Breast Cancer Induced by Radiation

Relation to Mammography and Treatment of Acne

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• **This communication reports cases of 16 women in whom cancer of the breast developed after radiation therapy for acne or hirsutism, suggesting another group at higher risk than is generally expected for cancer of the breast. It is prudent to regard the carcinogenic effect of radiation on the breast as proportional to dose without a threshold. Mammography in young women should be ordered only selectively, not for screening.**

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HIGH RISK of breast cancer is said to be associated with genetic factors, preexisting benign breast disease, artificial menopause, family history of breast cancer, failure to breast-feed, older age at time of first pregnancy, high socioeconomic status, specific blood groups, fatty diet, obesity, and hormonal imbalances. But none of these factors is as certain a cause of cancer of the breast as is ionizing radiation.

According to the Biological Effects of Ionizing Radiation report of the National Academy of Sciences,[1] an excessive incidence of breast cancer occurs in the following populations of women exposed to high doses of ionizing radiation: (1) tuberculous women subjected to repeated fluoroscopy,[2,3] (2) women who are atom bomb survivors,[4] (3) women who received localized x-ray treatment for acute postpartum mastitis,[5] and (4) women who received irradiation of the chest in childhood,[6] for gynecomastia and hemangioma.

In 1965, MacKenzie[2] reported 40 cancers of the breast in women who had repeated fluoroscopic examinations in sanatoriums for pulmonary tuberculosis. Later,[3] more than 1,500 tuberculous patients who were treated at a Nova Scotia sanatorium had an incidence of cancer more than ten times that expected in the general population. Cancer of the breast developed about 17 years after radiation exposure and in a younger group than is usual.

The Adult Health Study of 12,000 female survivors and controls living in Hiroshima and Nagasaki at the time of the atomic bombing[4] showed an increase in the incidence of cancer of the breast when the breast or total body received more than 90 rads, and when the patient was young at the time of the bombing.

In a follow-up study of more than 600 women treated with x-rays for mastitis,[5] there were 13 cases of subsequent breast cancer instead of the expected 5.9 cases in a comparable group of women. In five of the 13 women with cancer, only one breast had been treated; in each of these cases, the cancer arose in the irradiated breast.

Lowell[6] reported the case of cancer of the breast in a 46-year-old man who, 35 years previously, had had therapeutic radiation to the same breast for prepubertal gynecomastia.

We have recently seen 16 patients with carcinoma of the breast who had been treated with radiation for acne and one who was treated for hirsutism at or about the age of 20 years, and in whom carcinoma of the breast developed more than 20 years later.

The age range at the time of diagnosis of cancer of the breast was 43 to 70 years (mean, 55 years). The time interval between irradiation for acne and appearance of cancer of the breast ranged from 25 to 52 years (mean, 33 years).

Some of these patients had other sequelae presumed to be associated with the irradiation for acne: four had skin cancers, and three had thyroidectomies for nodules (two benign, one malignant). Two patients had family histories of cancer of the breast.

REPORT OF CASES

CASE 1.—A 49-year-old woman had a radical mastectomy for a stage II carcinoma of the medial half of the breast. She was a healthy-looking, slender woman with tanned face and atrophy of the skin. She had some telangiectasis of the face and anterior chest, consistent in appearance with the late effects of radiation given for acne in 1945, when she was 24 years old. The details of the acne treatment are unavailable, but according to the history, the acne was present on the lower neck and presternal regions. The patient's skin was "unusually dry." In this instance, the mastectomy was done 25 years after the radiation therapy for acne. Metastases in bones and lungs appeared within 18 months, and death occurred four years after mastectomy.

CASE 2.—A 45-year-old married woman had received a number of x-ray treatments[7] for acne of the chest about 25 years before she had a mastectomy in March 1974; at that time, she had a ductal carcinoma of the left breast, with involved lymph nodes at all levels of the axilla. There was no definite indication of radiation skin changes from this acne treatment. The details of the therapy are not available, because the treatment was administered by a dermatologist who has died. In June 1974, a mastectomy was done for carcinoma of the other breast; there

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was again extensive involvement of the axillary lymph nodes. The patient subsequently died, despite oophorectomy, chemotherapy, and radiation therapy.

CASE 3.—A 75-year-old woman had cancer of the endometrium in June 1975, cancer of the colon in 1973, and cancer of the breast in 1970. A right radical mastectomy had been done. There was no evidence of cancer of the breast at the time we treated her for endometrial cancer. Noteworthy were shrinkage of the mouth and chin, atrophy, scarring, and telangiectasis of the face—all late effects of irradiation. The patient had received radiation therapy for hirsutism over a period of months in the early 1920s. From the practice of the day, it is likely that the anterior chest wall and breasts were also irradiated, although the chief damage was to the lower face. A basal cell cancer of the skin of the chin had been excised in 1972.

CASE 4.—A 48-year-old unmarried woman had cancer of the breast with metastases and died three years after mastectomy. Her skin was atrophic and pitted from acne scars. During her teens she had been treated by dermatologists for several years. Her skin showed telangiectasis and dryness, as seen after radiation therapy for acne. This patient's older sister also died of cancer of the breast.

CASE 5.—A 61-year-old married woman had a left radical mastectomy for cancer of the breast. As a teenager she had received radiation for acne. Her skin showed telangiectasis of the face and infraclavicular regions.

CASES 6 through 16.—Details of the more recent 11 additional cases are similar to those reported previously. As the possibility of the relationship between irradiation of acne and subsequent development of cancer of the breast was realized, such cases were recognized more frequently.

COMMENT

Irradiation for benign conditions like acne may not, by itself, cause breast cancer, but it is possible that it affects the incidence by superimposing a carcinogenic effect on a susceptible patient. Details of radiation exposure given many years previously are difficult to obtain. The patient in case 3, whose blood relative had cancer of the breast, is an example of an irradiated, susceptible woman.

We are in a period of enthusiasm for early diagnosis of breast cancer, including mammography for the detection of early tumors. The amount of radiation received in mammography varies with technique and equipment.[8] The soft-tissue technique for mammography produces a much larger dose to the skin on the tube side (entrance dose) than to the skin overlying the film or detector (exit dose). The dose of radiation to the breast falls off sharply as the breast is penetrated. Gilbertson and his associates[9] reported exposures on the entrance side of the breast of 10 to 20 R, depending on techniques. Crosby and Ty[10] describe low-dose film systems that reduce the skin dose to a range of 1.5 to 3.5 rads per exposure. The dose absorbed by the breast tissue is less than these entrance doses.

In contrast, the dose of radiation received by the survivors of the atom bomb in whom cancer of the breast subsequently developed was more than 90 rads; the tuberculous women who were repeatedly treated by fluoroscopy were estimated to have received from 50 to 6,000 rads; the women who were treated for mastitis probably had 30 to 700 rads exposure; and our patients with acne received 75 to 1,000 rads.

Estimates of dose are imprecise, but mammographic doses are in the range of tens of rads to the breast at each examination, and the effects of successive doses are cumulative. The American Cancer Society prudently advised that women less than 35 years old should be examined by mammography only for medical indication, not for so-called screening. The Food and Drug Administration also voiced its "word of caution" on mammography.[11]

Until recently, there has been enthusiasm for unrestrained use of mammography as a screening procedure, even in the young, but restraint is now more generally accepted. In a recent publication, John C. Bailar III, MD, of the National Cancer Institute,[12] analyzes reasons why promotion of mammography as a general health measure is premature.

In young women, particularly, there are factors that limit the benefits and increase the risks from mammography. The hazard of radiation carcinogenesis is greater in the young. The dense breasts of the young require greater exposure of radiation for penetration in mammography. Diagnosis in the dense breast is difficult; a small tumor can rarely be discerned in the midst of dense breast tissue. The yield of cancer finds in mammography is low in the young.

CONCLUSION

While it is not improbable that breast cancer could have developed by chance in a woman who had irradiation for acne in her youth, it appears more likely that the radiation contributed causally to the breast cancers in our series of cancer patients with previously irradiated acne.

Because multiple fluoroscopies, exposure to the atomic bomb, and radiation therapy for mastitis and gynecomastia (to which is added radiation therapy for acne and hirsutism) are probable causal factors in the development of breast cancer, we should now suggest that any radiation, unless absolutely indicated, should be withheld, especially from the young. In the same context, we would consider repeated mammography in young women as potentially carcinogenic. More studies on the safety of this useful diagnostic procedure in screening programs are needed.

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