Original Article

Prevalence and implications of thyroid related embryological remnants: A prospective study of 1118 total thyroidectomies

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Abstract

Context: Modern thyroid surgery has undergone a paradigm shift from subtotal thyroidectomy to an extended total thyroidectomy (TT) even for benign disorders. This entails removal of all embryological remnants even in benign disorders. **Aims:** To study the prevalence of various embryological remnants of the thyroid and surgical utility and implications in preventing complications. **Settings and Design:** Retrospective study of total thyroidectomies done by a single endocrine surgeon by standardized technique. **Methods and Material:** A detailed search of all embryological rests including Pyramidal tract (PT), Tubercle of Zuckerkandl (TZ), and Thyro-thymic thyroid rests (TTR) were done in 1118 patients undergoing TT over 6 years. The cases with and without TTR were divided as Group A and B, respectively. Their prevalence and impact on parathyroid preservation and other clinical parameters were analysed. **Statistical Analysis Used:** Descriptive analyses. **Results:** Out of the 1118 TT cases, TTR was seen in 230 (20.57%) cases, TZ in 598 (53.48%), cases and PT in 641 (57.33%) cases. Among group-A (n = 230), 213 had unilateral and 17 had bilateral TTR with 51 (22.17%) having retrosternal extension. Compressive symptoms, presence of TZ and PT were also significantly higher in group A. On follow up the incidence of temporary hypoparathyroidism was significantly higher in group-A, where as permanent hypoparathyroidism, temporary and permanent vocal cord palsy were comparable between the two study groups. **Conclusions:** Embryological remnants related to thyroid are not uncommonly encountered during total thyroidectomy. A thorough search and complete removal is crucial for the successful outcome of the procedure.

Keywords: Embryological remnants, hypocalcemia, thyrothymic thyroid rests, total thyroidectomy

Introduction

Thyroid gland develops from the endodermal thyroglossal duct and migrates downwards in the neck anterior to the hyoid and thyroid cartilage from foramen cecum. Variations in this developmental process may lead to embryological remnants anywhere along the path of thyroid development. The major thyroid remnants are pyramidal tract (PT), tubercle of Zuckerkandl (TZ), and thyro-thymic thyroid rests (TTR). These embryological remnants may be significant either when they present as neck swellings or during thyroid surgeries. Embryological thyroid rests within the thyro-thymic area called

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Thyro-thymic thyroid rests (TTR) or "Reeve's Rests," and present as separate nodules from the thyroid lobe.[1]

Total thyroidectomy (TT) is the procedure of choice for majority of thyroid disorders. Thyroidectomy entails removal of not only the lobes of thyroid in the neck but also the various embryological remnants (or rests) associated with it.[2,3] The importance of removing the pyramidal tract/thyroglossal tract remnant during thyroidectomy has been emphasised time and again for completeness of the procedure.[4-6] However, literature regarding prevalence and importance of identification of TTR is scarce. Total thyroidectomies are extensively performed by general surgeons in the rural and urban setting, owing to volume of the disease and simplicity of the surgery. They are even practised as day care procedures. The emphasis on the frequent presence of TTR's, the necessity for complete removal is of utmost importance to all surgeons undertaking this procedure. Awareness in this regard will avoid future recurrences (30–50%), avoiding further surgical risk in case of recurrence. Redo procedures are extremely challenging, even in the most experienced hands. Hence, we studied the prevalence of embryological remnants with emphasis on TTR during total thyroidectomy and analyzed its associations and impact on complications of surgery.

Subjects and Methods

This prospective evaluation was performed by a single Endocrine surgeon (first author) from June 2011 to May 2017 with a minimum follow up of 1 year. Consecutive patients who underwent total thyroidectomy during this period were enrolled in the study. Informed written consent was obtained from all the patients regarding collection, storage of the data and photographs including the intra-operative specimens and institutional ethical clearance was obtained. Patients who presented for completion thyroidectomy or re-operative procedures for thyroid malignancies were excluded. The clinical details collected in addition to patient demographics included fine needle aspiration cytology (FNAC) report, imaging report (high resolution ultrasonography or computerized tomography findings), detailed intra-operative findings and procedures, postoperative period including morbidity if present in terms of hypocalcemia— temporary (up to 6 months) or permanent (>6 months), vocal cord palsy— (transient or permanent) and histopathology.

A thorough intra-operative search was diligently made to document the size of each lobe of thyroid, presence of embryological remnants including pyramidal tract (PT), tubercle of Zuckerkandl (TZ), and thyro-thymic thyroid rests (TTR). The site, size, side, and grade of the rests and intra-thoracic extension of TTR were documented. The grading of TTR was based on Sackett *et al.* classification as follows.[1] Grade I TTR defined as protrusion of thyroid tissue arising from the inferior border of the thyroid lobe in the region of the thyro-thymic ligament, distinctly recognizable from the line of the lower border of the thyroid gland. Grade II TTR comprises thyroid tissue remnants found within the thyro-thymic tract but attached to the thyroid gland by a narrow pedicle of thyroid tissue. Grade III TTR is similar to Grade II TTR, except their attachment is by a fibro-vascular core. Grade IV TTR do not have connection to the thyroid gland.

Tubercle of Zuckerkandl (TZ) was graded as follows; Grade I: <0.5 cm, Grade II: 0.5- 1 cm, Grade III >1 cm.[7] Parathyroid glands were identified and their number and location were noted. At the completion of the surgical procedure, the parathyroid glands were inspected again to evaluate their color and viability. The thyroidectomy specimen was also inspected for inadvertent parathyroid removal. All patients with thyroid malignancy (both papillary and medullary cancer) underwent central compartment lymph node dissection either prophylactic or therapeutic with or without modified radical neck dissection based on the lymph nodal positivity by FNAC or frozen section histology. The non-viable or inadvertently removed parathyroids were immediately auto-transplanted into the contra-lateral sternocleidomastoid muscle by the standard technique.[8]

As identification of TTR poses greater problems during surgery, the patients were divided into Group-A (TTR positive cases) and group-B (non - TTR cases) and various clinical parameters were analyzed between the 2 groups.

Statistical analysis

The data were tabulated and analyzed using IBM SPSS statistics 20.Ink. Patient demographics were expressed in mean+/-standard deviation. Chi square test for difference in proportions and student *t* test for difference means were used for test of significance. *P* value < 0.05 was considered statistically significant.

Results

One thousand one hundred and eighteen (1118) patients undergoing total thyroidectomy were included in the study of which 88.3% (987) were females. The mean age of the patients was 37.9 ± 12 (15–83) years.

The presenting symptom included: clinically noticeable but incidentally detected thyroid swelling in 392 (35.1%), presence of compressive features (persistent dysphagia or dysphonia) in 419 (37.5%), lateral lymph nodal mass in 52 (4.6%), thyrotoxic features in 69 (6.1%), and the remaining 186 (16.7%) presented as thyroid incidentaloma (diagnosed by ultrasound or other forms of imaging).

Majority of the FNAC were benign and they were categorized as follows: nodular colloid goitre (50.3%), MNG with associated thyroiditis (24.8%), follicular neoplasm (8.5%), papillary thyroid cancer (8.1%), medullary thyroid cancer (1.8%), and Hurthle cell neoplasm (1.5%). FNAC was not performed in 5% of patients who comprised thyrotoxicosis cases. Histopathology of the 1118 thyroidectomies showed an overall

malignancy rate of 21.2% of which papillary thyroid cancer was the commonest contributing 92% and the remaining were Follicular (3%), Hurthle cell carcinoma (2%) and medullary thyroid carcinoma (3%). Of the 1118 thyroidectomies, TTR were evident in 230 patients. Histopathology of the thyroidectomy specimens with TTR revealed that the majority (187/230, 81.3%) had multi-nodular goitre, while malignancy was present in 43/230 (18.7%) thyroidectomy specimens. Papillary thyroid cancer in 36/230 (15.65%), medullary thyroid cancer in 5/230 (2.17%) and follicular thyroid cancer in 2/230 (0.86%) of cases.

The common embryological remnants seen in our study were: PT (57.33%), TZ (53.48%), and TTR (20.57%). Pyramidal tract (PT) remnant was found in 641/1118 (57.33%) patients and seen arising from the right lobe in 310/641 (48.36%), isthmus in 197/641 (30.73%) and left lobe in 134/641 (20.9%) of thyroidectomy specimens. Ethical clearance was obtained on May 22, 2011.

Of the 1118 patients, TZ was seen in 598/1118 (53.48%) cases. TZ was predominant on the right side, present in 456/1118 (40.78%) and less on the left side 236/1118 (21.1%). Majority were grade II TZ than grade I and the exact split up is as follows: Right Side, Grade I (13%), II (23.9%), III (3.88%) and absent in 59.22% of cases. Left side, Grade I (7.1%), II (11.1%), III (2.9%), and absent in 78.9% of lobes.

Both PT and TZ were more commonly observed on the right side with 72.6% and 69.5% of them were seen associated with TTR, respectively.

TTR, the embryological remnant below the thyroid lobes were documented in 230/1118 (20.57%) of thyroidectomy procedures. Similar to PT and TZ, TTR was also encountered more on the right side—54.78% (126/230) and the various grading and distribution of TTR is given in Table 1.

The mean size of the 230 TTR were 2.48 ± 1.69 cm (0.5 -8.8 cm). Majority (58.3%) of these TTR were smaller than 2 cm, while 10.8% of TTR were larger than 5 cm. TTR with <1 cm was found in only 12% of thyroidectomy specimen. Few TTR with various grading encountered during our total thyroidectomy were depicted in Figure 1 [(a) shows a Grade III Thyrothymic rest (TTR) attached to the isthmus by a narrow fibrovascular pedicle. (b) Shows a Grade III TTR attached at the inferior aspect of the thyroid gland and a separate Grade IV TTR below the grade III TTR. (c) Shows a Grade II TTR attached to the lower end of right lobe of thyroid. (d) Shows a Grade IV TTR which is disconnected from the thyroid gland and found in the anterior mediastinum]. Figure 2 shows a total thyroidectomy specimen with all the three embryological rests (small arrow: pointing towards the pyramidal tract, medium arrow: the left grade III tubercle of Zuckerkandl, large arrow: the Grade III Thyro-thymic thyroid rest delivered from the anterior mediastinum), while Figure 3 shows total thyroidectomy specimen, with bilateral thyro-thymic thyroid rests (TTR), Grade II TTR on the left side and Grade III TTR on the right side.

Table 1: Grading of Thyro-Thymic Thyroid Rests (TTR)

Grading of TTR	Unilateral *n* (%)	Bilateral *n* (%)	Total *n* (%)
Grade I	102 (44.34%)	11 (4.78%)	113 (49.13%)
Grade II	70 (30.43%)	4 (1.73%)	74 (32.17%)
Grade III	36 (15.65%)	1 (0.43%)	37 (16.08%)
Grade IV	5 (2.17%)	1 (0.43%)	6 (2.60%)
Total *n* (%)	213 (92.6%)	17 (7.4%)	230 (100%)

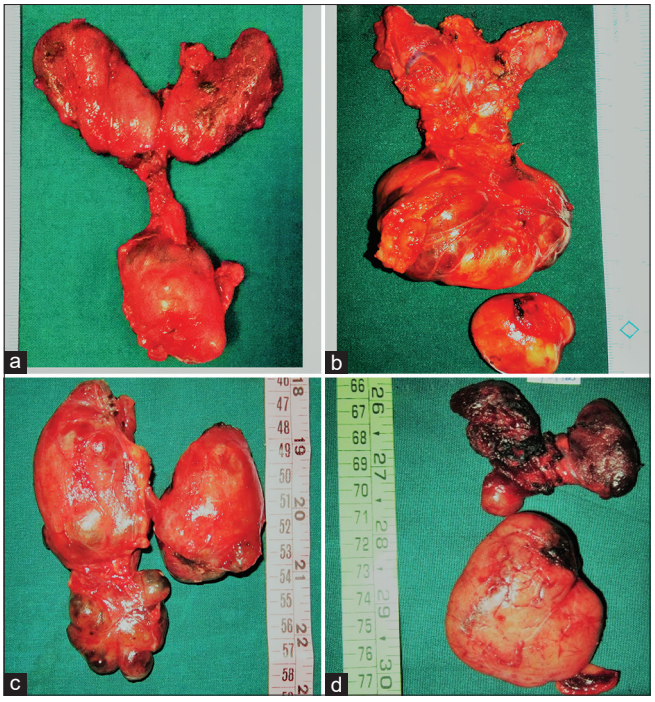

Figure 1: (a) shows a Grade III Thyrothymic rest (TTR) attached to the isthmus by a narrow fibrovascular pedicle. (b) Shows a Grade III TTR attached at the inferior aspect of the thyroid gland and a separate Grade IV TTR below the grade III TTR. (c) Shows a Grade II TTR attached to the lower end of right lobe of thyroid. (d) Shows a Grade IV TTR which is disconnected from the thyroid gland and found in the anterior mediastinum

Table 2 gives a detailed description on the associations of TTR on various parameters. The presence of TTR had a higher proportion of patients with compressive features, intra-thoracic extension and higher prevalence of other embryological rests (PT, TZ). The permanent morbidity like vocal cord palsy ($P = 0.67$) and permanent hypocalcemia ($P = 0.89$) was not statistically different with regard to the presence of TTR.

Discussion

In order of frequency, the common embryological remnants observed in our series were PT (57.33%) followed by TZ (53.48%) and TTR (20.57%), respectively. Both TZ and PT are usually easily identified during surgery and do not pose any problem. However, TTR may be overlooked especially grade 3 and 4 (Sackett) if the surgeon does not actively search for the same. This may result in incomplete surgery in well-differentiated thyroid cancer as well as in autoimmune causes of hyperthyroidism to the extent that

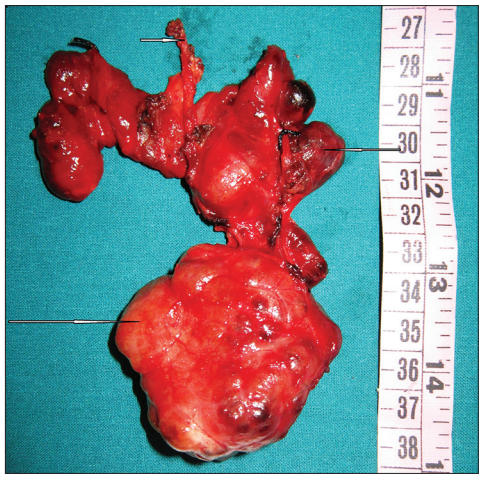

Figure 2: A total thyroidectomy specimen with all the three embryological rests, small arrow: pointing towards the pyramidal tract, medium arrow: the left grade III tubercle of Zuckerkandl, large arrow: the Grade III Thyro-thymic thyroid rest delivered from the anterior mediastinum

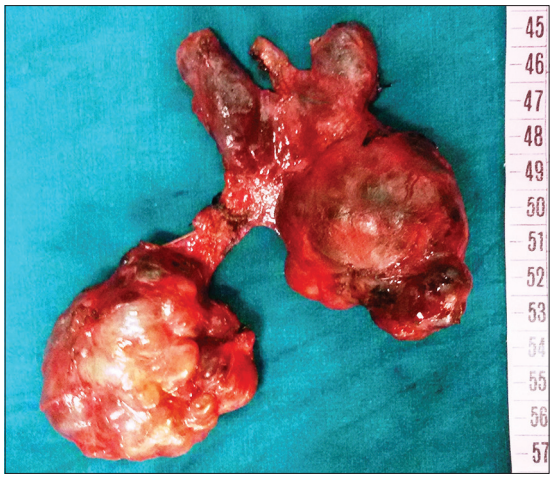

Figure 3: Total thyroidectomy specimen, with bilateral thyro-thymic thyroid rests (TTR), Grade II TTR on the left side and Grade III TTR on the right side

Table 2: The impact of presence of TTR on other clinical parameters

Parameters	Group A- TTR present (*n*=230) (%)	Group B- TTR absent (*n*=888) (%)	*P*
Age (in years) mean±SD (range)	39±12.5 (17-75)	37.4±10.7 (15-83)	0.17
Females	87.4%	89.5%	0.29
Presence of TZ	160 (69.56%)	438 (49.32%)	0.001
Presence of PT	167 (72.6%)	474 (53.37%)	0.01
Retrosternal extension	51 (22.17%)	63 (7.09%)	0.01
Compressive features	110 (47.82%)	309 (34.79%)	0.02
Malignancy rate	43 (18.7%)	194 (21.8%)	0.24
Parathyroid auto-transplantation	35 (15.21%)	124 (13.96%)	0.11
Temporary hypoparathyroidism	139 (60.34%)	251 (28.26%)	0.001
Permanent hypoparathyroidism	3 (1.30%)	11 (1.23%)	0.89
Temporary vocal cord palsy	8 (3.47%)	23 (2.59%)	0.36
Permanent vocal cord palsy	2 (0.86%)	7 (0.78%)	0.67

TZ=Tubercle of Zuckerkandl, PT=Pyramidal tract remnant, TTR=Thyrothymic thyroid rest

reoperation may be required in few cases. Further, the presence of TTR may require more surgical dissection, increasing the chances of devascularizing parathyroids or injuring recurrent laryngeal nerve.

Our finding of TTR in 20.57% is much less in comparison to the only other large series on thyroid embryological remnants by Sackett *et al.* where the prevalence of TTR among 100 thyroidectomies was 46%.[1] Another review Fernando *et al.* quoted a TTR prevalence of 30%.[9]

In the study by Sackett *et al.*, the occurrence of TTR were grade I (68%), grade II (12%), grade III (9%), and grade IV (11%), respectively. In contrast, in our series, grade I (49.13%), Grade II (32.17%), grade III (16.08%), and grade IV (2.60%). The incidence of grade II was quite high and grade IV was very low than Sackett *et al.*[1] With respect to size, most of the TTR observed in the Sacket series were <1 cm (88%) and largest was around 4.5 cm. In our study, majority were >1 cm with largest being a 8.8 cm intrathoracic Grade IV TTR. The above observations of higher proportion of grade II and larger size of TTR may be due to the larger size of the goitre found in the Indian subcontinent, late presentation and probable iodine deficiency compared to western countries.

It is very important to diligently search for these TTR in the region below the inferior aspect of the thyroid gland to identify them. Usually they are embedded within the thyro-thymic ligament or found in the central compartment of the neck. It may be easily mistaken for a parathyroid or lymph node as promptly suggested by Sackett *et al.*[1] A high index of suspicion is crucial to identify these rests.[10] Grade IV TTR usually pose a great risk of getting unattended during surgery when imaging is not done for the same in the preoperative period as happened in one of our case of thyroid malignancy with non-elevation of TSH in the postoperative period during thyroid hormone withdrawal.[11] These embryological rests especially, TTR (large grade II, III and IV) and TZ cause compressive features. Giant TZ (>5 cm), causing severe compression is rare but had been encountered by us (8 cm) in one patient.[12] We sent TTR that are not attached to the thyroid gland in separate containers for the final confirmation by histopathology. In addition to the observed findings of TTR, TZ were also noted. TZ act as a guide to identify the parathyroid glands in difficult thyroidectomies along with other pointers.[13] A prospective study published in 2019, stress the importance of thyroid embryological remnants, their incomplete removal leading to recurrence and their outcomes. Pyramidal lobe was noted in 54%; ZT in 72% and TTR in 34% patients in the study.[14] Rico *et al.* in a case report highlighted the importance of median and lateral anlages of thyroid- embryological remnants during surgery.[15] Another prospective study by Freitas *et al.* noted the

importance of TZ in 68% serving as a pointer to the recurrent laryngeal nerves.[16] Wang *et al.* reported a recurrence of Papillary carcinoma Thyroid in a Pyramidal lobe remnant, suggesting the importance of complete removal of embryological remnants.[17]

In conclusion, embryological remnants are frequently encountered during thyroid surgeries with pyramidal tract and tubercle of Zuckerkandl contributing to majority of them. Thyro-thymic thyroid rests are less common. However, they pose more surgical problems (especially grade III and IV) in both identification and removal. A high index or suspicion and a shift to embryological rather than anatomical approach is required by every operating surgeon operating in the community and elsewhere for complete removal of the latter remnants.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflict of interest

There is no conflict of interest.

References

1. Sackett WR, Reeve TS, Barraclough B, Delbridge L. Thyrothymic thyroid rests: Incidence and relationship to the thyroid gland. J Am Coll Surg 2002;195:635-40.
2. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, *et al.* American thyroid association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer. Thyroid 2016;26:1-133.
3. Snook KL, Stalberg PL, Sidhu SB, Sywak MS, Edhouse P, Delbridge L. Recurrence after total thyroidectomy for benign multinodular goitre. World J Surg 2007;31:593-8.
4. Agarwal A, Mishra AK, Lombardi CP, Raffaeli M. Applied embryology of the thyroid and parathyroid glands. In: Randolph GW (ed) Surgery of the Thyroid and Parathyroid glands, 2nd edn. Elsevier Saunders, Philadelphia; 2013. p. 15-24.
5. Delbridge L. Total thyroidectomy: The evolution of surgical technique. ANZ J Surg 2003;73:761-8.
6. Gauger PG, Delbridge LW, Thompson NW, Crummer P, Reeve TS. Incidence and importance of the tubercle of Zuckerkandl in thyroid surgery. Eur J Surg 2001;4:249-54.
7. Hisham AN, Aina EN. Zukerkandl's tubercle of the thyroid gland in association with pressure symptoms: A coincidence or consequence? Aust N Z J Surg 2000;70:251-3.
8. Delbridge L. Parathyroid autotransplantation: An essential technique for safe thyroid surgery. ANZ J Surg 2002;72:852-3.
9. Fernando R, Rajapaksha A, Ranasinghe N, Gunawardana D. Embryological remnants of the thyroid gland and their significance in thyroidectomy. World J Endoc Surg 2014;6:110-2.
10. Houck WV, Kaplan AJ, Reed CE, Cole DJ. Intrathoracic aberrant thyroid: Identification critical for appropriate operative approach. Am Surg Apr 1998;64:360-2.
11. Sadacharan D, Mahadevan S, Muthukumar S, Dinesh S. Non-elevation of TSH after total thyroidectomy: A surgical surprise. BMJ Case Rep 2015. doi: 10.1136/bcr-2015-209809.
12. Sadacharan D, Mahadevan S, Muthukumar S, Ravikumar K. A rare giant tubercle of Zuckerkandl with retrosternal extension encountered during total thyroidectomy. BMJ Case Rep 2015. doi: 10.1136/bcr-2015 2103071.
13. Bhattacharjee A. Role of Zuckerkandl's tubercle and neurovascular structures in parathyriod identification during thyroidectomy. J Am Coll Surg 2018;227:e190.
14. Abd-Elwahab EM, El-hady HA. Outcomes of total thyroidectomy with vs. without extensive intended dissection of the thyroid embryological remnants single centre experience. Med Sci 2019;23:363-8.
15. Rico F, Lung J. Thyroid embryonic anomalies involving the medial and lateral anlagen: Two surgical case reports. Case Rep Surg 2019;3174848:1-6.
16. Freitas CAF, Paroni AF, Santos AN, Silva RJS, Souza RO, Silva TF, *et al.* Can the Zuckerkandl tubercle assist in the location of the inferior laryngeal nerve during thyroidectomies? Rev Col Bras Cir 2019;46:e2249.
17. Wang M, Zou X, Li Z, Zhu J. Recurrence of papillary thyroid carcinoma from the residual pyramidal lobe: A case report and literature review. Medicine 2019;98:15:1-4.