

Radiation-induced sarcoma of the breast

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A small but growing number of radiation-induced sarcomas after breast-conserving surgery for carcinoma have been reported. Because breast-conserving surgery followed by irradiation is becoming increasingly popular, the potential for the emergence of these sarcomas is growing. Unfortunately, because of postirradiation changes in the affected breast, detection of a new lesion can be difficult, resulting in a delay in diagnosis. This case history describes a 48-year-old woman in whom a malignant fibrous histiocytoma was discovered 5 years after she had had a lumpectomy followed by radiation therapy for infiltrating ductal carcinoma. Although the exact mechanism of radiation-induced carcinogenesis is unclear, one theory is discussed. Also discussed are the histologic composition of the malignant fibrous histiocytoma, its latency period, and the best treatment modality for radiation-induced sarcomas.

(Key words: Breast cancer, breast irradiation, radiation complications)

Radiation-induced carcinogenesis is a well-recognized phenomenon. Since the first report by Friebe¹ in 1902, which described a case of squamous cell carcinoma on the hand of an x-ray technician, numerous reports have followed. Of particular interest, and with reference to this case, is the number of radiation-induced sarcomas that have been reported in the literature after treatment for breast carcinoma.² To date, fewer than 40 cases of sarcoma of the chest wall after irradiation for breast carcinoma have been reported in the literature. This case meets the criteria set forth by Cahan,³ which describe the necessary conditions for diagnosis of a radiation-induced neoplasm.

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Breast-conserving surgery followed by radiation is becoming increasingly popular for the treatment of early breast carcinoma. Since the work of Fisher⁴ and Veronesi,⁵ breast-conserving surgery followed by radiation has become a viable alternative to mastectomy for early breast lesions. As a result, greater numbers of women are being exposed to radiation and the attendant ill effects of this modality of treatment.

Radiation-induced sarcomas require a minimum latency period of 5 to 20 years.^{3,6} After the latency period, the risk of a sarcoma developing remains stable throughout life.³ This finding holds great interest with regard to our current therapy for early breast carcinoma. Breast-conserving surgery followed by irradiation has only become popular in a span of 8 to 9 years; this is also the approximate minimum latency period for the development of a radiation-induced sarcoma. Additionally, more women are living longer than the latency period necessary for radiation-induced sarcomas to develop. This case represents one of a potentially growing number of sarcomas of the chest wall developing after radiation therapy for breast carcinoma.

Report of case

The patient, a 48-year-old woman, was seen at the Chicago Osteopathic Hospital's General Surgery Clinic in November 1991 with a 6.0×5.0×3.0-cm exophytic weeping mass adherent to the medial inframammary soft tissues of the left breast (*Figure 1*). The patient reported that the tumor had been present for approximately 5 months. She delayed in reporting it to her physician because she thought the tumor was secondary to irritation from her brassiere.

The patient's history revealed that she had undergone a lumpectomy with axillary dissection for infiltrating duct cell carcinoma of the affected breast 5 years previously. At that time, the margins of resected breast tissue were free of tumor and none of the 11 sampled axillary lymph nodes showed evidence of tumor invasion.

One month after this surgery, the patient underwent postoperative radiation therapy. Treatment consisted of 25 fractions of cobalt 60 administered during a period of 45 days. Each fraction utilized 200 cG to the respective treatment field. Treatments were administered at a distance of 70 cm from the skin surface. No bolus was administered to the internal mammary nodes.

Five years after the initial surgery and radiation therapy, the patient was seen with the aforescribed mass

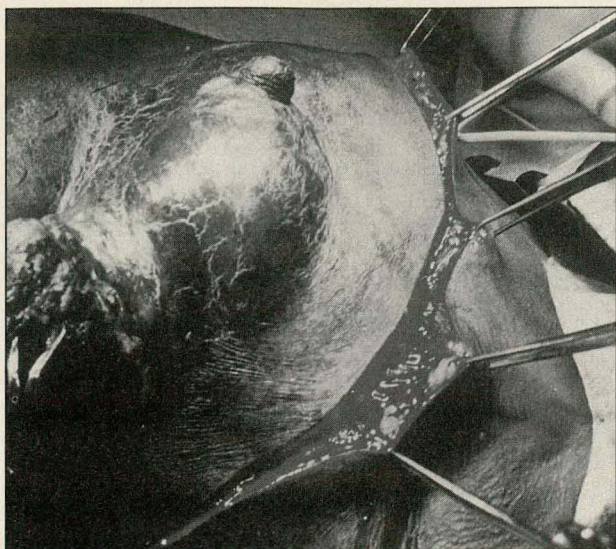


Figure 1. Postirradiation changes of left breast in patient with malignant fibrous histiocytoma adherent to lateral inframammary soft tissues.



Figure 2. High-power section shows pleomorphic fibroblast-like spindle cells arranged in a storiform pattern, typical of malignant fibrous histiocytoma. (Hematoxylin-eosin stain, original magnification $\times 400$.)

in the left breast. At the time of presentation, a core needle biopsy was performed. The biopsy specimen showed a "highly malignant" tumor on histologic inspection. No further diagnosis could be obtained from the specimen submitted. A completion mastectomy with split-thickness skin grafting to the chest wall defect was performed the next month. Further histologic inspection of the submitted tissue revealed a malignant fibrous histiocytoma with extension to the skin and deep resected margins.

Three months later, the pectoralis major muscle was excised in its entirety and split-thickness skin grafting

was performed as a delayed procedure. In May 1992, the patient returned with necrosis of the bone and soft tissues overlying the medial aspect of the fourth, fifth, and sixth ribs. This necrosis necessitated resection of the involved ribs in this region. Subsequent microbiologic and pathologic studies showed areas of osteomyelitis with no evidence of sarcomatous transformation. Currently, the patient continues to be alive and well without evidence of recurrent disease.

Discussion

The local effects of radiation after breast-conserving surgery are well known and include erythema, desquamation, hyperpigmentation, and edema of the skin as well as leukopenia, neuritis, and arm swelling.⁷ Of greater concern is the malignant potential caused by radiation therapy. Radiation exposure appears to increase the incidence of all cancers with the exceptions of chronic lymphocytic leukemia, Hodgkin's disease, cervical cancer, and a few others.⁸ Of interest with regard to this case is the induction of soft tissue sarcomas after breast irradiation.

Soft tissue sarcomas after breast irradiation are rare.^{2,9} The incidence of a sarcoma developing in an irradiated field is on the order of 0.3%, as reported by Karaparkar and associates.¹⁰ The prognosis after diagnosis is dismal. Survival times have ranged from 3 months¹¹ to 36 months,² with more recent studies showing a 32% 2-year survival rate.¹²

Multiple sarcomatous cell types have been described after breast irradiation. The most common cell types reported are osteogenic sarcoma and malignant fibrous histiocytoma.^{2,6,11} Other less common cell types have included chondrosarcomas and malignant mesenchymoma.^{6,9} Our report describes a malignant fibrous histiocytoma. This is a relatively new cell type classification describing a high-grade, highly malignant sarcoma. Histologically, the tumor is composed primarily of pleomorphic spindle and giant cells, with or without a storiform pattern, and demonstrating histiocytic or fibrocytic differentiation (Figure 2).¹³

The exact mechanism of radiation-induced carcinogenesis appears unclear. A potential sequence of events is described by Cole.¹⁴ His theory supposes that a radiation-sensitized cell mutates by primary exposure of the genetic apparatus or, indirectly, by damage to the extragenetic apparatus or activation of a latent virus. It is further theorized that radiation exposure causes a mutated cell to enter into mitosis earlier, with resultant regeneration.¹⁵ Although this is a simplification of the complex interaction of the effect of radiation at the cellular level, the net result is a neoplasm with malignant potential.

The diagnosis of a radiation-induced neoplasm can be difficult. Postradiation changes often result

in a cosmetically inferior, deformed breast. This makes detection of a new mass lesion difficult, even after close examination. Additionally, the postirradiation neoplasm is rare and will typically not express itself until more than 5 years after exposure.

These combined factors make diagnosis difficult and often result in a delay in diagnosis. The patient who is the subject of this report had a 5-month delay until the diagnosis was made. This difficulty in diagnosis is not unusual, as cited by Souba and colleagues.¹¹ The diagnosis of a radiation-induced sarcoma requires a high index of suspicion and must adhere to the requirements described by Cahan³ and modified by Souba and associates¹¹ to qualify as a "true" radiation-induced malignancy. The criteria are as follows:

- ☐ The sarcoma must develop in a previously irradiated field;
- ☐ a latent period of at least 5 years must exist from exposure until diagnosis of the sarcoma; and
- ☐ all cases must be proved histologically and be histologically different from the primary malignancy.

The treatment for radiation-induced sarcomas continues to be radical, with wide excision of the tumor with tumor-free margins.¹¹ Limited trials have been conducted with chemotherapeutic agents² for this aggressive tumor. However, the results of these treatment modalities have been largely disappointing. The reason for this poor response is unknown; however, it is thought to be caused by the fibrotic changes in the previously irradiated tissues. These changes are believed to result in poor levels of the agents in the target regions.² Currently, the best treatment for this aggressive tumor remains early diagnosis followed by wide excision of the affected region.

Comment

A sarcoma developed in the chest wall of a 48-year-old woman after treatment with breast-conserving surgery followed by irradiation. The latent period

for development of the sarcoma was 5 years after initial radiation exposure. Therapy consisted of a total of 5060 cG to the breast and axilla. This case adds to the rare but growing number of cases of sarcomas of the chest wall developing after breast-conserving surgery with subsequent radiation.

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