

Introduction

- Papillary thyroid cancer (PTC) is characteristically indolent. However, recurrence remains a major concern. The most common site of locoregional recurrence is the cervical lymph nodes. PTC may invade cervical muscles by direct extension from the primary tumor or local nodal disease.
- Skeletal muscle metastasis is an extremely rare manifestation of disease recurrence. Herbowski et al. calculated the probability of detecting follicular and papillary thyroid cancer skeletal muscle metastasis to be 4 out of 1,000,000 cases annually.^{1,2} The mechanism behind isolated cervical muscle metastases not due to extranodal extension (ENE), referred to here as intramuscular PTC, is not clearly understood.
- PTC deposits in the infrahyoid strap muscles is a predictor of distant recurrence.³ Interestingly, there is limited data on patients with intramuscular PTC involving the sternocleidomastoid muscle (SCM).
- In our review of the literature, we only found four patients with truly isolated SCM deposits of recurrent PTC;⁴⁻⁷ none of the reports included molecular testing. We add five more cases to the literature with detailed pathology and molecular analysis.

Methods

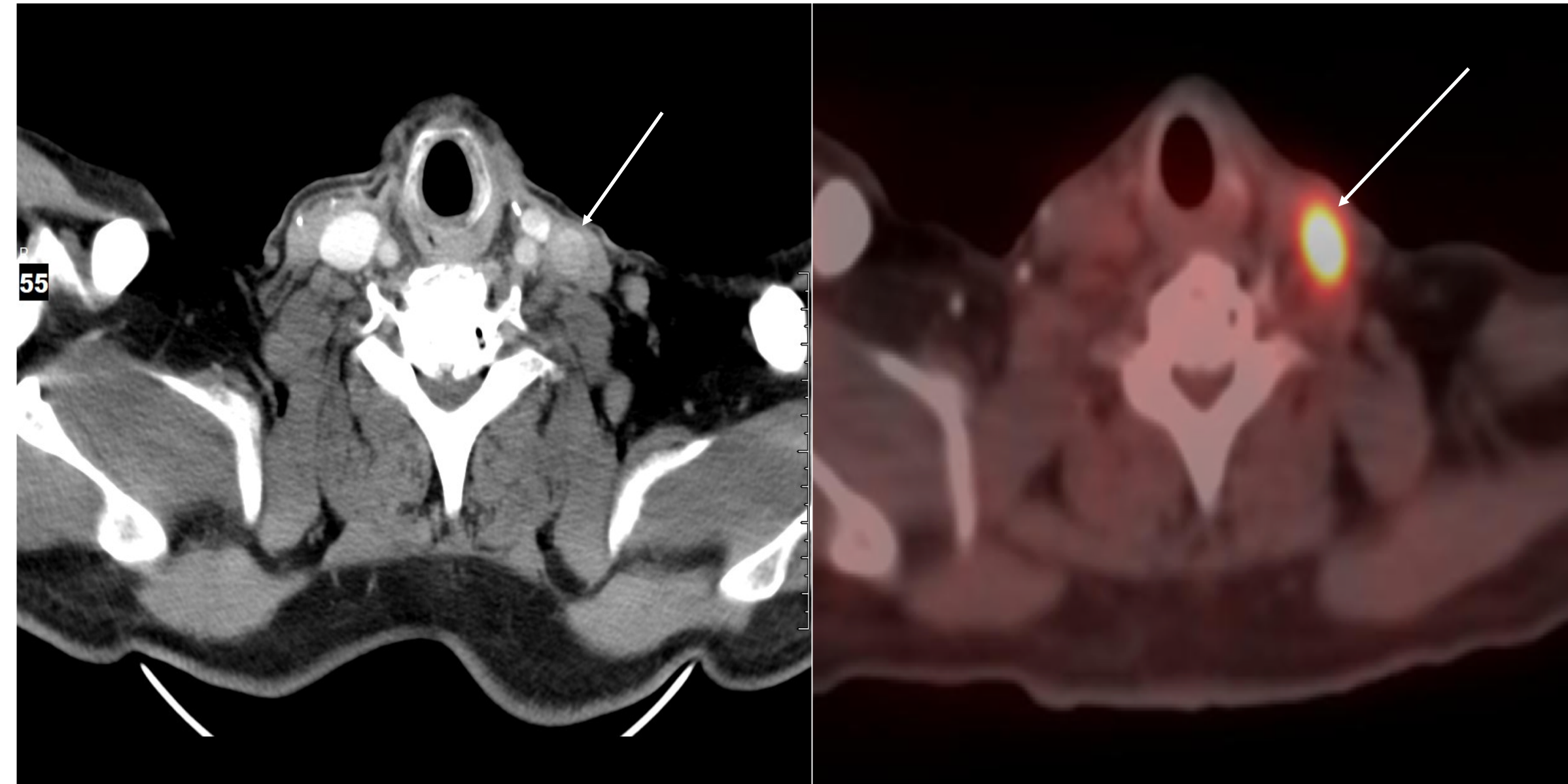
- This is a single institutional case series in a tertiary referral hospital.
- Molecular analysis of the SCM metastases was performed by Interpace Diagnostics.

Results

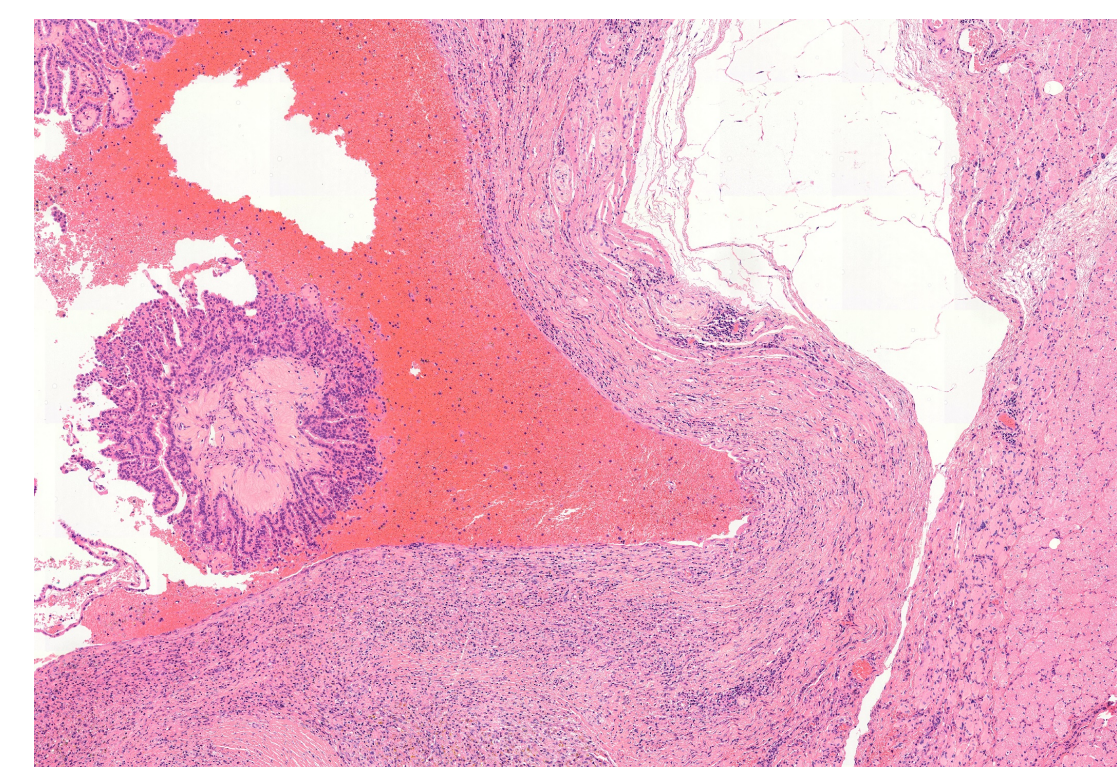
- All SCM PTC deposits were identified in the recurrent setting, and presented six to 17 years following initial treatment. All primary PTC tumors had high risk histologic features (HRFs) (**Table 1**).

Results Cont.

- These primary tumors also exhibited other aggressive characteristics including tall cell features, positive margins, and features of less well differentiated thyroid carcinoma.
- Of the two patients who underwent PET/CT scans, the SCM PTC deposit was FDG avid (case 1 and 3). Only one patient (case 3) had evidence of systemic disease when the intra-SCM was discovered.
- All cases were managed with resection of the metastasis along with a cuff of surrounding normal SCM.
- SCM metastases were positive for the *BRAF*^{V600E} and *TERT* mutation in three patients and *BRAF*^{V600E} in one patient. Loss of heterozygosity (LOH) was also reported in three of the five patients.



Case 3. Neck CT reveals a lesion measuring 1.4 x 1.5 x 1.5 cm within the sternocleidomastoid muscle in the expected location of the left IV nodal chain (arrow). PET/CT of neck reveals the lesion within the sternocleidomastoid muscle with SUV of 13.



Case 3. H&E × 40 magnification: Intramuscular focus of metastatic cystic PTC demonstrating hobnail features.

Table 1

Case	Age /Sex	Years since presentation	Histological variant of primary	Size of primary tumor on final pathology	Aggressive features of primary	Previous Treatment	RAI (mCi)	Histological variant of SCM recurrence	Aggressive Features of SCM Recurrence	Mutational Analysis (LOH, BRAF/TERT)
1	70/M	6	PTC, tall cell variant	3.5 cm*	ETE, lymphovascular space involvement, possible vascular tumor emboli	TT, RAI, ND,	368	PTC, tall cell variant	ENE	1p17q BRAF V600E, TERT C124T
2	62/F	13	PTC, follicular	1.6 cm*	ETE	TT, ND, RAI	142	PTC, follicular	ENE, necrosis	1p5q BRAF V600E, TERT C124T
3	72/M	6	PTC	6.5 cm	ETE, ENE	TT, ND, RAI	150	PTC, tall cell with hobnail	necrosis	NA
4	57/M	17	PTC	NA	NA	TT, RAI	NA	PTC, tall cell variant	NA	22q BRAF V600E, TERT C124T
5	26/F	3	PTC	4.2 cm, 1 cm	ENE	TT, ND, RAI	126	PTC, follicular	ENE	No LOH, BRAFV600E

*positive margins; PTC=papillary thyroid cancer; ETE= extrathyroidal extension; ENE= extranodal extension; TT= total thyroidectomy; ND= neck dissection; RAI= radioactive iodine; LOH= loss of heterozygosity

Discussion

- Skeletal muscle tissue is an uncommon site of metastasis due to its high levels of lactic acid, regular movement, and dense lymphocyte population.⁸
- The mechanism of metastasis of previous reported cases of recurrent intra-SCM thyroid cancer have been attributed to seeding along the FNA biopsy needle tract or endoscopic thyroidectomy probe tract.^{9,10} For our cases, all intra-SCM PTC recurrences occurred outside of regions that are presumed to be in the needle tract of prior biopsies.
- Several studies have elucidated the role of distinct mutations in driving thyroid malignancies. An association exists between *BRAF*^{V600E} and earlier age at diagnosis, advanced TNM stage, presence of ETE, lymph node metastases, but no association with distant metastases. The presence of *BRAF/TERT* mutations results in an additive effect, showing a greater association with the aforementioned characteristics.¹¹

Discussion Cont.

- In our case series, three of the five patients were found to have *BRAF*^{V600E} and *TERT* mutations simultaneously, which may explain the aggressive disease processes detailed above.
- While LOH in PTC has not been well-explored, LOH on chromosome 16p and 18q of anaplastic thyroid cancers has been reported.¹² Further, LOH has been associated with aggressive disease and poor prognosis in other malignancies such as gastric, pancreatic, and breast cancers. As 3/5 of our patients demonstrated LOH, we theorize that these genetic alterations contribute to this unique pattern of disease.

Conclusion

- We present this series of five cases of recurrent PTC in the sternocleidomastoid muscle to add to the existing literature and to provide more clarity on this uncommon presentation.
- All primary PTC tumors had HRFs including ETE and lymphovascular invasion. These primary tumors also exhibited other aggressive characteristics including tall cell morphology, positive margins, and genetic features of less well differentiated thyroid carcinoma.
- Our case series is the first to detail the molecular abnormalities of intramuscular PTC and opens a new avenue of research to better understand the etiologies and management of such unusual metastases.

References

- Herbowski L. Skeletal muscle metastases from papillary and follicular thyroid carcinomas: An extensive review of the literature. *Oncol Lett.* 2018;15(5):7083-7089.
- Herbowski L. Missing Skeletal Muscle Metastases of Papillary Thyroid Carcinoma. *Diagnostics (Basel).* 2020;10(7).
- Ito Y, Hirokawa M, Higashiyama T, et al. Clinical significance and prognostic impact of subcutaneous or intrastrap muscular recurrence of papillary thyroid carcinoma. *J Thyroid Res.* 2012;2012:819797.
- Macei DR, Babyak J, Ossakow SJ. Lateral neck mass. Sole presenting sign of metastatic thyroid cancer. *Arch Otolaryngol Head Neck Surg.* 1986;112(1):47-49.
- Portela RA, Choby GW, Manni A, Campbell D, Crist H, Goldenberg D. Unusual sites of metastasis of papillary thyroid cancer: Case series and review of the literature. *Ear Nose Throat J.* 2015;94(8):E43-47.
- Sindoni A, Gobitti C, Sulfaro S, Giacomarra V, Borsatti E. Unusual presentation of recurrent papillary thyroid microcarcinoma with neck muscles and skin dissemination [corrected]. *Hormones (Athens).* 2018;17(4):589-591.
- Virmani N, Dabholkar J. Distant skeletal muscle metastasis to sternocleidomastoid in the setting of recurrent papillary thyroid carcinoma. *Thyroid Research and Practice.* 2017;14(2):77-80.
- Molina-Garrido MJ, Guillen-Ponce C. Muscle metastasis of carcinoma. *Clin Transl Oncol.* 2011;13(2):98-101.
- Karwowski JK, Nowels KW, McDougall IR, Weigel RJ. Needle track seeding of papillary thyroid carcinoma from fine needle aspiration biopsy. A case report. *Acta Cytol.* 2002;46(3):591-595.
- Bakkar S, Frustaci G, Papini P, et al. Track Recurrence After Robotic Transaxillary Thyroidectomy: A Case Report Highlighting the Importance of Controlled Surgical Indications and Addressing Unprecedented Complications. *Thyroid.* 2016;26(4):559-561.
- Vuong HG, Altibi AMA, Duong UNP, Hassell L. Prognostic implication of BRAF and TERT promoter mutation combination in papillary thyroid carcinoma-A meta-analysis. *Clin Endocrinol (Oxf).* 2017;87(5):411-417.
- Kadota M, Tamaki Y, Sekimoto M, et al. Loss of heterozygosity on chromosome 16p and 18q in anaplastic thyroid carcinoma. *Oncol Rep.* 2003;10(1):35-38.