

Low Grade Cutaneous Angiosarcoma Of Chest Wall Skin Following Mastectomy 20 Months Postradiation

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Citation

Y Elshimali, M Feinberg. *Low Grade Cutaneous Angiosarcoma Of Chest Wall Skin Following Mastectomy 20 Months Postradiation*. The Internet Journal of Radiology. 2003 Volume 3 Number 2.

Abstract

Angiosarcoma of the skin of the chest wall or breast following radiation treatment after breast lumpectomy or mastectomy for breast carcinoma is a rare condition. The majority of cases of post radiation angiosarcoma occur in the upper extremities and are associated with edema. The latent period of postradiation angiosarcoma of chest wall or breast skin varies from 37 months to 13 years. Few cases are reported and most have high-grade angiosarcoma. The latent period in the case we are reporting was 21 months and the tumor histologically was low grade. The clinical history and histological findings are compared with cases found in a review of the literature.

INTRODUCTION

Angiosarcoma is a rare malignancy of vascular endothelium; approximately one third of reported cases occur in the skin. Cutaneous angiosarcomas arise in three types of clinical setting. 1. Primary cutaneous angiosarcoma most often in the skin of the face or scalp of elderly persons. 2. In sites of chronic lymphedema. 3. As a sequel of radiation therapy (4, 6). Lymphedema associated angiosarcoma most often occurs in a patient with upper extremity edema after mastectomy and axillary dissection; approximately 10 % of lymphedema associated angiosarcomas are not associated with mastectomy and lymph node dissection. Post irradiation angiosarcoma is the least common type. Four criteria have been suggested for diagnosis of this type of lesion

- Must be a history of radiation.
- The tumor must arise in the field of radiation or the adjacent skin.
- A latent period of several years must elapse
- There must be histological confirmation

CASE HISTORY

This was a 46-year-old white female who presented to Olive View-UCLA Medical Center for regular follow up and to check on a small firm reddish purple nodule in scar tissue of left chest skin. The patient had a history of stage 3A infiltrating ductal carcinoma of the left breast, status post

modified radical mastectomy and axillary lymph node dissection 30 months prior. Surgery was followed by 4 cycles of chemotherapy and 3 courses of radiation therapy. The last chemotherapy (adriamycine and cyclophosphamid) cycle was 5 months after mastectomy and last radiotherapy was 9 months after mastectomy. The patient underwent chest wall radiation. The dose to left chest wall was 4500 cGy in 25 fractions and the skin scar was given a boost for a total dose of 6100 cGy. The dose to the left supraclavicular fossa was 4500 cGy in 25 fractions at 3 cm depth. The energy was 6 Megavolt Linear accelerator.

Mammogram of the right breast 18 months after the surgery was negative. Her recent blood counts have shown normal white blood cells and platelets. On examination at the time of presentation at Olive View-UCLA Medical Center there was surgical absence of the left breast with a well-healed scar. A 0.5 cm firm mobile subcutaneous reddish nodule was present in the scar. No other masses were palpable on the chest wall or in the axilla. The right breast showed no suspicious masses and no right axillary lymphadenopathy. A 1.2 x 0.6 cm excisional biopsy was performed to remove the nodule in the scar.

MATERIAL AND METHODS

Tissue from the patient lesion was fixed in 10% formalin and embedded in paraffin. Four micrometer thick sections were cut and stained with Hematoxylin and Eosin. Unstained sections were incubated for 2 hours at 60 degrees for deparaffinization. Antigen retrieval was done by citrate for

20 minutes at 96-98 degrees, then incubated in hydrogen peroxidase for 5 minutes and finally in buffer at PH 7.8. The sections were then stained using antihuman antibody Ki 67 from mouse, clone MIB-1, produced by Dako with the Dako automated Ki 67 stain system.

RESULTS

Microscopic examination revealed involvement of the dermis by a patchy vascular lesion composed of irregular anastomosing vascular channels lined by prominent endothelial cells. The vascular channels infiltrated into collagen bundles (fig.1). The endothelial cells were atypical and showed moderate pleomorphism. (Fig. 2). A rare mitotic figure was present and an occasional endothelial cell contained a nucleolus. Ki 57 stain was positive in endothelial cells. The distribution of the lesion was patchy with areas of uninvolved collagen between the vascular areas. The lesion appeared confined to the upper reticular dermis. The margins of excision appeared clear of the lesion, although the patchy nature of the vascular areas precluded a complete assurance of excision. Small numbers of lymphocytes were associated with the vascular channels. There were scattered thick-walled arterioles within the dermis; atypical fibroblasts were not seen. The findings were consistent with angiosarcoma of skin, low grade. Wide reexcision of the area was done. Pathologic examination of the reexcision specimen showed foreign-body type reaction, chronic inflammation and dermal scarring. Residual angiosarcoma was not seen in sections of the entire specimen.

Figure 1

Figure 1: Anastomosing and irregular vascular channels infiltrating into collagen bundles with prominent endothelial cells x 20.

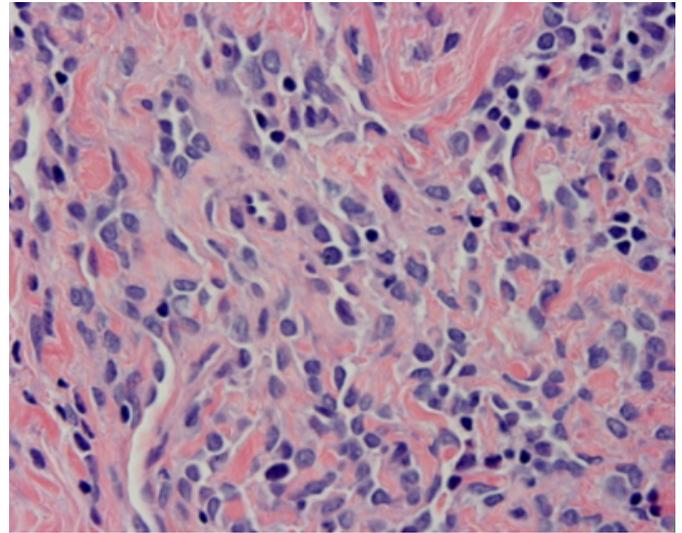
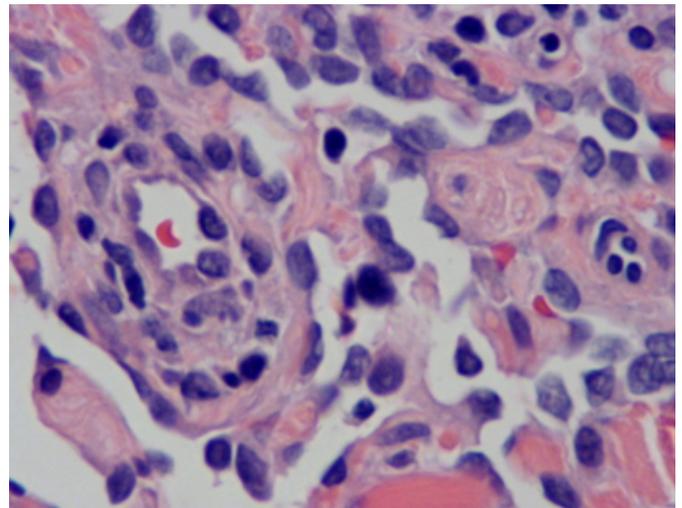


Figure 2

Figure 2: Atypical and pleomorphic endothelial cells lining irregular vascular channels x 40.



DISCUSSION

Dermal angiosarcoma may occur in areas previously radiated. This is a rare occurrence in the setting of post lumpectomy radiation of remaining breast tissue or chest wall following mastectomy. Small numbers of reported cases are usually secondary to radiation following lumpectomy; the reported cases following radical mastectomy are rare. Because of the high mortality associated with angiosarcoma consideration should be given to wide reexcision if clinically feasible.

Malignant neoplasms known to develop following external

beam radiation include squamous cell carcinoma, osteosarcoma, chondrosarcoma, malignant fibrous histiocytoma, mixed mullerian tumors, malignant schwannoma, myelogenous leukemia and angiosarcoma (13). Latency periods of many years characterize the onset of these tumors following the exposure (13). Unlike other radiation therapy-induced sarcomas, cutaneous angiosarcoma often occurs within a shorter time interval after radiotherapy compared to the above-mentioned sarcomas. By literature review we found 2 cases of low-grade angiosarcoma in the literature arising after 7 and 10 year postradiation therapy (3, 14). High-grade angiosarcoma was diagnosed between 37 months and 13 years after radiotherapy (13). In our case the time between radiation therapy and occurrence of low-grade angiosarcoma is shorter than other reported cases for development of radiation-induced angiosarcoma. The clinical features are usually several round blue-colored or purple nodules and patchy discoloration of the irradiated skin with some inflammation surrounding them (2,11).

Literature review reveals that these lesions are difficult to diagnose because of their rarity and their highly variable and benign appearance, which may mimic radiation-induced changes in the skin (3). The prompt diagnosis of cutaneous angiosarcoma is strongly dependent upon a high index of suspicion. Biopsy should be considered in patients who present with new skin lesions after radiation treatment for breast cancer. Recognition of the mammography changes in residual breast and clinical manifestations may help in the earlier diagnosis of additional cases. On mammography the angiosarcomas showed development of skin thickening and increase in breast density (14).

Lesions arising in irradiated mammary skin include extensive lymphangiectasia, atypical vascular lesions, and cutaneous angiosarcoma.

The histologic differential diagnosis of low-grade angiosarcoma would include atypical vascular lesion, of which three cases were described by Fineberg and Rosen (5). This lesion consists of circumscribed groups of dilated vascular spaces, lined by a single layer of plump and sometimes hyperchromatic endothelial cells. The lesion invades between collagen bundles but not into collagen fibers. The reported cases in this category need larger case studies and further cases must be evaluated to determine the biological potential of the cases. At the present time none of the reported case have evolved into angiosarcoma (5).

Requena, Kutzner, Mentzel et al (10) reviewed fourteen cases of benign vascular proliferation in irradiated skin of the breast. Twelve cases consisted of irregular dilated vascular spaces lined by a discontinuous single layer of endothelial cells. These were classified as benign lymphomatous papules or plaques. Two cases consisted of poorly circumscribed and focally infiltrating irregular jagged vascular spaces lined by inconspicuous endothelial cells. These latter 2 cases were classified as atypical vascular proliferation. The follow up in this series showed a benign biological behavior. It is felt that collagen invasion, pleomorphism, diffuse atypism and Ki 67 staining of the endothelial cells as described in our case is more indicative of angiosarcomas.

The presence of chronic lymphedema in the breast after radiation therapy may contribute to the development of angiosarcoma and is an early warning sign for later development of angiosarcomas. Dermal angiosarcoma is not always associated with chronic lymphedema. Some patients never have evidence of lymphedema (3,15). Furthermore, almost all cases previously reported have been high grade. Our case suggests that radiation therapy for breast carcinoma may also be complicated by low-grade angiosarcoma. Angiosarcomas behave aggressively and the outcome is very poor. Survival has not been more than 22 months in high-grade angiosarcoma (2). Atypical vascular lesions at the skin margins of mastectomy may be predictive of recurrence after resection of angiosarcoma (15).

The prognosis of low-grade cutaneous angiosarcoma is unknown due to the small number of cases and the number of cases of high-grade angiosarcomas which arise through a low-grade phase is unknown as well.

Most women who undergo lumpectomy or mastectomy followed by radiotherapy do not develop angiosarcoma in the chest wall skin. A few of these may develop a high-grade angiosarcoma after years. From this case report and other cases of low-grade angiosarcoma following radiation therapy we conclude that radiation therapy could have a role in development of a low-grade angiosarcoma that occurs as early as 21 months after radiotherapy. The number of cases of postradiation low-grade cutaneous angiosarcoma is very small and further studies are needed. Long-term clinical surveillance is recommended for all patients who have received breast surgical therapy or chemotherapy with radiation therapy.

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