The Laryngoscope

Case Report

EGFR Expression in Primary Squamous Cell Carcinoma of the Thyroid

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We present the case of a 57-year-old male with primary squamous cell carcinoma of the thyroid (PSCCT). Epidermal growth factor receptor (EGFR) staining was strongly positive. Pharmaceuticals targeting EGFR may provide an additional therapeutic option for this rare disease with extremely poor prognosis.

Key Words: Thyroid, EGFR, squamous cell carcinoma.

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INTRODUCTION

A 57-year-old male presented with a two-month history of an enlarging neck mass. His past medical history was significant only for a vascular malformation of the tongue, which was treated with radiation as a child. Physical exam revealed a 4-cm firm mass within the thyroid isthmus. The remainder of the head and neck exam, including flexible laryngoscopy, was normal. Computed tomography (CT) scan confirmed the mass within the thyroid gland. Positron emission tomography (PET) was positive in the thyroid region with no other areas of enhanced activity.

A fine needle aspiration of the mass yielded atypical cells suspicious for malignancy. The patient underwent a total thyroidectomy with selective central neck dissection and bilateral neck exploration. The thyroid mass was found to nearly completely replace the isthmus and extend into both the left and right thyroid lobes. Several palpable lymph nodes were removed separately.

Pathologic analysis demonstrated a 4.5-cm necrotic tumor mass within the thyroid. Microscopic examination was remarkable for a well-differentiated squamous cell carcinoma arising from a background of Hashimoto's thyroiditis (Fig. 1). Sections labeled with antibodies against epidermal growth factor receptor (EGFR) were strongly positive (Fig. 2). Four lymph nodes were positive for metastatic squamous cell carcinoma (SCC).

The patient had an uncomplicated postoperative course. A repeat PET scan showed no areas of increased tracer uptake. He underwent postoperative radiation therapy to the thyroid bed and bilateral necks, and concurrent cisplatin-based chemotherapy. The patient is currently alive one year after surgery with no evidence of disease.

DISCUSSION

Primary squamous cell carcinoma of the thyroid (PSSCT) is rare; the largest case series included 10 patients assembled over 25 years.[1] Patients are predominantly female and usually over 50 years old at presentation, although pediatric and young adult patients have been reported in conjunction with Hashimoto's thyroiditis. Diagnosis requires exclusion of other sites of squamous cell carcinoma, since metastatic disease to the thyroid is much more common than primary thyroidal SCC.

The squamous cells are thought to arise from metaplasia of follicular epithelial cells; alternatively, they may be remnants of the thyroglossal duct or ultimobranchial body. Factors inciting metaplastic change and malignant degeneration are unknown. Squamous metaplasia is a common finding in other thyroid conditions including papillary and anaplastic carcinomas. Squamous cell carcinoma has also been found to coexist with other thyroid carcinomas and Hashimoto's thyroiditis. This patient had radiation exposure in childhood, a known risk factor for other types of thyroid cancers.

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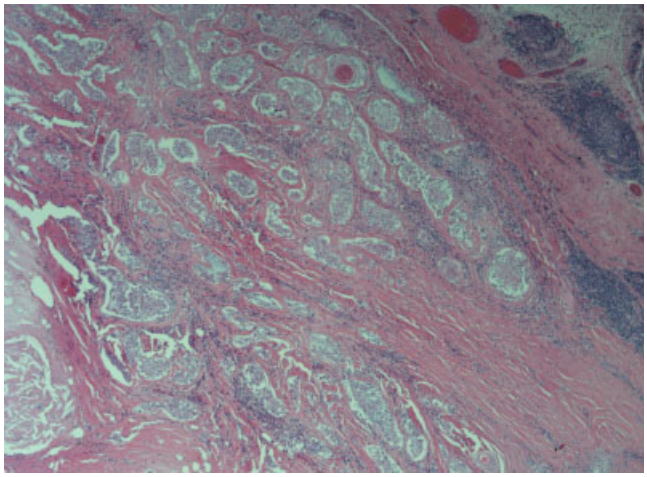

Fig. 1. Hematoxylin and eosin stain of thyroid tumor specimen. Tumor necrosis is seen on the left, squamous cell carcinoma in the center, and Hashimoto's thyroiditis on the right. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

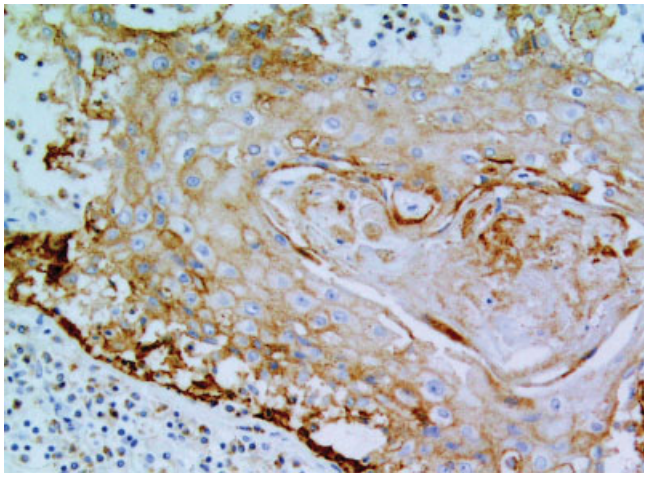

Fig. 2. Epidermal growth factor receptor (EGFR) immunohistochemistry (peroxidase stain) is strongly positive in the carcinoma cells. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

However, no other cases of PSCCT occurring after radiation were identified in the literature.

PSCCT has a dismal prognosis, with most patients dying within one year. The mainstay of treatment has been complete surgical resection followed by radiotherapy. Radiosensitizing chemotherapy and postradiation chemotherapy have also been advocated but performed in only limited numbers of patients.

Epidermal growth factor receptor (EGFR) is a tyrosine kinase-signaling molecule active in many epithelial cancers, including squamous cell carcinoma in the head and neck. Its constitutive activation or overexpression promotes cell proliferation and survival. EGFR is found in the cytoplasm and nuclei of normal and goiterous thyroid tissues where it also promotes cell proliferation and inhibits differentiated thyroid function.[2] Several studies have also demonstrated EGFR in anaplastic thyroid carcinoma, with a total of 107 of those 158 tumors (67%) rated as overexpressing EGFR.[3–7] Less evidence for EGFR activity in differentiated thyroid carcinomas exists.

Only one prior study addressed epidermal growth factor in thyroid SCC. EGF binding to 43 benign and malignant thyroid specimens was quantified. One SCC was included, although it was unclear whether that was a primary thyroidal or a metastatic tumor. The SCC exhibited 16 times the binding capacity for EGF of normal thyroid tissues, with equivalent affinity coefficients. These data suggested EGFR upregulation without change in receptor binding affinity. One-third of the other thyroid cancer specimens also bound more EGF than normal thyroid, but none were as dramatically increased as the SCC.[8]

CONCLUSIONS

This report documents EGFR overexpression in a primary SCC of the thyroid. Given the prevalence of EGFR in SCC of other sites, it may also be commonly overexpressed or activated in PSCCT. These preliminary results prompt consideration of EGFR as a therapeutic target for this aggressive disease.

BIBLIOGRAPHY

1. Booya F, Sebo TJ, Kasperbauer JL, Fatourechi V. Primary squamous cell carcinoma of the thyroid: report of ten cases. *Thyroid* 2006;16:89–93.
2. Marti U, Ruchti C, Kämpf J, et al. Nuclear localization of epidermal growth factor and epidermal growth factor receptors in human thyroid tissues. *Thyroid* 2001;11: 137–145.
3. Wiseman SM, Masoudi H, Niblock P, et al. Anaplastic thyroid carcinoma: expression profile of targets for therapy offers new insights for disease treatment. *Ann Surg Oncol* 2007;14:719–729.
4. Lee DH, Lee GK, Kong SY, et al. Epidermal growth factor receptor status in anaplastic thyroid carcinoma. *J Clin Pathol* 2007;60:881–884.
5. Murakawa T, Tsuda H, Tanimoto T, Tanabe T, Kitahara S, Matsubara O. Expression of KIT, EGFR, HER-2 and tyrosine phosphorylation in undifferentiated thyroid carcinoma: implication for a new therapeutic approach. *Path Int* 2005;55:757–765.
6. Schiff BA, McMurphy AB, Jasser SA, et al. EGFR is overexpressed in anaplastic thyroid cancer, and the EGFR inhibitor gefitinib inhibits the growth of anaplastic thyroid cancer. *Clin Cancer Res* 2004;10:8594–8602.
7. Ensinger C, Spizzo G, Moser P, et al. EGFR as a novel therapeutic target in anaplastic thyroid carcinoma. *Ann NY Acad Sci* 2004;1030:69–77.
8. Kanamori A, Abe Y, Yajima Y, Manabe Y, Ito K. Epidermal growth factor receptors in plasma membranes of normal and diseased thyroid glands. *J Clin Endocrinol Metab* 1989;68:899–903.