Secondary Breast Angiosarcoma: Lethal Response to Anti-angiogenic Therapy with Paclitaxel Chemotherapy. A Case Report

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Abstract. Angiosarcoma of the breast is a malignant tumour of vascular endothelial cells. It is a rare and difficult tumour to treat. The authors report a case of cutaneous radiation-associated angiosarcoma treated with paclitaxel chemotherapy. A few days after drug administration, bleeding of skin lesions was observed and the patient died.

Angiosarcomas are rare, aggressive tumors with pathological and morphological properties similar to the vascular endothelium that can occur in any region of the body. The incidence of angiosarcomas among malignant breast is 0.02%. Angiosarcomas have been frequently reported to arise in the irradiated breast after breast-conserving therapy but, despite the distinction between primary and secondary angiosarcomas of the breast, the natural history is remarkably comparable, with a median survival period of 14.5-34 months and a 5-year survival rate of approximately 15%. Optimal treatment has not been well defined: surgical procedure is recommended if the disease is localised, while radiotherapy could contribute to local or palliative control. If the disease is extensive, chemotherapy regimens based on paclitaxel have shown activity in few patients with involved sites other than the breast. The exact cytotoxic action of this drug is not fully understood, but it appears to be mediated through two different mechanisms: the mitotic arrest leading to apoptosis in the tumor cells and anti-angiogenic activities targeting endothelial cells currently demonstrated in vitro and in vivo.

Case Report

Herein the case of an 83-year-old woman, presenting with erythematous and violaceous nodular skin lesions rapidly growing on her right breast, is reported (Figure 1).

Five years before, this patient had been treated with a bilateral surgical breast-conserving therapy for bilateral early breast carcinomas. She had an uncomplicated postoperative course and subsequently received bilateral chest-wall tangential-field whole breast irradiation (4500 and 4500 cGy) and tamoxifen therapy based on the presence of oestrogen and progesterone receptors.

A complete staging work-up was performed. The disease appeared to be extended only to the skin without visceral metastases.

A biopsy on the breast mass allowed for the diagnosis of high-grade angiosarcoma (Figure 2), while a histological review of both previous malignancies confirmed the diagnosis of breast ductal carcinomas (Figure 3).

The patient received paclitaxel 60 mg/m² as a 1-h infusion on an in-patient basis. Two days later, the mass started flattening irregularly and extraordinarily, changing in colour from bruise-like to red nodular lesions, with bleeding and fluctuant ulcerating nodules (Figure 4).

Such changes were ascribed as response criteria of the disease (1). On the third day after starting the therapy, the patient developed progressive and remarkable hypovolemia and anaemia. On the subsequent days, shock symptoms and progressive renal failure increased, despite blood transfusions, plasma expanders, monitoring of central venous pressure and the support of the anaesthesiologists. Uric acid, hepatic enzymes and coagulation parameters were normal. An increased capillary permeability with progressive bleeding from the ulcerating tumour mass was responsible for this progressive haemodynamic compromise. The patient died on day 5 from chemotherapy.
Discussion

Angiosarcoma seems to originate from the endothelial cell and its pattern of spread is characterised by a diffuse and aggressive course. Given the rarity of this tumour, relatively little is known concerning the optimal treatment (1).

Surgical resection remains the cornerstone of therapy, while radiation therapy or chemotherapy play a role in local or systemic control and palliation, respectively, of the disease. The overall prognosis remains dismal even with multimodal therapy (1, 2).

For the chemotherapy approach, most information comes from small case reports and a hypothesis under investigation is whether chemotherapy targeting angiogenesis would give better results. When angiosarcomas respond to treatment, they flatten and their colour fades from bruise-like to red nodular lesions with some decrease in size (1-3).

Paclitaxel showed activity in angiosarcomas of the scalp and face and its antitumor activity was reported in Kaposi Sarcoma, an unusual form of haemangiosarcoma (4).

The taxanes, paclitaxel and docetaxel, demonstrated significant activity against many solid tumors and their activity depends either on direct cytotoxic activity or on their anti-angiogenetic effect on tumor epithelial cells (5).

Recent information suggests that the mechanism of action of taxanes may primarily include inhibition of growth factor secretion, e.g., vascular endothelial growth factor (VEGF) in tumour cells and a direct effect on endothelial cells causing the cells to arrest in the G2/M phase. It is
known that taxanes bind and stabilise microtubules by inhibiting tubulin depolarisation (5-7).

Angiogenesis is a crucial field of interest for oncologists, but many questions still surround the safety profile of the drugs under investigation. VEGF, a specific mitogen of endothelial cells, might be a new target for inhibiting the growth of many tumours, including angiosarcoma (8).

Antibodies against neo-angiogenesis are now promising in non-small cell lung cancer, renal cancer, colon cancer and a variety of other solid tumours, but additional data on their safety are necessary (9).

To the best of our knowledge, paclitaxel in patients affected by angiosarcoma seems to be a promising drug that should aid clinicians in managing this infrequent malignancy, but aggressive kinetics of this disease need consideration in the clinical management.

The intriguing idea of selectively inhibiting massive tumour vasculature with vascular-targeting agents and inducing rapid tumour necrosis is promising, but not lacking in risk for these patients. The extension of the disease to the cutaneous and non-cutaneous lesions should be considered carefully in order to minimise the risk of a haemorrhagic and fatal response to therapy.

References


