Advanced Breast Angiosarcoma Completely Responding to Gemcitabine-Containing Chemotherapy

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Keywords

Breast neoplasm · Angiosarcoma · Lung metastases · Gemcitabine · Vincristine · Cisplatin · Chemotherapy

Summary

Background: For patients with anthracycline-resistant metastatic angiosarcoma, there is currently no available standard for second-line therapy, and a need exists for novel effective regimens to improve response rates.

Case Report: We report here on a case of a primary angiosarcoma of both breasts in a 34-year-old woman presenting with lung metastases. Upon completion of 3 cycles of the MAID regimen (mesna, adriamycin, ifosfamide, dacarbazine), computed tomography showed disease progression. Subsequently, a second-line chemotherapy was started using the GVP regimen (gemcitabine, vincristine, cisplatin). Complete response of the lung metastases was achieved after 6 cycles of treatment. **Conclusion:** In the absence of an effective therapy among patients with anthracycline-resistant metastatic breast angiosarcoma, a GVP chemotherapy regimen can be performed as a selective option.

Schlüsselwörter

Mammatumour · Angiosarkom · Lungenmetastasen · Gemcitabin · Vincristin · Cisplatin · Chemotherapie

Zusammenfassung

Hintergrund: Für Patienten mit anthrasyklinresistentem metastasierten Angiosarkom existiert momentan keine Standard-Zweitlinientherapie, und es besteht Bedarf an neuen effektiven Regimen zur Verbesserung der Ansprechraten. **Fallbericht:** Wir berichten von einem Fall von primärem, bilateralen Angiosarkom der Brust bei einer 34-jährigen Patientin mit Lungenmetastasen. Nach 3 Zyklen des MAID-Regimes (Mesna, Adriamycin, Ifosfamid, Dacarbazin) zeigte die computertomographische Untersuchung ein Fortschreiten der Erkrankung. Daraufhin wurde eine Zweitlinienchemotherapie mit dem GVP-Regime (Gemcitabin, Vincristin, Cisplatin) begonnen. Nach 6 Behandlungszyklen konnte ein komplettes Ansprechen der Lungenmetastasen verzeichnet werden. **Schlussfolgerung:** In Abwesenheit einer effektiven Therapie für Patienten mit anthrasyklinresistentem metastasierten Angiosarkom der Brust stellt das GVP-Chemotherapieregime eine Behandlungsmöglichkeit dar.

Introduction

Primary angiosarcoma of the breast is a rare and highly aggressive malignancy which accounts for about 0.05% of malignant breast neoplasms [1, 2]. The 3-year disease-free survival and overall survival are 14 and 38%, respectively [3]. Bilateral primary breast angiosarcoma is even more infrequent. Only 1 case of metachronous bilateral angiosarcoma of

the breast has been reported thus far [4]. We herein report a case of complete remission of anthracycline-resistant lung metastases of a bilateral primary angiosarcoma of the breast after treatment with the GVP chemoregimen.

Case Report

A 34-year-old female patient had noticed diffuse enlargement of both breasts by more than one-third over a 1-year period, accompanied by nipple retraction, occasional galactorrhea, local skin thickening, and

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Fig. 1. Atypical endothelial cells with numerous mitotic figures and hyperchromatic nuclei lining the vascular structures (H&E ×400).

Fig. 2. Poorly differentiated tumor with area of necrosis and massive hemorrhage (H&E ×200).

roughness. She was also experiencing severe pain not associated with menstruation. Erythematous infiltrated surface lesions had gradually developed to 6 cm in diameter within 8 months (right breast) and to 3 cm in diameter within 3 months (left breast). The patient was referred to our hospital on 14 July 2009. On physical examination, there were 2 clearly defined 6-cm and 3-cm erythemas, towering 1 mm above the skin, in the upper outer quadrant of right and left breast, respectively. The breasts were diffusely swollen with cutaneous hypertonicity and nipple retraction. There were no associated ulcerated lesions or nipple suffusions. On palpation, the breasts were solid with large lumps occupying almost the whole breast and adherent to the skin with limited mobility. The patient had previously refused surgical treatment and radiation exposure to the breast.

A core needle biopsy was taken from the right breast, and a possible angiosarcoma was diagnosed. On immunostaining (2009-09148), the tumor cells were positive for factor VIII, CD31, vimentin, and Ki-67 (+, 30%), and negative for SMA, CD68, AE1/AE3, and CAM5.2, indicating an endothelial nature. A bilateral simple mastectomy was performed on 28 July 2009. Postmastectomy pathology confirmed a poorly differentiated bilateral breast angiosarcoma (figs. 1 and 2). Tumor dimensions on macroscopic examination were 10.0 × 6.0 × 3.0 cm for the left breast and 14.0 × 9.0 × 4.0 cm for the right breast. The nipple dermis and subcutaneous tissue were focally involved. The tumor was close to the inferior margin with only 0.2 cm clearance.

On 8 November 2009, 3 months after surgery, a computed tomography (CT) scan with contrast enhancement revealed a high-density mass in the right lung field (fig. 3). For palliative therapy, a combination chemotherapy with the MAID regimen (mesna, adriamycin, ifosfamide, dacarbazine) was initiated. After 3 cycles, a CT scan for reevaluation showed progression of the disease. Subsequently, the patient was changed over to the GVP chemoregimen (gemcitabine, vincristine, cisplatin) as a salvage therapy. Doses and administration schedule were as follows: gemcitabine (1,000 mg/m² body surface area (BSA)) over 30 min days 1 and 8, vincristine (1.4 mg/m² BSA, maximum 2 mg) day 1, and cisplatin (25 mg/m² BSA) days 1–3. The protocol was repeated in 3-week intervals. After 2 and 4 cycles, CT showed the metastatic lesions in the right lung field to be gradually decreasing in size, to the point of partial remission. By March 2010, clinical complete remission was evident after 6 cycles of treatment (fig. 4). During subsequent follow-up, the patient developed a 1 × 0.6 cm discolored skin nodule on the right chest wall (June 2010), which was treated by local surgical excision and radiotherapy. Multiple subcutaneous nodules on the waist and back have since emerged.

Discussion

Breast angiosarcomas are very rare and tend to affect women in their 3rd or 4th decade of life (mean age 38 years). Half of the patients may be misdiagnosed due to the scarcity of the disease and clinical similarity with benign lesions. A typical clinical manifestation is a rapidly enlarging painless mass deeply embedded in the breast tissue. 12% of patients present with initial diffuse enlargement and blocks of calcification of the affected breast. Some cases with persistent subcutaneous bleeding tend to be ignored as the tumor may be masked. A purple discoloration of the overlying skin due to tumor infiltration is a frequent symptom; however involvement of the underlying muscles is rare [1, 3, 5]. Breast angiosarcomas are aggressive and tend to recur locally and metastasize widely. They mainly spread hematogenously while lymphatic metastasis is generally absent. The most frequent sites of distant metastasis are lung, liver, bone, and skin [3]. The prognosis is generally poor and based primarily on tumor size, tumor grade, completeness of surgery, and performance status. Angiosarcomas secondary to irradiation, local relapses, and distant metastases are adverse prognostic indicators [4, 6–8].

Surgical resection is recommended as the primary treatment. Adjuvant radiotherapy and chemotherapy are considered helpful to reduce the local recurrence rate in poorly differentiated tumors [9], but a real effect on survival is not proven. Palliative chemotherapy is the basic concept of treatment in advanced disease. Anthracycline-based regimens have emerged, by consensus, as the standard first-line therapy for angiosarcomas as well as most other subtypes of soft tissue sarcomas [6]. Paclitaxel and liposomal doxorubicin have also shown some activity [10]. However there is still no general agreement about a standardized therapy in patients progressing on anthracycline. It has been reported that trifluoromethine plus gemcitabine are feasible and can be safely

Fig. 3. Computed tomography scan at first presentation (8 November 2009) prior to chemotherapy showing pulmonary metastasis.

Fig. 4. Computed tomography scan after 6 cycles of GVP chemotherapy (29 March 2010) revealing complete disappearance of the pulmonary lesions.

administered [11]. Furthermore, docetaxel has demonstrated a certain efficacy [12], and capecitabine alone or combined with docetaxel have also shown some effect [13–16]. However the efficacy of these regimens is limited, and only a few patients can benefit from second-line treatment [17]. In the case reported here, we used a GVP regimen after failure of 3 cycles of MAID chemotherapy and achieved complete remission of the lung metastases upon completion of 6 treatment cycles. Hence, the GVP regimen seems to be an option as a

second-line treatment modality for anthracycline-resistant breast angiosarcomas. More trials are needed to confirm its clinical value.

Disclosure Statement

The authors confirm that there was no conflict of interest.

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