CI:1.09–11.54).

Conclusion

A panel of exosomal miRNAs may serve as a potential biomarker for vulvar carcinoma to benefit the cancer diagnosis. MiR-223-3p and miR-143-3p seem predictive for HPV-positivity of tumours. The dysregulation of miR-16-5p and miR-451a might be associated with a worse outcome. This study indicates the potential diagnostic and prognostic power of a combined exomiR-panel. Validation studies with larger cohorts are required to consolidate the results.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.