Case Report

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Complete Response of Radiation related Angiosarcoma of the Breast with CMF Chemotherapy

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Abstract

Angiosarcoma of breast or chest wall is a rare recognized side effect in breast cancer survivors secondary to Adjuvant radiation. The treatment of angiosarcoma of the breast is carried out in number of ways. We would like to report the case of a 50-year old woman. She developed an angiosarcoma of the breast following adjuvant radiation to her conserved breast and was successfully treated with classical Cyclophosphamide, Methotrexate, and 5- fluorouracil (CMF) chemotherapy leading to a successful local surgical salvage.

Keywords: Angiosarcoma; Breast; Radiation; Chemotherapy

Introduction

One of the side effects of treating breast cancer with radiation to the chest wall or the conserved breast is the development of angiosarcoma [1,2].

This is a rare event and often occurs many years beyond the successful therapy of breast cancer itself [3]. The treatment of radiation related angiosarcoma (RAAS) of the breast in such settings is carried out by surgery, radiation, and chemotherapy. Nevertheless, the fact that the angiosarcoma itself is brought about by radiation therapy may result in a debate amongst clinicians as to the best modality of therapy in any given case. Chemotherapy regimens include many agents including the taxanes which have an antiangiogenic as well as a cytotoxic effect [4].

We would like to propose that CMF chemotherapy in the classical mode should be considered as an antiangiogenic and chemotherapy option in such cases.

Case Report

The lady is a 50-year-old of Pakhtoon ethnicity diagnosed having invasive ductal carcinoma of breast, grade III, T2N1Mo disease with ER/PR and Her 2 neu negative in 2008. She underwent breast conserving surgery with axillary clearance followed by adjuvant chemotherapy and radiation to breast and axilla, she was doing well subsequently. However, in 2014 she noticed a small lump in the conserved breast in lower outer quadrant; She underwent a biopsy and was felt to have a recurrent breast cancer. She received two cycles of docetaxel and carboplatinum. The tumor continued to grow and had mastectomy elsewhere. This resulted in a poor outcome with positive tumor margins and bleeding which later became an open wound. At this time she sought an opinion from us. A reassessment of the original biopsy and the second biopsy with an additional pathology opinion showed the entire biopsies specimen to be a high grade angiosarcoma and not breast cancer. The immunohistochemical markers were consistent with the diagnosis of angiosarcoma **(Figures 1 and 2)**.

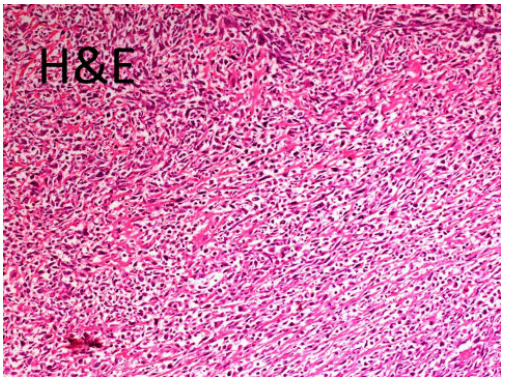

Figure 1 Angiosarcoma.

She was felt to be inoperable given the very large area involves clinically and the first option was felt to be chemotherapy. It was decided to start classical CMF. Midway through the second cycle of CMF the open wound had closed. By the end of the third cycle clinical traces of the disease had disappeared and she was considered fit for surgery. Excision of the tumor area was done easily with a quick and easy recovery. Histopathology showed only scarring, no tumor was seen. It was felt to be a complete and a successful excision.

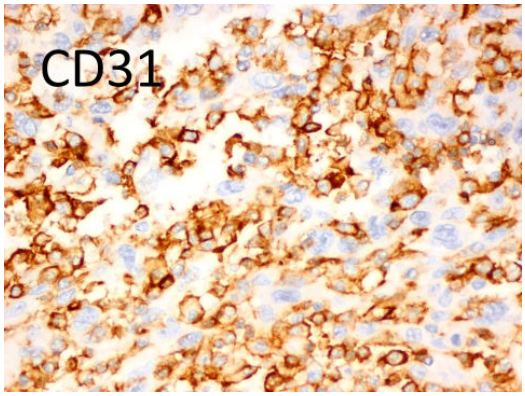

Figure 2 CD 31 Marker.

Discussion and Conclusion

Angiosarcoma of the breast is a rare condition and may develop de novo or may be related to radiation treatment delivered to the chest region in breast cancer [1]. The early description of the Treves syndrome was angiosarcoma developing in patients who underwent a mastectomy which was followed by the development of angiosarcoma [2]. In the breast conserved setting angiosarcomas of the breast can also develop but the average time to such an event is approximately 72 months [3]. In our own case the period was approximately 62 months.

Treating RAAS follows the usual lines of integrating surgery, irradiation and in some cases chemotherapy. Systemic therapies used in these settings have included doxorubicin, liposomal doxorubicin, Ifosfamide, Gemcitabine, Docetaxel and even pazapanib [4]. In the PhaseII Angiotax weekly paclitaxel was employed in 30 cases of which 3 had breast angiosarcoma. In these 3 cases partial responses were seen after paclitaxel which let to successful surgery [5]. In one case report a 30-year remission in metastatic angiosarcoma is recorded following the use of methotrexate [6]. We could find any report relating to the use of Bevicizumab although the vascular endothelial growth factor may be overexpressed in breast angiosarcoma [7]. Finally, metronomic chemotherapy in the form of trofosfamide, pioglitazine, rofecoxib has been used as well [8].

In a recent analysis Depla et al. published a systemic review on treatment and prognostic factors of RAAS after primary breast cancer. In 74 articles encompassing 222 patients only 6% received chemotherapy with surgery with another 9% in which either radiation or chemotherapy alone were employed [9]. The treatment of RAAS with chemotherapy has few publications. We have found no report where CMF in a classical mode has been used in RAAS. CMF was appealing to us for a number of reasons. In this case the prior use of adjuvant FAC and the unaffordability of more expensive options such as liposomal doxorubicin were evident. Docetaxel was used with no effect. The high toxicities of Ifosfamide based regimens were not considered as was gemcitabine. There is a metromomic part to the use of CMF which is the two weekly oral cyclophosphamide treatments. Metronomic chemotherapy is highly antiangiogenic and it is easily affordable in the poorer economic settings. Often cyclophosphamide is its backbone [10]. The response of this patient was quick as within 6 weeks the wound closed completely. After 2 cycles she has undergone surgery with no angiosarcoma seen in the resected specimen and is undergoing re irradiation to the anterior chest wall.

An overall review of chemotherapies used in RAAS indicates no predictable pattern of treatments employed given that RAAS is a rare disease and no studies have been forthcoming prospectively.

Finally, the biology of angiosarcomas in breast conservation and radiation may be different the chest wall chest wall related angiosarcomas or the so called Treves syndrome. CMF may also need to be considered a chemotherapy choice in RAAS based on our experience.

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