CASE REPORT

Primary squamous cell carcinoma of the thyroid with complete response to radical radiotherapy and concurrent cisplatin-based chemotherapy

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SUMMARY

Chemoradiotherapy and/or surgery are both potentially radical treatments for squamous cell carcinomas. Squamous cell carcinomas are considered chemosensitive tumours compared to adenocarcinomas or anaplastic thyroid malignancies. A 76-year-old man was found to have T4bN0M0 primary squamous cell carcinoma of the thyroid with encasement of the internal carotid artery. The disease was deemed unresectable. Therefore, he was treated with radical radiotherapy with concurrent cisplatin-based chemotherapy. We discuss herein the aetiology, diagnosis and management of primary squamous cell carcinoma of the thyroid. We demonstrate success of chemoradiotherapy in an unresectable case of a rare and aggressive disease.

BACKGROUND

Primary squamous cell carcinoma of the thyroid (PSCCT) is an extremely rare neoplasm of the thyroid with a reported incidence of <1% of thyroid malignancies.¹ Localised PSCCT is treated with surgical resection followed by chemoradiation. In cases with metastatic disease at presentation or when radical treatment is not feasible, prognosis is usually poor with an overall survival of 1 year.² We report herein a patient with PSCCT who was not a surgical candidate but responded well to radiation therapy plus cisplatin-based chemotherapy.

CASE PRESENTATION

A 76-year-old white man presented with left-sided neck tightness. He was diagnosed several months prior to presentation with gastro-oesophageal reflux disease. He had an extensive workup, including esophagogastroduodenoscopy, which showed

gastritis. Despite the use of a proton pump inhibitor, his symptoms did not improve. At presentation, he reported of tightness of the left lower neck but no pain. He had minimal dysphagia with solid food but not to liquids. He also had mild associated hoarseness.

The patient's medical history included irritable bowel syndrome, non-melanomatous skin cancer removal from the back and bunions. His surgical history included tonsillectomy, bilateral cataracts, bunion removal, and wide local excision of the skin cancer from his back.

The patient denied any allergies. Family history was only significant for uterine cancer in his mother. He was a former smoker with an 8-pack year history, who quit over 50 years prior. He denied alcohol excess and any illicit drugs. He was a world class distance runner, although his ability to run slowed down over the past several months.

On physical examination, the patient was not in acute distress. A non-pulsatile, firm, non-tender single nodule was palpated in the left medial low neck. The rest of physical examination was within normal limits.

Laboratory panel showed normal values for haemoglobin, white cell count, platelets, electrolyte panel and thyroid function tests. A CT of the chest showed a large (7 cm) mass in the thoracic inlet, which appeared to arise from the left lobe of the thyroid gland (figures 1A and 2A). Mass effects on the trachea and oesophagus were seen, although there was no invasion of either of these structures. The mass encased a portion of the left common carotid artery.

Subsequent positron emission tomography CT (PET-CT) scan confirmed hypermetabolic activity

Figure 1 (A–D): (A) CT of the chest at presentation. There is a large, hypodense lesion in the thoracic inlet which appears to originate from the left thyroid measuring 5.5×5×7 cm. There is mass effect with displacement of the trachea towards the right side and mild luminal narrowing. (B) CT of the chest after completing chemoradiation treatment pointing out a decrease in size of the mass. (C) Follow-up CT at 1 year showing a 24.6×31.3 mm mass at the inferior left neck at the cervicothoracic junction, not significantly changed in size representing radiation-induced fibrosis. (D) Follow-up CT at 2 years showing a triangular mass in the inferior left neck at the cervicothoracic junction, not significantly changed in size from prior CT.

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Figure 2 (A, B): (A) CT of the chest at presentation showing a large 7 cm mass with mass effect displacing the trachea. (B) T of the chest after completing chemoradiation treatment, where a 3.1×2.8×5 cm left neck mass seen arising from the left thyroid lobe is again demonstrated. The left common carotid artery is displaced by the mass and the left jugular vein is effaced. Inferiorly, the mass extends in the midline the retromanubrial notch and superiorly just inferior to the hyoid bone. Superiorly, the rest of the neck anatomic spaces have normal symmetrical morphology. There is no carotid space lymphadenopathy, and the mass appears to have decreased in size since presentation.

Figure 3 Fine-needle aspiration showing squamous characteristics by cytological Diff-Quik stain.

Figure 4 Cell block H&E stain showing carcinoma with squamous cell features.

within the thoracic inlet mass. No other evidence of disease was noted. Ultrasound-guided core needle biopsy yielded the diagnosis of poorly differentiated primary squamous cell carcinoma of the thyroid (figure 3). The tumour was p63 positive, CK5/6 positive and TTF-1 negative confirming squamous cell carcinoma (figure 4). The malignancy was staged T4bN0M0.

As the tumour encased the left common carotid artery, the patient was deemed unsuitable for surgery. Therefore, his primary squamous cell carcinoma of the thyroid was treated with cisplatin-based concurrent chemoradiotherapy (CRT).

As a main therapeutic modality, intensity modulated radiation therapy was used to deliver 70 Gy to the primary tumour while concurrently giving 50 Gy to the clinically uninvolved neck nodes (figure 5). Concurrent cisplatin at a dose of 100 mg/m² was given during the first, fourth and seventh week of radiation therapy. The patient completed treatment as scheduled, over a total of 47 days. The patient tolerated treatment remarkably well with minimal fatigue, skin erythema and oesophagitis.

The first post-treatment CT scan performed 3 months after treatment showed the mass to have shrunk considerably; maximum dimension of 3.1 cm compared to 7 cm prior to treatment (figure 1B and 2B). Subsequent PET/CT scan performed 6 months after therapy completion showed continued shrinkage of the mass, which showed normal metabolism, consistent with treatment-related scar tissue (figure 6). The mass continued to shrink on succeeding scans at 1 and 2 years (figure 1C, D) and there has been no development of regional

or distant metastases. The patient remains disease-free 2 years after completing treatment with an excellent quality of life.

DISCUSSION

PSCCT is a very uncommon malignancy of the thyroid which represents 1% of all thyroid cancers.¹ Since the normal thyroid gland lacks squamous cell epithelium, the origin of PSCCT is unclear. There have been multiple theories regarding the origin of squamous epithelium in the thyroid.³ One theory proposes that the squamous cells might be derived from basaloid cells of the branchial cleft. Another proposal is that the squamous cells are remnants of the thyroglossal duct. The squamous cells can also be a result of metaplasia from the native follicular, papillary or anaplastic cells in the thyroid. Owing to advanced age of our patient at presentation, it is reasonable to assume that he developed the PSCCT from metaplasia of his existing thyroid cells.

PSCCT most commonly affects women with history of goitre in their 5th to 6th decade of life.⁴ At presentation, these patients display a rapidly enlarging neck mass, followed by dyspnoea and hoarseness due to infiltration and compression of adjacent neck structures.⁴ Metastases to cervical lymph nodes are often present at diagnosis.

The differential diagnosis of a subacute neck mass includes squamous cell carcinoma of the upper aerodigestive tract, amyloidosis, lymphoma, metastatic squamous cell carcinoma and carcinoma showing thymus like elements (CASTLE). Diagnosis is made via biopsy and confirmed via immunohistochemical

Figure 5 (A, B): (A) Intensity-modulated radiation therapy planning superiorly (A) and Inferiorly (B) in the neck. Isodose curves show differential dosing between the thyroid mass and the clinically negative neck.

Figure 6 Follow-up PET/CT 6 months after treatment showing continued shrinkage of the thyroid mass and a significantly diminished metabolic score compared to the pretreatment value. PET/CT, positron emission tomography CT.

staining. Biopsy of the patient's mass demonstrated poorly differentiated squamous cell carcinoma (figures 3 and 4).

Our patient was a never smoker and the location of the neck mass in the thyroid gland ruled out upper aerodigestive tract

squamous cell carcinoma. A subset of squamous cell carcinomas of the upper aerodigestive tract includes those related to human papillomavirus infection.⁵ The patient's pathology specimen was negative for human papillomavirus via p16 immunohistochemistry. MEN syndrome is also a possibility in the initial evaluation of a thyroid malignancy. Since the biopsy showed a squamous cell cancer and not a medullary carcinoma of the thyroid, MEN 2A/2B syndromes were effectively excluded. Another rare disease, CASTLE, may resemble PSCCT histologically. Both PSCCT and CASTLE demonstrate presence of central degeneration with squamous differentiation and distinct cell borders.⁶ However, CASTLE stains positive for CD5, whereas PSCCT does not. The patient's tumour was positive for p63 and CK5/6 and negative for CD5 indicating squamous cell carcinoma.⁶

Further, clinicians should be aware that squamous cell carcinoma of the thyroid could also represent a metastasis from an adjacent cancer or even from cancers originating from distant organ sites. In fact, squamous cell carcinoma in the thyroid gland is more likely to be due to a metastasis rather than a primary thyroid tumour.⁷ Physical examination of the patient was negative for thyroid nodules, and a complete skin examination was negative for any lesions. Full body PET-CT scan was negative for any abnormal hypermetabolic activity or distant disease (figure 6). The patient also had a colonoscopy prior to the presentation which showed no masses or polyps.

Owing to the rarity, optimal management has not been clearly identified. Optimal management requires complete surgical resection. Postradical resection, these patients should be ideally offered adjuvant radiotherapy or adjuvant chemoradiotherapy

Table 1 Selected cases of PSCCT treated with non-surgical modalities

Case	Year published	Age, sex	TNM staging	Treatment	Survival	ANED, DOD
Lui <i>et al</i> ¹²	2014	36M	T4bN1bM1	None, Hospice/Palliative	17 days	DOD
Ghoshal <i>et al</i> ¹³	2016	70M	T4bN0M0	Palliative radiotherapy 30 Gy in 10 fractions over 2 week's period	<1 year	DOD
Tunio MA <i>et al</i> ¹⁴	2012	54F	T4aN0M0	Palliative radiotherapy (30 Gy in 10 fractions)	3 months	DOD
Our Case	2016	76M	T4bN0M0	Radical radiotherapy with concurrent chemotherapy	2 years	ANED

ANED, alive with no evidence of disease (alive with disease); DOD, dead of disease; TNM, tumour, nodes, metastases; PSCCT, primary squamous cell carcinoma of the thyroid.

to a high dose to provide better local control/reduce risk of local regional relapse. Our patient was not a surgical candidate because the tumour encased the left common carotid artery. At the time of writing this report, there were no published guidelines or studies on non-surgical treatment of PSCCT. We treated our patient according to principles applying to other squamous cell carcinomas of head and neck origin.⁸⁻⁹ The standard of care for locally advanced head and neck cancers is concurrent CRT, which was proven to yield a better local disease control than sequential CRT.⁸⁻⁹ CRT also results in similar outcomes to surgical resection in this group of patients, with the added advantage of preserving laryngopharyngeal function.¹⁰

Following treatment, the patient had shrinkage of the mass seen on follow-up CT scans (figures 1 and 2). In addition, subsequent PET/CT scan showed a mass without metabolic activity consistent with radiation-induced fibrosis (figure 6). Although the differential diagnosis for the palpated mass included recurrent tumour,¹¹ the lack of metabolic activity on PET/CT scan with no signs of growth makes that possibility highly unlikely. Furthermore, a biopsy was not pursued in order to avoid wound healing and worsening of the fibrosis.¹¹

The patient was followed up at 1 week at treatment, 6 months, 1 year and 2 years, accordingly (figures 1B–D). We have decided on following the patient with this protocol because he owns a vacation home in the area and only travels locally during the summer and winter. The patient tolerated the treatment well without any significant post-treatment complications.

We have studied and analysed all published case reports of primary squamous cell carcinoma of the thyroid in the peer-reviewed literature (table 1). We found only three reports where radiation and/or radiation and chemotherapy were the primary modality for treatment. In comparison to these cases, our case demonstrated an important survival advantage 48 months compared with the median of 5.16 months. However, we do realise that inferences on survival due to a specific treatment modality cannot be made due to a small number of cases and possibly different stages of the disease. A prospective trial would be necessary in this regard.

In conclusion, advanced PSCCT is an aggressive malignancy with a generally poor prognosis. Nonetheless, our patient has done very well with organ-preserving, concurrent CRT. Several factors have likely contributed to his excellent outcome, two of which seem significant. First, the tumour was confined to the thyroid gland and therefore amenable to aggressive local therapy. Second, he was in excellent state of health prior to treatment, which allowed him to complete the entire course of therapy as scheduled. Further studies are certainly needed to define the management of this rare disease; however, concurrent CRT should be considered for patients with unresectable PSCCT.

Learning points

- ▶ Primary squamous cell carcinoma of the thyroid is a rare malignancy with an incidence of <1%.
- ▶ Squamous cell carcinomas normally stain positive for p63 and CK5/6.
- ▶ Surgery is considered the gold standard.
- ▶ Radical chemoradiotherapy can be a good alternative in patients who are either unfit for surgery or not willing to pursue a surgical option.

Contributors MDR compiled data, researched and reviewed articles, and constructed the manuscript. CD carefully reviewed, revised, and approved the manuscript for submission. HT saw and diagnosed the patient after careful evaluation and efficient testing. HT also carefully reviewed and revised the manuscript. RJ treated and managed the patient. RJ also carefully reviewed, revised, and approved the manuscript for submission.

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REFERENCES

- 1 Syed MI, Stewart M, Syed S, *et al*. Squamous cell carcinoma of the thyroid gland: primary or secondary disease?. *J Laryngol Otol* 2011;125:3–9.
- 2 Booya F, Sebo TJ, Kasperbauer JL, *et al*. Primary squamous cell carcinoma of the thyroid: report of ten cases. *Thyroid* 2006;16:89–93.
- 3 LiVolsi VA, Merino MJ. Squamous cells in the human thyroid gland. *AM J Surg Pathol* 1978;2:133–40.
- 4 Sapalidis K, Anastasiadis I, Panteli N. Primary squamous cell carcinoma of the thyroid gland. *J Surg Case Rep* 2014;2014:rju133.
- 5 D'Souza G, Kreimer AR, Viscidi R, *et al*. Case-control study of human papillomavirus and oropharyngeal cancer. *N Engl J Med* 2007;356:1944–56.
- 6 Ebina A, Sugitani I, Motoi N. Intrathyroidal epithelial thymoma: carcinoma showing thymus-like differentiation mimicking squamous cell carcinoma of the thyroid. *J Nippon Med Sch* 2015;82:2–3.
- 7 Chen KH, Chou YH, Cheng AL. Primary squamous cell carcinoma of the thyroid with cardiac metastases and right ventricle outflow tract obstruction. *J Clin Oncol* 2012;30:e260–3.
- 8 Pignon JP, le Maître A, Maillard E, *et al*. Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): an update on 93 randomised trials and 17,346 patients. *Radiother Oncol* 2009;92:4–14.
- 9 Forastiere AA, Goepfert H, Maor M, *et al*. Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer. *J Clin Oncol* 2003;21:2091–8.
- 10 VA Laryngeal Cancer Study Group. Induction chemotherapy plus radiation compared with surgery plus radiation in patients with advanced laryngeal cancer. The Department of Veterans Affairs Laryngeal Cancer Study Group. *N Engl J Med* 1991;324:1685–90.
- 11 Herrmann T, Baumann M, Dörr W. *Clinical radiation biology*. Munich: Elsevier, 2006.
- 12 Lui JT, Khalil MN, Chandarana SP. Primary squamous cell of the thyroid—an abbreviated clinical presentation. *J Otolaryngol Head Neck Surg* 2014;43:17.
- 13 Ghoshal S, Bhattacharyya T, Sood A, *et al*. Palliative radiation in primary squamous cell carcinoma of thyroid: a rare case report. *Indian J Palliat Care* 2013;19:192–4.
- 14 Tunio MA, Al Asiri M, Fagih M, *et al*. Primary squamous cell carcinoma of thyroid: a case report and review of literature. *Head Neck Oncol* 2012;4:8.

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