

effects, and improved self-care irrespective of age, partner status, or stage of disease. Women's fear of cancer spread should be a central part of counselling at the time of diagnosis.

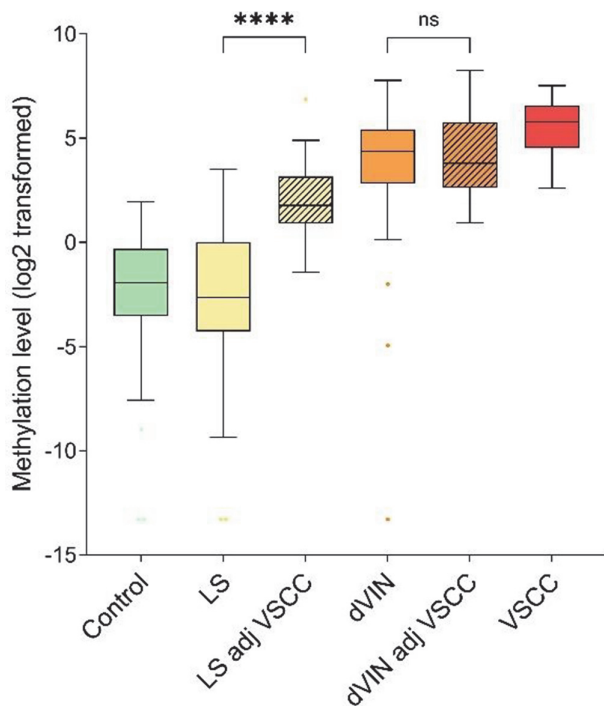
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DNA METHYLATION MARKERS IN HPV-INDEPENDENT PRECURSORS OF VULVAR SQUAMOUS CELL CARCINOMA

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Introduction/Background The majority of vulvar squamous cell carcinomas (VSCC) develop independently of human papillomavirus (HPV) and are associated with lichen sclerosus (LS). A small subset of patients with LS progress to VSCC (5%), usually via differentiated vulvar intraepithelial neoplasia (dVIN) which is an aggressive lesion with a high cancer risk (50%). However, dVIN is rarely diagnosed prior to VSCC and accurate diagnosis can be challenging. Our aim was to study the potential value of prognostic DNA methylation biomarkers in vulvar lesions involved in the HPV-independent route towards cancer.



Abstract 2022-RA-412-ESGO Figure 1 DNA methylation levels (log₂ transformed $\Delta\Delta C_t$ ratios) increase with increasing severity of disease across six HPV-independent vulvar disease categories, including healthy controls, LS, LS adjacent to VSCC, dVIN, dVIN adjacent to VSCC and VSCC. Differences between categories were tested by the Kruskal-Wallis test, followed by post-hoc testing using the Mann-Whitney *U* test with Bonferroni multiple testing correction; *****p*<0.0001

Abbreviations: adj, adjacent; dVIN, differentiated vulvar intraepithelial neoplasia; LS, lichen sclerosus; ns, not significant; VSCC, vulvar squamous cell carcinoma

Methodology A series of 220 HPV-independent vulvar samples were collected, including healthy controls, LS, dVIN, LS adjacent to VSCC, dVIN adjacent to VSCC and VSCC. Samples were tested for 12 DNA methylation markers with quantitative multiplex methylation-specific PCR (qMSP), including genes *ASCL1*, *CADM1*, *FAM19A4*, *GHSR*, *LHX8*, *MAL*, *miR124-4*, *PHACTR3*, *PRDM14*, *SST*, *ZIC1* and *ZNF582*.

Results Across all twelve markers, significantly higher methylation levels were shown with increasing severity of disease (*p*<0.001, Kruskal-Wallis test) (figure 1). Comparable low methylation levels were found in healthy vulvar controls and LS samples. Interestingly, LS adjacent to VSCC showed significantly higher methylation levels compared to LS of patients without cancer, whereas none of the markers showed a significant difference in methylation levels between dVIN and dVIN adjacent to VSCC. In fact, methylation levels in dVIN, dVIN adjacent to VSCC and VSCC were consistently high across almost all markers.

Conclusion Our findings indicate the potential of DNA methylation biomarkers to detect HPV-independent precursor lesions with a high cancer risk. As a next step, we aim to further explore these markers in vulvar lesions of patients with a known cancer outcome. Timely identification and treatment of vulvar lesions with a high cancer risk can substantially reduce the risk of malignant progression.

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VULVAR MELANOMA

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Introduction/Background Vulvar melanoma is a very rare gynecological tumor. It represents only 1% of all melanomas. It affects, in order of frequency, the vagina, the uterus and the ovaries. Less than 200 cases have been reported in the literature.

Methodology We report a clinical case of a metastatic vulvar malignant melanoma treated at the Radiotherapy oncology Department of the Farhat Hached Hospital in Sousse.

Results The case represents a 67 year old hypertensive woman who was being monitored for ACFA. We were consulted for a painful vulvar swelling evolving for 6 months. On examination, it appeared to be an ulcerating lesion on the vulva, crusty, superinfected, bleeding 7 cm GA with a fixed right inguinal adenopathy of 2 cm long axis; speculum examination finds a healthy cervix, the recto-vaginal septum is free. A biopsy of the lesion was performed, showing a spindle cell tumor proliferation, probably malignant, with a melanoma of the vulvar commissure on IHC. On thoracic-abdominal-pelvic CT scan, multiple deep cutaneous, pulmonary, splenic and left renal nodules associated with a peripheral hepatic mass and retroperitoneal adenomegaly, of secondary appearance, were observed. The patient underwent analgesic radiotherapy at a dose of 20 Gy in 5 fractions. Two weeks after treatment, the patient died.

Conclusion Vulvar melanoma is an aggressive tumour and has a poor prognosis. Although surgical treatment is the gold standard for localized forms, the therapeutic modalities are not codified for metastatic forms.