Ochsner Journal 17:438–441, 2017

Invasive Insular Thyroid Carcinoma Presenting as Nonparalytic Dysphonia

Blake S. Raggio, MD,[1] Blair M. Barton, MD,[1] Maria C. Grant, MD,[1] Judith A. Fornadley, MS, CCC-SLP,[2] Jeffrey P. Marino, MD[2]

[1]Department of Otolaryngology – Head and Neck Surgery, Tulane University School of Medicine, New Orleans, LA [2]Department of Otolaryngology, Ochsner Clinic Foundation, New Orleans, LA

Background: Patients with suspected thyroid malignancy often undergo preoperative laryngeal examination with a focus on vocal fold mobility. We present the unique case of a patient with invasive thyroid carcinoma who presented with dysphonia despite intact vocal fold motion.

Case Report: A 73-year-old female with a remote thyroid lobectomy presented with dysphonia. Thyroid ultrasound and fine-needle aspiration revealed a 1.1-cm nodule consistent with a colloid cyst. Videostroboscopy demonstrated mild laryngeal stenosis at the glottis and infraglottis with no evidence of paralysis. After failed medical therapy, the patient underwent microlaryngoscopy with biopsy of her infraglottic fullness, with histopathology reporting squamous epithelium without nucelar atypia. After several weeks of worsening dysphonia and persistent infraglottic fullness, she underwent repeat microlaryngoscopy with biopsy. On postoperative day 1, she developed dyspnea and stridor refractory to maximal medical management. To secure the airway, she underwent an awake tracheostomy, during which the thyroid isthmus was found to be densely adherent to the larynx. Histopathology identified insular thyroid carcinoma. Subsequent imaging confirmed a large, invasive thyroid tumor. Further workup revealed metastases to the bone and liver. The patient underwent a successful palliative resection of the thyroid followed by neck radiation and received palliative spinal surgery with adjuvant radiation. A clinical trial of vandetanib was initiated but withdrawn because of myelosuppression. She deferred any further treatment and was alive with few symptoms despite persistent disease 1.5 years after initial diagnosis.

Conclusion: Physicians should consider the diagnosis of invasive thyroid carcinoma in a dysphonic patient with an infiltrative endolaryngeal process despite intact vocal fold mobility.

Keywords: *Aged, dysphonia, hoarseness, larynx, thyroid neoplasms*

Address correspondence to Jeffrey P. Marino, MD, Department of Otolaryngology, Ochsner Clinic Foundation, 1514 Jefferson Hwy., New Orleans, LA 70121. Tel: (504) 842-4080. Email: jeffrey.marino@ochsner.org

INTRODUCTION

Insular carcinoma (IC) is a rare, poorly differentiated form of thyroid carcinoma that accounts for approximately 0.1%-6.2% of thyroid malignancies.[1,2] This distinct variant of thyroid cancer is thought to be an intermediate between well-differentiated and anaplastic thyroid carcinoma, with discrete nests (insulae) of cells displaying frank capsular and vascular invasion.[3] IC is capable of presenting as advanced, local, or even metastatic disease.[1,2] The optimal treatment for IC involves total thyroidectomy, lymph node dissection, and radioactive iodine therapy; nevertheless, prognosis is poor. To our knowledge, this is the first report of IC in which the primary concern was acute nonparalytic dysphonia.

CASE REPORT

A 73-year-old female presented with increased vocal effort, decreased vocal projection, vocal fatigue, and vocal strain that she reported had been present for 6 months since attending a wedding. Her Voice Handicap Index-10 score (a 10-item questionnaire that subjectively measures voice handicap [an abnormal score is >11]) was 4.[4] Her voice was worse with use but showed mild improvement after periods of voice rest. She denied any dyspnea or sonorous breathing. The patient had undergone left thyroid lobectomy 40 years prior to presentation for an unknown, reportedly benign, tumor. Recent surveillance thyroid ultrasound performed by an experienced ultrasound technologist certified by the American Registry for Diagnostic Medical Sonography had identified a 1.1-cm nodule with coarse calcifications in the remaining thyroid bed (Figure 1), and fine-needle aspiration (FNA) demonstrated scant colloid material consistent with a colloid cyst. Because of her lack of compressive symptoms and her history of previously resected benign thyroid tumor, the patient

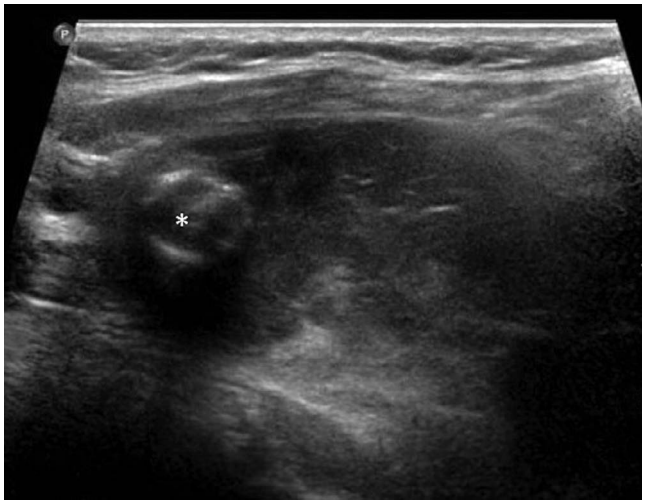

Figure 1. Thyroid ultrasound in vertical axis shows a 1.1-cm nodule (asterisk) with coarse calcification identified within the superior aspect of the right lobe.

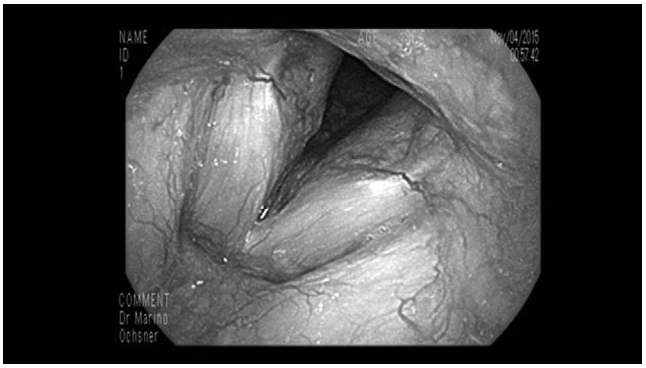

Figure 2. Flexible videostroboscopy demonstrates diffuse, nearly symmetric, submucosal fullness of the bilateral true vocal folds with increased convexity and hypervascularity of the immediate infraglottic free edges.

deferred a repeat FNA and elected continued observation with serial ultrasounds. Her medical history was otherwise noncontributory.

During examination, the patient's voice was characterized by mild roughness and strain. An overall score of 30 was obtained with the Consensus Auditory-Perceptual Evaluation of Voice scale (visual analog scale for rating the parameters of overall severity, strain, breathiness, roughness, pitch, and loudness [maximum severity equals 100]).[5] Maximum phonation time (clinical measurement of the longest time one can phonate a vowel [normal is 20.96 seconds]) was 13 seconds.[6] Her connected speech fundamental frequency, a measure of the frequency of a person's voice, was 179 Hz; the normal value for a female her age is 170.6.[7] Flexible laryngeal videostroboscopy demonstrated diffuse, nearly symmetric, submucosal fullness of the bilateral true vocal folds and infraglottis, with hypervascularity and increased convexity of the immediate infraglottic free edges of the vocal folds, resulting in overclosure of the glottis during phonation. Pliability was preserved but reduced bilaterally. Both cricoarytenoid joints were fully mobile, without any evidence of paralysis or paresis (Figure 2). Initial differential diagnoses included amyloidosis, granulomatosis with polyangiitis, idiopathic laryngeal stenosis, chronic infectious laryngitis, severe reflux laryngitis, intrinsic laryngeal neoplasm, and thyroid neoplasm. She was initially treated with a 6-day course of an oral steroid taper (4-mg Medrol [methylprednisolone] Dosepak) and antireflux medication (40-mg omeprazole daily) for 2 weeks. After experiencing no improvement in her symptoms, the patient elected to undergo a suspension microlaryngoscopy with biopsy of her infraglottic fullness. Initial pathologic evaluation was nondiagnostic but negative for neoplasia or amyloidosis.

During the next several weeks, the patient exhibited worsening dysphonia with persistence of her infraglottic fullness. She underwent repeat suspension microlaryngoscopy and CO_2 laser relief of her persistent laryngeal stenosis. The patient was discharged home the same day without complications. On postoperative day 1, however, the patient presented to the emergency department with acute dyspnea and stridor that minimally improved with systemic steroids (8-mg intravenous dexamethasone [Decadron] every 8 hours), 900-mg intravenous clindamycin every 8 hours, nebulized breathing treatments, and humidified oxygen. The recommendation was made to stabilize the airway via awake tracheostomy because of her persistent laryngeal stenosis in the setting of acute dyspnea. During tracheostomy, the thyroid isthmus was found to be densely adherent to the laryngotracheal complex. Biopsies of the thyroid and endolaryngeal fullness revealed follicular Hürthle cell–type thyroid carcinoma with areas of IC (Figure 3).

Postoperative imaging confirmed the presence of a large and invasive thyroid tumor (Figure 4) with evidence of bony (spine, pelvis) and liver metastases that were confirmed by respective biopsies. Palliative surgical resection of the thyroid tumor was performed that included a total thyroid-

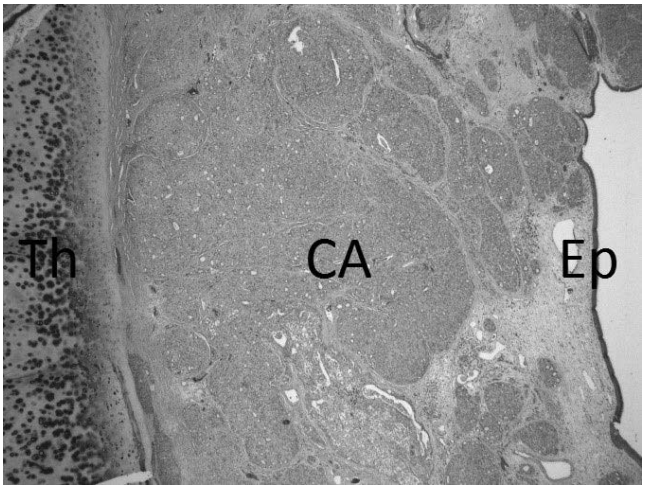

Figure 3. Hematoxylin and eosin stain at 10× magnification demonstrates thyroid cartilage (Th), invasive thyroid carcinoma (CA), and intact endolaryngeal columnar respiratory epithelium (Ep).

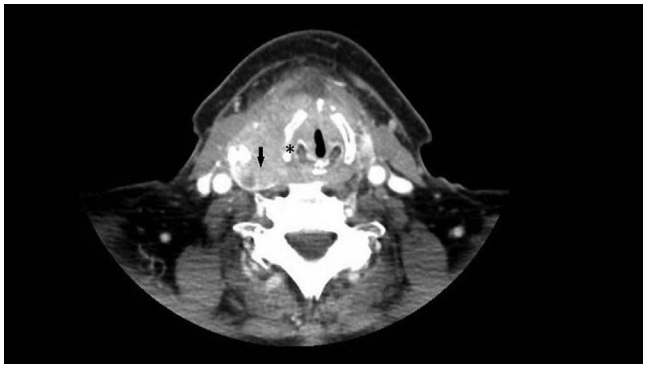

Figure 4. Axial computed tomography scan with contrast demonstrates a heterogeneous thyroid mass (arrow) with areas of necrosis as well as calcification and invasion of the paraglottic space (asterisk).

ectomy, total laryngectomy, and paratracheal lymphadenectomy with adjuvant neck radiation therapy (60 Gy). She also underwent a posterior thoracic laminectomy and spinal fusion for decompression of the intraspinal extradural tumor, followed by radiation therapy to the spine and pelvic lesions (30 Gy). A clinical trial of vandetanib 300 mg once daily was initiated but withdrawn because of myelosuppression. She deferred any further treatment (ie, radioactive iodine, clinical trials) or imaging because of her lack of significant symptoms and was alive, with preservation of her activities of daily living despite persistent disease, during follow-up 1.5 years after diagnosis.

DISCUSSION

Dysphonia affects nearly one-third of the population at some point in their lives and has multiple etiologies, including thyroid malignancy.[8] As many as 8%[9] of patients with malignant thyroid disease present with vocal fold motion impairment preoperatively, including 70%[10] of patients with invasive thyroid malignancy.[11] The American Academy of Otolaryngology recommends that a laryngeal examination be performed in dysphonic patients prior to thyroidectomy as well as in patients without dysphonia who are suspected to have invasive thyroid malignancy.[11] These recommendations, however, are focused on identifying the presence or absence of vocal fold motion impairment.

Interestingly, our patient's dysphonia was not secondary to vocal fold motion impairment. This case demonstrates that a patient with invasive thyroid carcinoma may present with nonparalytic dysphonia because of submucosal invasion of the paraglottic space. Thus, evidence of an infiltrative endolaryngeal process should raise suspicion for invasive thyroid malignancy despite intact vocal fold mobility.

Regarding the use of imaging in the workup of dysphonic patients, Schwartz et al recommend that imaging should be used to assess for specific pathology only after the larynx has been visualized.[8] After laryngoscopy, evidence supports the use of imaging to further evaluate either vocal fold paralysis or a mass or lesion of the larynx that suggests malignancy or airway obstruction.[12] Our patient exhibited neither of these findings on laryngoscopy to warrant imaging, nor did she report any signs or symptoms consistent with invasive thyroid malignancy other than dysphonia. Evidence of laryngeal invasion was not discovered until after her third procedure.

IC portends a significantly worse prognosis compared to well-differentiated thyroid carcinoma but has improved survival compared to anaplastic thyroid carcinoma.[1] IC frequently presents with local invasion, lymph node metastasis (26.3%),[1] and distant metastasis (36.4%-84.6%)[2] as in our case. Although our patient presented with isolated nonparalytic dysphonia, symptoms vary depending on severity of disease and are known to include the presence of a neck mass, compressive symptoms (dysphagia, dyspnea), or breathy dysphonia resulting from vocal cord paralysis. The optimal treatment for IC involves total thyroidectomy, lymph node dissection, and radioactive iodine therapy. Positive margins are common (32.7%),[1] and ICs are often unresponsive to cytotoxic agents,[2] imparting an overall 5-year survival of $<$60%.[1]

CONCLUSION

Physicians should consider the diagnosis of invasive thyroid carcinoma in a dysphonic patient whose laryngeal examination demonstrates an infiltrative endolaryngeal process despite intact vocal fold mobility.

ACKNOWLEDGMENTS

The authors have no financial or proprietary interest in the subject matter of this article.

REFERENCES

1. Pezzi TA, Sandulache VC, Pezzi CM, et al. Treatment and survival of patients with insular thyroid carcinoma: 508 cases from the National Cancer Data Base. *Head Neck*. 2016 Jun;38(6): 906-912. doi: 10.1002/hed.24342.
2. Chao TC, Lin JD, Chen MF. Insular carcinoma: infrequent subtype of thyroid cancer with aggressive clinical course. *World J Surg*. 2004 Apr;28(4):393-396.
3. Carcangiu ML, Zampi G, Rosai J. Poorly differentiated (''insular'') thyroid carcinoma: a reinterpretation of Langhans' ''wuchernde Struma''. *Am J Surg Pathol*. 1984 Sep;8(9):655-668.
4. Arffa RE, Krishna P, Gartner-Schmidt J, Rosen CA. Normative values for the Voice Handicap Index-10. *J Voice*. 2012 Jul;26(4): 462-465. doi: 10.1016/j.jvoice.2011.04.006.
5. Kempster GB, Gerratt BR, Verdolini Abbott K, Barkmeier-Kraemer J, Hillman RE. Consensus auditory-perceptual evaluation of voice: development of a standardized clinical protocol. *Am J Speech Lang Pathol*. 2009 May;18(2):124-132. doi: 10.1044/1058-0360(2008/08-0017).
6. Maslan J, Leng X, Rees C, Blalock D, Butler SG. Maximum phonation time in healthy older adults. *J Voice*. 2011 Nov;25(6): 709-713. doi: 10.1016/j.jvoice.2010.10.002.
7. Nishio M, Niimi S. Changes in speaking fundamental frequency characteristics with aging. *Folia Phoniatr Logop*. 2008;60(3): 120-127. doi: 10.1159/000118510.
8. Schwartz SR, Cohen SM, Dailey SH, et al. Clinical practice guideline: hoarseness (dysphonia). *Otolaryngol Head Neck Surg*. 2009 Sep;141(3 Suppl 2):S1-S31. doi: 10.1016/j.otohns.2009.06.744.
9. Rowe-Jones JM, Rosswick RP, Leighton SE. Benign thyroid disease and vocal cord palsy. *Ann R Coll Surg Engl*. 1993 Jul; 75(4):241-244.
10. Randolph GW, Kamani D. The importance of preoperative laryngoscopy in patients undergoing thyroidectomy: voice, vocal cord function, and the preoperative detection of invasive thyroid malignancy. *Surgery*. 2006 Mar;139(3):357-362.

11. Chandrasekhar SS, Randolph GW, Seidman MD, et al; American Academy of Otolaryngology-Head and Neck Surgery. Clinical practice guideline: improving voice outcomes after thyroid surgery. *Otolaryngol Head Neck Surg*. 2013 Jun;148(6 Suppl): S1-S37. doi: 10.1177/0194599813487301.

12. Pretorius PM, Milford CA. Investigating the hoarse voice. *BMJ*. 2008 Oct 8;337:a1726. doi: 10.1136/bmj.a1726.

This article meets the Accreditation Council for Graduate Medical Education and the American Board of Medical Specialties Maintenance of Certification competencies for Patient Care and Medical Knowledge.