

Adult Thyroglossal Duct Carcinoma of Thyroid Epithelial Origin: A Retrospective Observational Study

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Abstract Thyroglossal duct or cyst carcinoma (TGDCCa) is uncommon. Current treatments follow those of thyroid cancer but controversy exists over the extent of thyroid and lymph node surgery. Our aim was to study the presentation, treatment strategies and clinical outcomes in patients presenting with TGDCCa. Of 637 patients diagnosed with thyroid cancer over 15-years, 4 patients (0.6 %) with TGDCCa were identified. Two patients were diagnosed outside this time period. Details of demographics, presentation, diagnosis, management and outcomes of all 6 patients were reviewed. 5 females and 1 male with a median (range) age of 41 (21–70) years were treated for TGDCCa. Five patients were diagnosed after initial surgery for thyroglossal cyst—cyst excision ($n = 2$) and Sistrunk's procedure ($n = 3$). This was followed by a total thyroidectomy (TT) in 4 of these patients. One patient underwent Sistrunk's operation, total thyroidectomy and central neck dissection at the first operation. I131 therapy was used in patients who had TT. Three patients had additional tumour foci in the thyroid. However, lymph node recurrence occurred in 2 patients at 6 and 16 months. At a median follow up of 55 months, all 6 patients were disease free. All patients had papillary TGDCCa and did well with conventional treatment as for thyroid cancer. The extent of treatment required is debatable as half the patients

had additional thyroid foci and no patient had clinically or radiologically involved lymph nodes at presentation. A systematic review of published cases will help summarise the existing knowledge base.

Keywords Papillary thyroid carcinoma · Thyroglossal duct carcinoma · Thyroid cancer

Introduction

The thyroid descends from the floor of the pharynx to the anterior neck [1, 2]. Residual tissue along this path of migration is known as the thyroglossal duct or tract [2]. This obliterates by the 10th week of gestation, but may persist in some individuals [1]. Accumulation of fluid resulting in cysts or residual thyroid tissue may be present anywhere along the path of descent from the floor of the mouth to the suprasternal notch [2]. Approximately 67 % of thyroglossal duct remnants are at the level of the hyoid bone; 33 % suprahyoid, 13 % suprasternal and 0.1 % are intralingual [3].

This developmental abnormality occurs in around 7 % of the population [4]. Of the people with a thyroglossal duct cyst, 1 % develop a malignancy [4]. The mean age at presentation is 6 years in the paediatric population and a median of 38 years in the general population with an equal sex distribution [5].

The cyst moves up with deglutition as it is closely associated with the hyoid bone [6, 7]. Thyroglossal duct cysts are smooth, spherical, mobile and usually non tender, unless there is infection, which can result from pathogen transmission through the foramen cecum [2, 8]. Malignancy should be suspected if the lump is fixed, irregular and hard, especially in an older child or adult [9].

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Clinically, there is no reliable way to distinguish between thyroglossal duct malignancies and benign cysts. Thyroglossal duct cancer generally affects women twice more often than men [10]. An irregular, hard mass, with invasion of local structures or suspicious lymphadenopathy may sometimes suggest malignancy [11].

On ultrasound, thyroglossal cysts are anechoic or hypoechoic [11]. The cancer may appear as a mural lesion within the cyst, sometimes associated with microcalcification [11]. The most common finding on computed tomography and magnetic resonance imaging is a solid nodule within the cyst [11]. Some authors recommend the routine use of fine needle aspiration cytology (FNAC) in all patients except children [1]. This is particularly useful if the sample is positive for carcinoma [1]. However, even if up to 50 % of such cancers can be diagnosed on FNAC, the low likelihood of malignancy in thyroglossal duct cysts (1 %) reduces the utility and cost effectiveness of FNAC, especially in children [1, 11–13]. Given a higher rate of malignancy in a thyroglossal duct in the elderly and if the lesion has a solid component, FNAC may be considered in these instances [2]. If malignancy is suspected during surgery, an intra-operative frozen section can assist in diagnosis [14] and facilitate the performance of an adequate operation at the first surgery [12].

Symptomatic cysts, or those with a history of infection are managed by surgical excision [1, 15]. There are two commonly carried out procedures; simple cyst excision, or the more extensive Sistrunk's procedure [1]. The Sistrunk's operation involves an *en bloc* excision of the cyst with the tract and the mid-section of the hyoid bone [1]. In a study, patients who underwent a simple excision had a recurrence rate of 55.6 % whereas patients who underwent Sistrunk's procedure had a recurrence rate of 5.3 % [16]. The overall recurrence rate was 9.7 % [16].

The majority of malignancies in thyroglossal duct cysts are papillary thyroid carcinomas; rarer types include follicular and squamous cancers. [2, 11]. As thyroid parenchyma may be seen in around 2/3 of thyroglossal tracts, it is thought that papillary carcinomas develop *de novo* from the duct remnants rather than metastasize from primary tumours within the thyroid gland [11]. The features described for the diagnosis of a primary thyroglossal duct carcinoma arising from thyroid epithelium are that malignancy should not be present in the thyroid or any other primary site; the carcinoma should be within the wall of the thyroglossal duct remnant; the epithelial lining should be squamous or columnar; and normal thyroid follicles present within the thyroglossal duct remnant [17].

Patients with papillary carcinoma of the thyroglossal duct have a very good prognosis—95.6 % survival rate at 10 years [18].

The general consensus is that total thyroidectomy with the Sistrunk procedure should be performed in cases of differentiated thyroid cancer in the thyroglossal duct [11, 18]. Some authors also advocate the performance of a prophylactic central compartment lymph node dissection at the time of thyroidectomy [19]. However, due to the rarity of the disease, there is currently no strong evidence to support an optimal management strategy for thyroglossal duct carcinoma. Key questions include whether thyroidectomy and central neck dissection should be routinely performed and whether postoperative thyroid stimulating hormone suppression and/or radioactive iodine ablation are indicated in all cases [1, 2, 11].

The aim of this study is to present a series of patients with thyroglossal duct cancer and discuss the management strategies and clinical outcomes.

Methods

Of 637 patients diagnosed with thyroid cancer over a 15-year period, 4 patients (0.6 %) with TGDCa were identified. Another two patients included in this study were diagnosed outside this 15 year period and were identified from hospital records. The medical records of the six patients were reviewed and information regarding demographics, presentation, diagnosis, management and outcomes was collected. The outcomes included data on biochemical, radiological and histologic evidence of recurrence. The analysis was primarily descriptive.

Results

Table 1 presents the demographic details, presentation, methods of diagnosis, treatment details, staging and prognosis for all six patients treated for papillary thyroid cancer arising from the thyroglossal duct. The median (range) age of diagnosis was 41 (21–70) years. No patients had clinical evidence of lymph node involvement at presentation. At a median (range) follow up of 55 months (6 months–29 years), all patients were free of disease.

Case 1

A 45 year old female patient with a 12 month history of neck lump, associated with discomfort and nausea. There was no significant past medical history or family history of thyroid disease. An ultrasound scan of the neck revealed a 1.5 cm solid, midline mass that moved on deglutition and tongue protrusion. A fine needle aspiration cytology from the lesion showed features suspicious of thyroid cancer (Thy4 cytology). The patient underwent Sistrunk's

Table 1 Presents the demographic details, presentation, methods of diagnosis, treatment details, staging and prognosis for all five patients

Age/sex	Presentation	Preoperative imaging	Preoperative FNA	Initial surgery	Further treatment	Histology	Staging	Recurrence	Outcome (months between date of diagnosis and last known to be disease free)
45/F	Neck lump	1.5 cm midline mass (USS)	Thy4	Sistrunk's operation, TT and CND	RIA (1.1 GBq I ¹³¹) and TST	Papillary thyroid carcinoma Further 2 mm focus of PTC in right thyroid lobe	pT3(m)N0MxR0	Central compartment recurrence at 6 months-had re-operative surgery	Free of disease at 44 months
39/F	Neck lump	Thyroglossal cyst and normal thyroid (USS)	Not done	Thyroglossal duct cyst excision	TT, RIA (3.76 GBq I ¹³¹) and TST	Papillary thyroid carcinoma	pT1bNxR0	None	Free of disease at 65 months
21/F	Unknown	Unknown	Not done	Sistrunk's operation	TST	Papillary thyroid carcinoma	Not available	None	Free of disease at 29 years
21/F	Neck lump	Complex cystic abnormality (MRI)	Not done	Sistrunk's operation	TT, RIA (1.1 GBq I ¹³¹) and TST	Papillary thyroid carcinoma	pT3NxR1	Lateral compartment recurrence at 16 months	Free of disease at 21 months
42/M	Neck lump	Thyroglossal cyst (USS)	Not done	Thyroglossal duct cyst excision	TT, RIA (3.7 GBq I ¹³¹) and TST	Multifocal papillary thyroid carcinoma Further 5 mm focus of PTC in right thyroid lobe	pT1(m)NxMxR0	None	Free of disease at 81 months
70/F	Neck lump	1.5 cm midline mass (USS and MRI)	Thy 3	Sistrunk's operation	TT, CND, RIA (1.1 GBq I ¹³¹) and TST	Papillary thyroid carcinoma (classical type and FVPTC) Multiple foci of classical PTC seen within the thyroid	pT3(m)N0MxR0	None	Free of disease at 6 months

procedure. Frozen section examination confirmed papillary thyroid cancer and therefore total thyroidectomy with central neck dissection was performed at the same procedure. Final histology demonstrated a 35 mm papillary cancer of the thyroglossal tract extending into adjacent skeletal muscle with clear resection margins. There was a further 2 mm focus of papillary carcinoma in the right lobe of the thyroid gland, which was completely excised. None of the 14 lymph nodes identified were involved and excision margins were clear. Final histological staging was pT3(m)N0MxR0.

Further treatment involved radio-iodine ablation (1.1 GBq I [1, 13]) and TSH suppression therapy. At 6 months, the follow up radio-iodine scan was unremarkable. However, the stimulated thyroglobulin level was elevated at 6.9 ng/mL. A subsequent ultrasound scan identified a 1 cm lymph node with micro calcification in level VI of the neck; FNA biopsy of which confirmed residual papillary thyroid carcinoma. A CT scan showed no suggestion of disease elsewhere. A re-operative neck exploration and excision of this lesion was performed. Post-operative laryngoscopy confirmed normal movement of vocal chords.

Thyroglobulin levels were undetectable after the second operation and the patient is free of disease 44 months following her initial diagnosis.

Case 2

A 39 year old lady presented to her GP with a short history of a lump in the anterior neck. An ultrasound scan revealed a thyroglossal cyst and a normal sized thyroid gland. In view of the increasing size, the patient underwent a thyroglossal duct cyst excision. Histology demonstrated a 12 mm completely excised papillary thyroid carcinoma. The patient underwent a total thyroidectomy. No further disease was identified in the thyroid. The pathological staging was pT1bNxR0. The patient underwent radioiodine ablation (3.76 GBq I [1, 13]). She underwent TSH suppression for 5 years. The patient was well and free of disease 65 months following diagnosis.

Case 3

A 21 year old woman presented with a swelling in her neck. A clinical diagnosis of thyroglossal cyst was made. The patient underwent Sistrunk's procedure. Histology demonstrated a 1 cm invasive papillary thyroid carcinoma. There was no vascular invasion or involvement of the hyoid bone. Five years after the initial surgery she had 1 lymph node removed that was benign. She did not have radioiodine ablation (as she did not undergo a thyroidectomy) but was treated with TSH suppression. She has remained well and disease free for 29 years now.

Case 4

A 21 year old lady presented with a 2 month history of a swelling in the left submandibular area. Ultrasound and MRI demonstrated a complex cystic abnormality in the floor of the mouth extending down into the submandibular region. Excision of the cystic nodule along with Sistrunk's procedure was performed as the lesion was wrapped around hyoid bone. Histology revealed widely invasive papillary thyroid carcinoma in thyroglossal duct cyst with lymphovascular invasion. Following this, she went on to undergo total thyroidectomy; no further focus of carcinoma was identified. The tumour involved the circumferential margin. The final histology was pT3NxR1. She underwent radioiodine ablation therapy (1.1 GBq I¹³¹) and is on TSH suppression treatment. She developed lymph node metastases in both lateral compartments around 16 months after diagnosis and has had bilateral selective neck dissections following which she is currently disease free (21 months after initial diagnosis).

Case 5

A 42 year old male presented with a midline lump in the neck. Following ultrasound scan, a diagnosis of thyroglossal cyst was made. The patient initially decided not to undergo surgery but due to increase in size of the cyst underwent cyst excision 4 years later. Histology showed thyroglossal cyst with a 17 mm non-invasive well differentiated papillary carcinoma. A further 1 mm focus of well differentiated follicular variant papillary carcinoma was present in the background. A total thyroidectomy was then performed and histology showed another 5 mm focus of completely excised well differentiated follicular variant papillary carcinoma in the superior pole of the right thyroid lobe. The overall staging was pT1(m)NxMxR0 papillary carcinoma of the thyroid. He underwent radioiodine ablation therapy (3.7 GBq I¹³¹) and TSH suppression treatment. The patient remains disease free at 93 months.

Case 6

A 70 year old female presented with a long standing submental 14–15 mm mass. In addition, two benign appearing thyroid nodules were detected on ultrasound and on MRI, the submental mass appeared as an irregular soft tissue lesion. FNA showed indeterminate cytology (Thy 3) and this was followed by Sistrunk's operation. Histology from Sistrunk's operation showed papillary thyroid cancer (21 mm mixture of classical and follicular variant papillary thyroid cancer) extending into the skeletal muscle (pT3). She subsequently underwent total thyroidectomy with central neck dissection. Multiple foci of classical papillary

thyroid cancer were seen within the thyroid but no lymph nodes were involved. The overall staging was pT3(m)N0R0Mx. She later underwent radioiodine ablation (1.1 GBq I¹³¹) and TSH suppression treatment. The patient remains disease free at 6 months after diagnosis.

Discussion

In this retrospective observational Study, we describe our experience in managing 6 patients with this rare disease. All patients had papillary thyroid cancer, and although the management strategy has changed over the years for these patients, outcomes have been favourable.

As described in Table 1, initial surgical treatment and extent of surgery varied between cases in this study. A number of reasons underlie these differences. These include time of diagnosis (preoperative vs. postoperative), extent of disease, changes in practice over the duration of study period, differences between clinicians and the lack of good evidence given the rarity of the disease.

Thyroid malignancy arising from the thyroglossal duct is very rare and diagnoses are often made incidentally and postoperatively on histology [20]. The majority of malignancies are papillary thyroid carcinomas [2, 11, 20]. Clinicians debate about whether the origin of the tumour is a metastases from occult thyroid carcinoma or whether it is due to a malignant transformation of a remnant of thyroid tissue in the thyroglossal tract [21]. In an autopsy study on 58 infants and children, 41.3 % had remnants of the thyroglossal duct or ectopic thyroid [22]. According to LiVolsi et al., papillary carcinoma in the thyroglossal duct most likely arises from islands of ectopic thyroid tissue adjacent to the cyst wall instead of the lining of the duct [23].

Differences in opinion exist regarding whether patients with thyroglossal duct cyst carcinoma should undergo thyroidectomy. Some authors do not recommend a total thyroidectomy in low-risk patients with clinically and radiologically normal thyroid glands [1]. These authors define low-risk patients as: age over 15 years and younger than 45 years, no history of radiation, <4 cm diameter without soft tissue extension and/or distant metastases [1, 12]. Others have argued for a total thyroidectomy, especially if another focus in the thyroid cannot be ruled out [24]. It is thought that 1.7–7.6 % of thyroglossal cysts contain thyroid tissue [20, 25]. The rationale for thyroidectomy in patients with a clinically normal thyroid is the increased risk (11–27 %) of co-existing intraglandular thyroid cancer [1, 5, 26]; facilitation of treatment with radio-iodine and monitoring for disease recurrence by measuring thyroglobulin levels [5]. However, a thyroidectomy is associated with increased morbidity; complications include hypocalcaemia and recurrent laryngeal nerve injury [27].

Therapeutic lymph node dissection of central and/or lateral compartments would be indicated on the basis of suspicious or pathological lymph nodes in the relevant part of the neck. However, the role of prophylactic lymph node dissection is controversial. Some suggest that, all patients should undergo TSH suppression whether they undergo thyroidectomy or not [20] and others propose TSH suppression as an alternative to thyroidectomy in low-risk adult patients [1]. However, long term TSH suppression is associated with risks of osteoporosis and cardiovascular complications [28].

Currently, the TNM staging for thyroid cancer is applied for cancers arising from the thyroid epithelium of thyroglossal ducts [2]. The validity of this is however unclear. Multiple foci of malignancy in the thyroid gland is denoted in the TNM stage by (m). It is unclear in TGDCa whether a separate tumour focus in the thyroid should be considered as a multifocal tumour or a separate thyroid cancer. In addition, given the small size of thyroid epithelial remnants in TGDCa, extension beyond the capsule often occurs and such tumours are labelled pT3 regardless of size. Due to its rarity, there is a lack of evidence to support the prognostic differences between the TNM stages in TGDCa and any potential differences between TGDCa and thyroid cancer of similar TNM stage.

In our study, 2 in 6 patients showed evidence of multifocality. One of these patients had recurrence in the central compartment of the neck despite having had a prophylactic central neck dissection at the first operation. The fourth patient in Table 1 was diagnosed with bilateral lymph node recurrence in the lateral compartments and has had bilateral selective neck dissections. On this basis, we support the argument for total thyroidectomy, radio-iodine ablation and TSH suppression in high risk patients. Given the lack of evidence, prophylactic lymph node of the central compartment may be performed in accordance to local practice in the management of thyroid cancer.

This study is limited by its retrospective nature. In addition, given that patients have been included over a long time period and have been subject to different management strategies, it is difficult to draw conclusions on appropriateness of the treatments used.

In summary, patients with papillary TGDCa seem to do well with standard treatment in accordance to thyroid cancer guidelines. There are few published case reports and small series and this report adds to the evidence in literature. We recommend that a total thyroidectomy, radio-iodine ablation and TSH suppression treatment is considered in all patients with pT3 tumours and in those where imaging suggests further tumour foci in the thyroid. Prophylactic lymph node dissection is controversial but should be considered in high risk tumours in centres where the morbidity can be minimised.

A systematic review will help summarise the existing knowledge base and clarify the similarities and differences with primary thyroid cancers. Careful analyses of risk factors will help better stratification of risk categories and enable better tailoring of treatments.

Compliance with Ethical Standards

Conflict of interest All authors declare that they have no conflict of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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