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Metastasizing vulvar carcinosarcoma with squamous carcinomatous and leiomyosarcomatous differentiation: genetic evidence of clonal origin

Patrick Adam MD[a,*], Andreas Zettl MD[a], Ursula Zollner MD[b], Johannes Dietl MD[b], Hans Konrad Müller-Hermelink MD[a], Matthias Eck MD[a]

[a]*Pathologisches Institut, Universität Würzburg, 97080 Würzburg, Germany*
[b]*Frauenklinik, Universität Würzburg, 97080 Würzburg, Germany*

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Summary In this report, we present the first case of a vulvar carcinosarcoma with squamous carcinomatous and leiomyosarcomatous differentiation. Comparative genomic hybridization was used to analyze clonality of the two tumor components. A widely identical pattern of genetic imbalances in the comparative genomic hybridization analysis in both the carcinomatous and the sarcomatous tumor component strongly supported the concept of a bidirectionally differentiated neoplasm. In both tumor components and two lymph node metastases, an amplicon was detected on chromosome 11q12-q13, homing the cyclin D1 gene locus. In contrast, exclusively in the sarcomatoid component, a characteristic amplicon on 12q13-q14 was found. The cytogenetic profile of the lymph node metastases revealed an increase in imbalances compared with the primary tumor. In summary, we found strong indications for a clonal origin of the two tumor components in a vulvar carcinosarcoma and a good correlation of the histological morphology with the pattern of genetic imbalances.

1. Introduction

Carcinosarcoma is a malignant neoplasm showing both epithelial and mesenchymal differentiation in changing composition. In the female genital tract, carcinosarcomas occur in several different localizations, including the uterus, cervix, fallopian tube, and ovary [1-3]. So far, only one detailed histopathologic report on a vulvar carcinosarcoma exists in literature [4]. With respect to the biphasic nature of carcinosarcomas, there is debate on whether they occur by collision of two independent neoplasms or they are of clonal origin. In the latter case, the two distinct cell phenotypes would result from two dichotomous ways of differentiation of a common cell of origin or by transdifferentiation (metaplasia) from one type of tissue to the other.

A recent study on carcinosarcomas of the uterus [1] indicated the components of carcinosarcomas being clonally related. To the best of our knowledge, no genetic investigation on carcinosarcomas of the vulva exists. In this report, we performed a comparative genomic hybridization (CGH)–based analysis of genetic imbalances and clonal relationship

* Corresponding author.
E-mail address: patrick.adam@mail.uni-wuerzburg.de (P. Adam).

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of the two tumor components and two inguinal metastases of a vulvar carcinosarcoma.

2. Clinical history

A 73-year-old patient presented with an ulcerated tumor between the clitoris and urethral ostium, 2.5 × 1.5 cm in size, with infiltration of the distal urethra. For histopathologic diagnosis, a biopsy was taken four days before tumor vulvectomy was performed. Eleven months after tumor surgery, the patient presented with bilateral inguinal lymph node metastases. Clinical examination was followed by lymphadenectomy. On both sides, several lymph node metastases measuring up to 2.1 cm and widespread soft tissue infiltration were seen.

Because of the advanced age of the patient, no further treatment was done, and the patient died of metastatic disease 13 months after initial presentation.

3. Materials and methods

Excised tumor specimens and lymph nodes were routinely fixed in 4% formaldehyde. Representative tissue specimen was embedded in paraffin, sectioned, and stained in hematoxylin and eosin. Immunohistochemical-staining panel included antibodies against pankeratin (AE1/3), cytokeratin (CK) 5/6, desmin, vimentin (all DakoCytomation, Hamburg, Germany), α smooth muscle actin, CD34 (both Immunotech Beckman Coulter, Krefeld, Germany), and cyclin D1 (Novocastra Laboratories, Newcastle upon

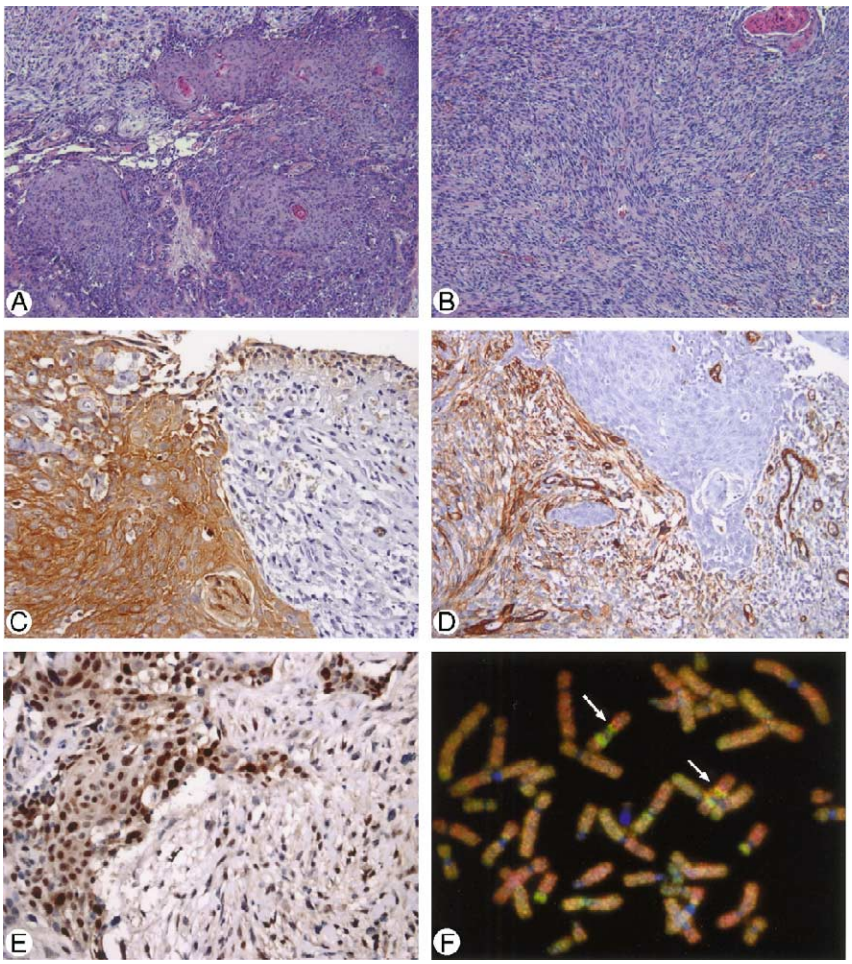

Fig. 1 Vulvar carcinosarcoma with a squamous cell carcinoma and a leiomyosarcoma component. Morphology and immunohistochemistry. A, The two tumor components showed an abrupt transition into one another. Forty percent of the tumor tissue displayed a carcinomatous differentiation (hematoxylin-eosin, original magnification ×40). B, Sixty percent of the tumor showed a spindle cell sarcomatous differentiation (hematoxylin-eosin, original magnification ×40). C, The carcinomatous component stained immunohistochemically positive for CK 5/6. D, The sarcomatoid component was strongly positive for smooth muscle actin (both original magnification ×200). E, Strong nuclear expression of cyclin D1 was detected in the carcinomatous component (upper left); the sarcomatous part showed weaker staining (lower right, original magnification ×400). F, Comparative genomic hybridization analysis yielded a high-level amplification on chromosome 11g12-q13 (arrows) among other genetic imbalances.