Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofSurgicalResearch.com

Squamous differentiation in papillary thyroid carcinoma: a rare feature of aggressive disease

Toni Beninato, MD,[a,b] *Wouter P. Kluijfhout, MSc, PhD,*[a,c] *Frederick Thurston Drake, MD, MPH,*[a,d] *Elham Khanafshar, MD,*[e] *Jessica E. Gosnell, MD,*[a] *Wen T. Shen, MD,*[a] *Quan-Yang Duh, MD,*[a] *and Insoo Suh, MD*[a,*]

[a] *Department of Surgery, University of California, San Francisco, San Francisco, California*
[b] *Department of Surgery, New York Presbyterian Hospital-Weill Cornell Medicine, New York, New York*
[c] *Department of Surgery, University Medical Center Utrecht, Utrecht, The Netherlands*
[d] *Department of Surgery, Boston University School of Medicine, Boston, Massachusetts*
[e] *Department of Pathology, University of California, San Francisco, San Francisco, California*

ARTICLE INFO

Article history:
Received 6 July 2017
Received in revised form
15 September 2017
Accepted 12 October 2017
Available online xxx

Keywords:
Papillary thyroid cancer
Squamous differentiation

ABSTRACT

Background: Papillary thyroid carcinoma with squamous differentiation (PTC-SD) is a poorly understood pathologic finding of unknown clinical significance. Selected case reports have suggested that PTC-SD is an aggressive tumor with a poor prognosis. Here we present the largest case series of PTC-SD reported in the United States.

Materials and methods: The cancer registry at our tertiary care referral center was reviewed to identify all patients from 1995-2015 who had been diagnosed with PTC-SD on initial total thyroidectomy or lymph node dissection for recurrent disease. All cases were reviewed by an endocrine pathologist to confirm the diagnosis. Patient demographic, pathology, and outcomes data were collected and reviewed.

Results: During the study period, ten patients were diagnosed with PTC-SD, six in the primary tumor at the time of initial surgery, and four in lymph node metastases during surgery for recurrent disease. The median age at diagnosis was 56 y and half of the patients were male. Aggressive features such as multifocality (67%), extrathyroidal extension (67%), positive margin (89%), lymph node metastases (80%), and extranodal extension (60%) were far more prominent than is typically seen in classic PTC. Long-term follow-up (median 56.5 mo) demonstrated high rates of locoregional recurrence (60%), pulmonary metastases (30%), and mortality (10%).

Conclusions: Squamous differentiation is a rare finding in PTC that is associated with aggressive pathologic features and poor long-term outcomes. This phenomenon may represent a step in progression toward dedifferentiation; thus, patients with PTC-SD should have close, life-long surveillance and should be treated according to evidence-based guidelines for high-risk thyroid cancers.

* *Corresponding author*. University of California, San Francisco, Mount Zion 1600 Divisadero Street, San Francisco, CA 94115. Tel.: +1 415 885 7616; fax: +1 415 885 7617.
E-mail address: insoo.suh@ucsf.edu (I. Suh).
0022-4804/$ – see front matter © 2017 Elsevier Inc. All rights reserved.
https://doi.org/10.1016/j.jss.2017.10.023

Introduction

Squamous cells are rarely found in normal thyroid tissue. They may represent embryologic remnants of the thymus, ultimobranchial body, or thyroglossal duct. They may also occur as benign squamous metaplasia of follicular epithelium in inflammatory conditions such as Hashimoto's thyroiditis or adenomatous goiter. Finally, they can rarely occur as neoplasms.[1]

Neoplastic squamous cells in the thyroid, though rare, can take multiple forms. They may present as a primary squamous cell carcinoma of the thyroid or as a metastatic squamous cell carcinoma from the oropharyngeal tract.[1] Malignant squamous cells may also be associated with a well-differentiated thyroid cancer as either a squamous cell carcinoma or with anaplastic components as an anaplastic spindle cell squamous carcinoma.[2-4] Pure squamous cell carcinoma of the thyroid associated with a well-differentiated thyroid cancer and without anaplastic or poorly differentiated components is often referred to as squamous differentiation (SD). The malignant squamous cells are postulated to have "dedifferentiated" from the well-differentiated component.[5]

The incidence of well-differentiated thyroid cancer has been increasing, and survival for these tumors remains excellent, which has led to less aggressive recommendations for surgical and adjuvant therapy. However, there still remain subtypes of thyroid cancer that have a poorer prognosis and therefore should be identified and treated aggressively.[6] Well-differentiated thyroid cancer with SD is a rare finding, and there are multiple case reports suggesting that this association predicts a poor prognosis.[7-13] However, it remains a poorly understood pathologic finding of unknown clinical significance. Here, we present a series of patients with papillary thyroid carcinoma with squamous differentiation (PTC-SD).

Materials and methods

The cancer registry at our tertiary care referral center at the University of California, San Francisco was reviewed to identify all patients from 1995-2015 who had been diagnosed with PTC-SD on initial total thyroidectomy or on lymph node dissection for recurrent disease. A retrospective chart review was completed to collect information on patient demographic and clinical data such as age, sex, preoperative diagnosis, and extent of surgery. Pathology reports were reviewed to determine tumor size, subtype, aggressive features such as extrathyroidal extension and presence of tumor cells at the inked surgical margin, and presence or absence of lymph node metastases and extranodal extension of tumor. The presence of SD was confirmed by reviewing the pathology slides. SD was defined as malignant-appearing squamous elements consisting of cells with dense keratinized and eosinophilic cytoplasm, high nuclear-to-cytoplasmic ratio, irregular nuclear contour, coarse or dark chromatin, prominent nucleoli, and occasional squamous pearl formation. The squamous portion of the tumor comprised less than half of the primary tumor. Details on postoperative treatment such as radioactive iodine (RAI), external beam radiation, and chemotherapy were collected. Follow-up data including time to recurrence, length of follow-up, distant metastases, and patient mortality were also reviewed. Patients with benign-appearing squamous metaplasia, primary squamous cell carcinoma of the thyroid, anaplastic carcinoma, or concurrent squamous cell cancer of the oropharyngeal tract were excluded. All cases were reviewed by an endocrine pathologist to confirm the diagnosis. This study was done with approval of the Committee on Human Research which is the institutional review board at the University of California, San Francisco.

Results

From 1995-2015, there were ten patients who had PTC-SD on final pathology. Six patients had PTC-SD in their primary tumor specimen at the time of initial thyroidectomy, and four patients had PTC-SD in lymph node metastases found during surgery for recurrent disease.

Table 1 – Descriptive characteristics of patients with papillary thyroid carcinoma with squamous differentiation at primary surgery.

Patient	Age	Sex	Procedure	Pathology	Complications	Follow-up (months)
1	8	Female	Total thyroidectomy with lymph node dissection	PTC-SD	None	158
2	58	Female	Total thyroidectomy	PTC-SD	None	3
3	15	Female	Total thyroidectomy with lymph node dissection	PTC-SD	None	72
4	60	Male	Total thyroidectomy	PTC-SD	Right vocal cord paralysis (involved with tumor)	31
5	53	Female	Total thyroidectomy with lymph node dissection	PTC-SD	Lymphatic leak requiring thoracic duct embolization	10
6	48	Male	Total thyroidectomy	PTC with <50% tall cells and SD	None	17