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BRIEF COMMUNICATION

Cytogenetic Study of Angiosarcoma of the Breast

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Angiosarcoma of the breast is quite rare, and the development of cutaneous angiosarcoma after segmental mastectomy and radiation therapy is even less common. A cytogenetic analysis of a mammary angiosarcoma arising in a breast after previous irradiation and segmental mastectomy for infiltrating ductal carcinoma revealed multiple clonal rearrangements involving chromosomes X, 1, 2, 3, 4, 5, 6, 7, 8, 9, 15, 17, 20, and 22. No cytogenetically analyzed angiosarcomas of the breast have been reported before. *Genes Chromosom Cancer 10:210–212 (1994).*

Angiosarcoma (AS) of the breast is an aggressive neoplasm, accounting for less than 0.04% of primary breast malignant tumors (Chen et al., 1980). Predisposing factors include chronic lymphedema following radical mastectomy (the Stewart-Traves syndrome) (1948) and external beam radiation therapy (EBRT) and iridium needle implants after total or segmental mastectomy or lumpectomy (Givens et al., 1989; Edeiken et al., 1992, Moskaluk et al., 1992; Stokkel and Peterse, 1992).

Cytogenetic studies on vascular tumors are rare, and to the best of our knowledge, only two cases of AS have been reported. The first case (Mandahl et al., 1990) was an angiomatous lesion in the left nasal cavity. It had the appearance of a cavernous hemangioma with intermingled, bizarre endothelial cells and was diagnosed as an angiosarcoma. Trisomy 5 and loss of the Y chromosome were the sole anomalies. The second case (Heimann et al., 1993) was a hepatic angiosarcoma that displayed a rather complex karyotype with multiple, clonal rearrangements involving chromosomes 1, 11, 17, and 19 and with double minutes, triradial figures, and dicentric markers. In this paper, we describe the cytogenetic findings of an AS of the breast occurring 5 years after conservative surgery for ductal carcinoma followed by EBRT.

A 61-year-old white woman was admitted to the hospital with a tumor approximately 3 cm in diameter in the outer upper quadrant of the right breast. A preoperative frozen section (May, 1987) revealed an infiltrating ductal carcinoma, and the patient underwent a segmental mastectomy with subsequent right axillary lymph node dissection, which yielded 12 lymph nodes with no evidence of metastatic disease. Computed tomography and a chest radiograph were also negative for metastatic disease. The neoplasm was staged as T2, N0, M0. Postoperatively, the patient received local radiation therapy with a dose of 4,600 cGy in 23 fractions for 5 weeks. In May, 1992, the patient was examined for a discoloration in the scar area of her breast. An incisional biopsy was performed and the specimen interpreted as an angiosarcoma grade II. Mastectomy followed. The AS recurred in the re-excised area in September, 1992.

The second mastectomy specimen showed a tumor composed predominantly of areas of well-differentiated angiosarcoma located in the dermis. The overlying epidermis was not involved. In some areas, apparent continuity with dermal capillaries was found. Focal areas of hemorrhage, necrosis, and endothelial cell pleomorphism with mitosis were seen. The tumor cells were spindle-shaped and formed extensive blood-filled clefts. The nuclei were large, oval, and possessed dense vesicular chromatin (Fig. 1A). The tumor was interpreted as a grade II angiosarcoma. Immunohistochemical studies were performed on fresh-frozen and paraffin-embedded tissue. The neoplastic cells expressed factor VIII-related antigen and vimentin, but were negative for desmin and cytokeratin, indicating an endothelial differentiation (Fig. 1B). Material from the second relapse showed a similar histological pattern, but with more undifferentiated structures, extensive necrosis, and epidermal invasion.

Cytogenetic analysis was performed on short-term cultures from fresh tumor samples. Tissue pieces were finely minced, rinsed in sterile phos-

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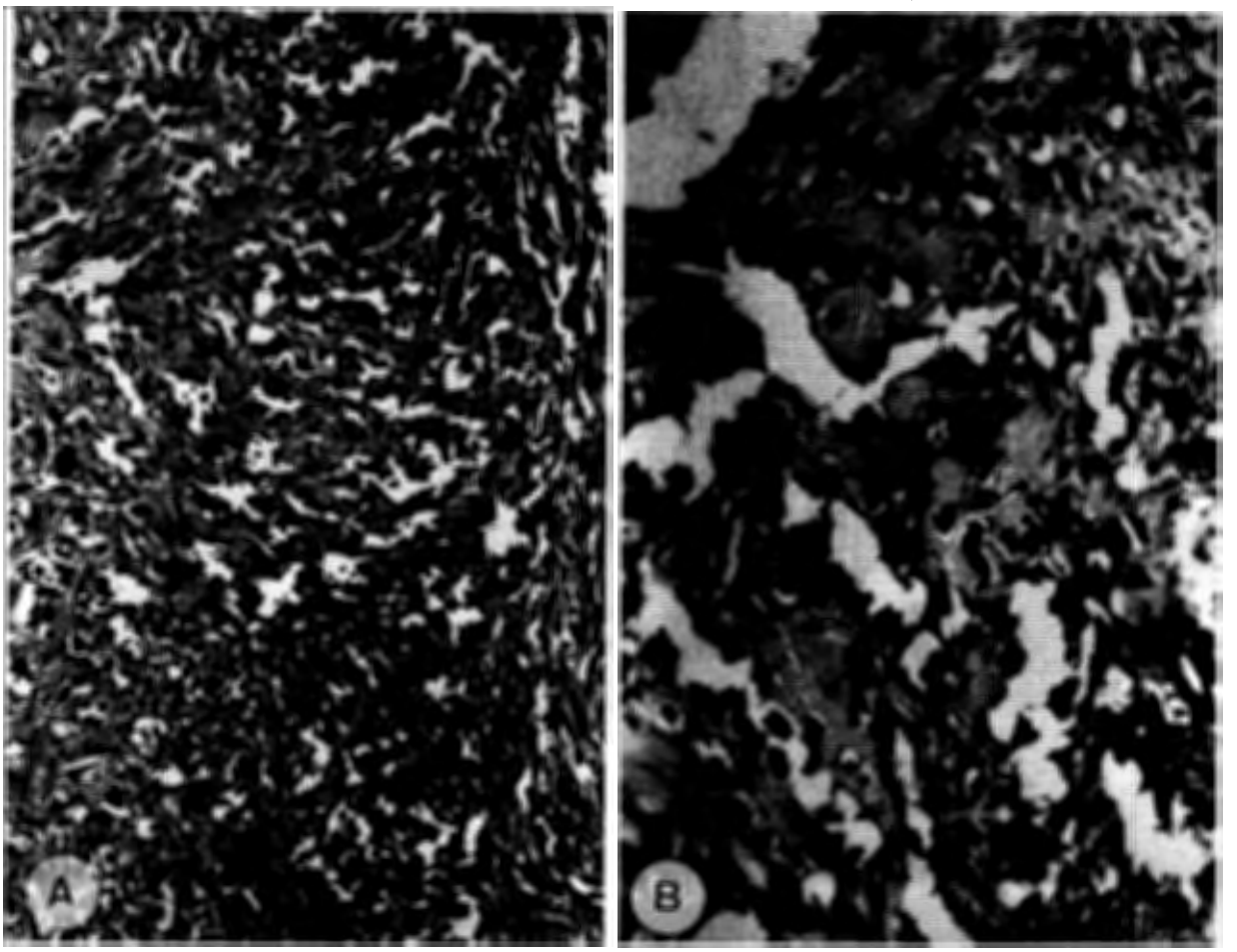

Figure 1. **A:** Initial biopsy of cutaneous angiosarcoma. The neoplasm shows plump endothelial and spindle cells forming atypical vascular spaces (H&E, ×200). **B:** Angiosarcoma showing vimentin-positive cells (×400).

phate-buffered saline (PBS), and enzymatically disaggregated with 2 mg/ml of collagenase II (Sigma). The cultures were initiated in flasks using minimum essential medium (MEM)-F12 medium supplemented with 7% fetal bovine serum, L-glutamine (200 mM), penicillin (5,000 U/ml), and streptomycin (5,000 mg/ml) and incubated at 37°C in a humidified atmosphere with 5% CO_2 in air. After 6 days, the cells were exposed to Colcemid (0.02 μg/ml) for 1.5 hours and harvested according to standard techniques. Air-dried slides were banded by trypsin-Giemsa. The metaphase cells were analyzed and karyotyped according to the ISCN (1991).

The 18 metaphases counted had chromosome numbers ranging from 43 to 47, with a modal number of 47. Chromosome analysis revealed a complex karyotype: 47,X,der(X)t(X;9)(q11;q12),t(1;3)(p13;q29),t(1;17)(p13;p13),-2,-2,del(4)(q25q31),+der(4)del(4)(p14)t(2;4)(p13;q35),del(7)(p11),add(8)(q13),+12,der(15)t(5;15)(p11;p11),+der(20)t(6;20)(q13;q23),der(22)t(6;22)(q15;q13) (Fig. 2).

As far as we know, this is the first report on chromosomal findings in mammary angiosarcoma. Only one aberrant clone with a near diploid modal chromosome number was found. The structural rearrangements affected chromosomes X, 1, 2, 3, 4, 5, 6, 7, 8, 9, 15, 17, 20, and 22 and led to the loss of the whole of chromosome 2 as well as the segments Xq11→qter, 2p13→qter, 7p11→pter, 8q13→qter, and 22q13→qter. Some of these segments might be present in the rearranged chromosome 8. Trisomy 12 was present, and also segments of chromosomes 4, 5, 6, and 20 were in excess.

With respect to the two reported angiosarcomas found in different locales, the hepatic angiosarcoma (Heimann et al., 1993) also showed rear-

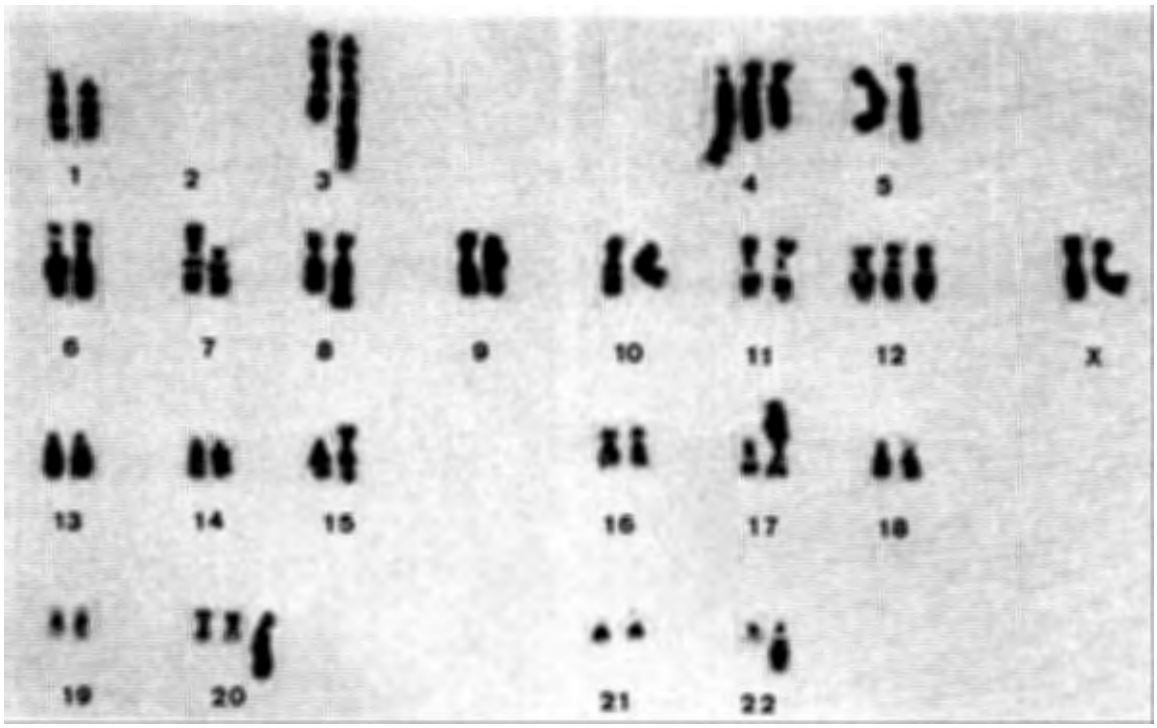

Figure 2. Karyotype: 47,X,der(X)t(X;9)(q11;q12),t(1;3)(p13;q29),t(1;17)(p13;p13),-2,-2,del(4)(q25q31), +der(4)del(4)(p14)t(2;4)(p13;q35),del(7)(p11),add(8)(q13), +12,der(15)t(5;15)(p11;p11), +der(20)t(6;20)(q13;q23),der(22)t(6;22)(q15;q13)

rangements of chromosomes 1 and 17, whereas the cavernous hemangiosarcoma showed trisomy 5 and loss of Y as the sole cytogenetic anomalies (Mandahl et al., 1990). In our case, partial 5p trisomy was also found. No chromosomal feature characteristic of angiosarcoma can be discerned on the basis of the three cases available for evaluation.

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