

## RADIATION CARCINOGENESIS: AN UNUSUAL FAMILIAL OCCURRENCE OF NEOPLASIA FOLLOWING IRRADIATION IN CHILDHOOD FOR BENIGN DISEASE

DAVID G. SMITH, MD,\* AND SEYMOUR H. LEVITT, MD†

A patient is presented who developed a mucoepidermoid carcinoma of the parotid gland 30 years after irradiation to the area for benign disease. Family history revealed four siblings had likewise developed neoplasia in locations previously irradiated for benign disease. Types of neoplasia included basal and squamous cell carcinoma of the skin, thyroid adenomata, and benign mixed tumor of parotid gland. The patient's mother, occupationally exposed to irradiation, developed acute monocytic leukemia. Comparison of these findings with those in the literature is presented.

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**R**ADIATION CARCINOGENESIS IS AN ENTITY that is poorly understood but increasingly well documented. The unfortunate cases of early radiologists who developed radiation dermatitis and skin carcinoma from overexposure to radiation are well remembered.<sup>7</sup> More recently, an association between irradiation of the thymus in children and the later development of thyroid carcinoma has been convincingly presented.<sup>2,8,10,11</sup> Other types of neoplasia associated with prior irradiation include leukemia, carcinoma of mucous membranes, sarcoma, and salivary gland tumors.<sup>3-6,9</sup>

We recently treated a patient for mucoepidermoid carcinoma of the parotid gland who had a history of irradiation to the head for a benign condition as a child. In addition, the patient has four living siblings, all of whom have a past history of radiation treatments as children and the subsequent development of neoplasm in the treated area. This unusual family history forms the basis of this report.

From the Department of Therapeutic Radiology, University of Minnesota Medical School, Minneapolis, MN.

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\* Assistant Professor; American Cancer Society Junior Faculty Clinical Fellow.

† Professor and Head.  
Address for reprints: David G. Smith, MD, Dept. of Therapeutic Radiology, University of Minnesota Medical School, Box 494 Mayo, Minneapolis, MN 55455.

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### CASE REPORT

The patient, age 42, presented to her family physician in December of 1972 with painless swelling of the right parotid gland of 4 months' duration. The patient's past history included receiving irradiation to the neck and ear between the ages of 5 and 10 for an "ear problem." The irradiation had been administered by the patient's father, a radiologist, and also by her mother who worked as her father's office assistant. In her family history were her four living siblings who had also received irradiation as children to the head and neck area for benign processes and had later developed neoplasm in the treated areas. Other family history included a grandfather that had developed a malignancy on his cheek which was presumably a skin carcinoma. The patient's mother died of acute monocytic leukemia. She had worked in the father's office and was, therefore, frequently exposed to radiation. The patient's father died suddenly of an unknown cause, but presumably related to cardiovascular disease.

On physical examination, the patient was found to have a firm swelling anterior to the right ear in the area of the parotid gland. The remainder of the physical examination was unremarkable. Routine laboratory studies and chest roentgenogram were within normal limits.

The patient was taken to surgery and a total right parotidectomy was performed. Because of the questioned adequacy of surgical margins, the patient was referred to our de-

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partment for postoperative irradiation. On our examination, the patient had skin changes secondary to the surgery but only minimal changes secondary to the previous radiation. This included a slight degree of hyperpigmentation of the treated skin. The patient was treated with a wedge pair technique over the parotid bed, utilizing cobalt. The treated volume was carried to 5000 rad in 5 weeks time; a similar dose was delivered to the ipsilateral neck. The patient tolerated the treatment well. No sign of recurrence has been noted now 10 months following the radiation.

#### Family History

In pursuing the history of neoplasia developing in the patient's siblings, a questionnaire was sent to the siblings and responses documented. Their personal physicians were contacted; they contributed information regarding diagnoses and treatment. Slides were obtained from the physicians, and reviewed in the Pathology Department at the University of Minnesota. In talking with the siblings, the following information was obtained. Treatments were directed to the area of the external ear, mastoid, nasopharynx, and neck areas because of problems with otitis media, lymphadenitis, adenoid hypertrophy, etc. Some of the siblings remembered receiving more than one course of treatment. Radiation was administered with an orthovoltage machine, energy unknown, and also by a radium source

which was kept in the patient's father's office. Records of radiation treatments have been since destroyed and hence an accurate assessment of dose delivered is impossible. A summary of the family history is presented in Table 1.

Three siblings developed more than one site of neoplasia in the treated areas; Sibling 1 developed two basal carcinomas of the skin of the neck 3 years apart. Sibling 2 developed a basal cell carcinoma of the earlobe and simultaneously had three benign thyroid adenomata removed. Sibling 4 developed a squamous cell carcinoma of the postauricular area and 2 years later a basal cell carcinoma of the skin of the opposite neck. Only Sibling 5 has not developed a malignancy in the treated area, but did develop a mixed tumor of the parotid gland. One other sibling not mentioned in the history died at approximately age 40 of an unknown cause. As far as is known, he did not develop neoplastic disease.

#### DISCUSSION

Our patient, developing a mucoepidermoid carcinoma of the parotid at age 42, seems to confirm Ju's<sup>6</sup> observation that development of salivary gland tumors is a late phenomenon after radiation exposure. On the average, 25 years' lag existed between irradiation and development of salivary gland tumors in his

TABLE 1. Family History of Neoplasmas Following Childhood Irradiation

Subject sex	present age	Age when irradiated for benign disease	Age at discovery of neoplasm	Lag between radiation and neoplasm (yrs)	Type of neoplasm	How treated
#1 F	46	5-10	37	27-32	Basal cell carcinoma, left neck	Excision
			40	30-35	Basal cell carcinoma left neck	Excision and cautery
#2 F	44	5-10	31	21-26	Basal cell carcinoma, left earlobe	Excision and graft
			31	21-26	Benign thyroid adenomata	Left hemithyroidectomy
#3 F	42 (current patient)	5-10	42	32-37	Mucoepidermoid carcinoma, parotid gland (right)	Excision and postop. radiotherapy
#4 M	40	5-10	32	22-27	Squamous cell carcinoma, post-auricular area	Radiotherapy
			34	24-29	Basal cell carcinoma, right neck	Curretage and cautery
#5 M	36	5-10	23	13-18	Mixed tumor parotid gland	Excision
#6 F (Mother—deceased)		Occupational exposure	Acute monocytic leukemia			

series. However, all of Ju's cases developed skin carcinoma at an earlier period—an average of 14 years following irradiation. Our patient did not develop skin malignancy prior to the development of her salivary gland tumor; however, her siblings developed skin carcinoma at an earlier age than that at which she developed the parotid tumor.

That salivary gland tumors can be related to prior irradiation exposures is further corroborated by study of atomic bomb survivors by Belsky et al.<sup>1</sup> Salivary gland tumors were increased more than five-fold amongst survivors of atomic bombs who had been exposed to high doses of radiation. This was felt to be

highly significant in regard to development of malignant salivary gland tumors following irradiation.

Unfortunately, we are unable to determine the dose of irradiation received by our patient and her siblings. However, the unusual familial occurrence of neoplasm in areas previously treated with irradiation appears highly significant and related to radiation carcinogenesis. The additional fact of the patient's mother developing leukemia following prolonged exposure to radiation likewise appears significant in view of the strong relationship existing between prior irradiation and incidence of leukemia.

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