REFERENCES

CLINICAL VIGNETTE

Radiation-Induced Thyroid Cancer

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Case Report
A 63-year-old woman with a history of breast cancer presented to her primary care physician concerned about her weight gain and mouth sores. Canker sores and thyromegaly were noted, and the initial workup included thyroid function tests and a thyroid ultrasound. She was euthyroid but the ultrasound revealed a 6 mm right lobe nodule and a 7 mm nodule in the left lobe, both well circumscribed. She was referred to an Endocrinologist for further workup.

Aside from weight gain, she had no hyper or hypothyroid symptoms, no recollection of having been told of a goiter or obstructive symptoms. She initially denied a history of head and neck irradiation or shoebox irradiation in youth, but on further questioning recalled receiving about ten x-ray treatments to her axillae for hidradenitis in her early teens. She recalled that everyone stepped out of the room for the treatments. Previous medical history was remarkable for excision of in-situ breast cancer. She denied a family history of thyroid disorders or thyroid cancer. Her father developed colon cancer at age 90.

Her examination was remarkable for mild obesity and surgical scars in the axillae and breasts. She had radiation skin changes in the axillae but no axillary or cervical adenopathy. Palpation of the thyroid disclosed a normal sized gland with bilateral prominence of the lobes and suggestion of a left upper lobe nodule. She appeared clinically euthyroid and the remainder of the exam was unremarkable. Thyroid function tests were normal, thyroid antibodies were negative, and the thyroid ultrasound showed the two small hypoechoic nodules described above.

Ultrasound-guided fine needle aspiration biopsy of the nodules disclosed papillary carcinoma in the left lobe nodule.

Discussion
In the 1940's and 1950's radiation treatments were given for a variety of conditions and fluoroscopy boxes were even used to help fit children's shoes. The radiation exposure may be difficult to confirm, but x-rays were most likely used if the patient's mother had to leave the room for the therapy. Patients who received UV treatments on the other hand often recall
parents or nurses in the room with them and a purple light. Dermatology treatments for cystic acne or hidradenitis may have involved penetrating x-rays. Lower levels of radiation exposure to the thyroid occurred with placement of radiation-tipped rods through the nose to shrink tonsils and adenoids. The thyroid is very radiation-sensitive, however, and even low doses increase the risk of cancer with a linear dose response curve. Even when the thyroid gland is outside of the field of radiation, an increased risk of thyroid cancer has been noted following radiation treatment in childhood for Hodgkin and non-Hodgkin lymphomas, acute lymphocytic leukemia, Wilm's tumor, neuroblastoma, and central nervous system tumors. No increased risk for thyroid cancer is seen after diagnostic I\(^{131}\) testing in childhood. Younger age at exposure increases the risk of thyroid cancer up to about 16-years-old, and the effects persist for decades. Even small doses of radiation exposure cause DNA damage including somatic rearrangements of the two transmembrane tyrosine kinase genes RET and NTRK1. Growth pathways are stimulated by activating rearrangements of the RET oncogene after exposure to ionizing radiation. Papillary carcinomas result from mutations in these oncogenes, as studied in children exposed to external radiation treatments and those exposed in the Chernobyl nuclear accident.

The history of childhood radiation exposure must alert the physician to look especially carefully for thyroid nodules. If a palpable lesion is found, ultrasonography should be done to look for multiple nodules, more common in radiation-exposed patients. All nodules should be biopsied whether palpable or found by ultrasound. Even with no palpable nodule, ultrasonography is recommended if there is a clear history of high dose radiation exposure at young age, history of another radiation-related tumor, or a sibling with a history of radiation-related tumor. Screening irradiated populations revealed that many of the thyroid cancers found were small (52% less than 10mm.) and early detection at a small size was associated with a lower recurrence rate after surgery.

Fine needle aspiration biopsy of thyroid nodules must guide management. Unless all nodules are confirmed benign on biopsy, surgery is recommended. A total thyroidectomy is recommended for radiation-induced thyroid cancer because of frequent multicentric tumors. Age, tumor size, metastases, invasiveness, and histology affect the prognosis of thyroid cancers found in radiation-exposed patients as in non-exposed thyroid cancers, and post surgical treatment is similar. If the thyroid nodules are benign, and surgery is not recommended the physician must monitor patients as high risk for life, with annual palpation and repeat ultrasonography periodically. This is one case where Endocrinologists agree that thyroid hormone suppression therapy should be used in management of benign nodules. The physician must also monitor these patients for development of other radiation-sensitive tumors including parathyroid and salivary gland tumors, as well as schwannomas or meningiomas of neural origin.

REFERENCES