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Harshwardhan D Pokharkar
Associate Consultant,
Kokilaben Dhirubhai Ambani
Hospital, Mumbai,
Maharashtra, India

Neharika
Assistant Professor,
Department of General
Surgery, Hind Medical College,
Barabanki, Uttar Pradesh,
India

Thyroid cancer in benign thyroid diseases: Incidence and role of total thyroidectomy

Harshwardhan D Pokharkar and Neharika

Abstract

Introduction: Most of the thyroid nodules are benign and fewer than 5% of them are actually malignant. There is always a clinical dilemma when FNAC is benign or inconclusive. The presence of solitary or dominant nodule in thyroid should be investigated to exclude carcinoma.

Aim: There is significant prevalence of thyroid micro carcinomas among benign thyroid diseases; this study was done to suggest total thyroidectomy (TT) as the preferred method in suspicious thyroid diseases.

Material and methods: This is a hospital based analysis of all thyroid surgeries performed in a thyroid service unit over a period of 4 years between 2006 to 2009. The total number of thyroid surgeries during this period was 277. 30 patients had undergone completion thyroidectomy following confirmation after hemi thyroidectomies which were done outside. FNAC was the guiding investigation to surgery in all the remaining 247 patients.

Results: In the present study, FNAC was done for 247 patients. Cytopathological analysis showed 132 cases of papillary thyroid cancer, 7 cases of MTC and 2 cases of ATC. Out of 106 FNAC proven benign cases, 90 cases had undergone total thyroidectomy, 51 cases were found malignant in final HPR. The incidence of malignancy was 48 % in overall benign thyroid lesions in which association of malignancy was highest for follicular neoplasm [71%] followed by adenomatous hyperplasia [57%].

Conclusions: We found that in certain variant of benign thyroid diseases total thyroidectomy can be performed with very low incidence of complications to prevent the future recurrences and reoperations.

Keywords: Hashimoto's thyroiditis, papillary thyroid cancer, medullary thyroid cancer, anaplastic thyroid cancer

Introduction

The burden of thyroid disease in the general population is enormous. Thyroid disorders are the most common among all the endocrine diseases in India [1]. It is different from other diseases in terms of its ease at identifying, as it is readily visible in neck and its amenability for treatment. But the only issue is ruling out of a malignancy in a thyroid swelling. Thyroid nodules are most often be only benign or can be associated with malignancy or develop malignancy over a period of time. The basic contradiction is the method of management if a diagnosis on cytology is equivocal or uncertain. Most of the thyroid nodules are benign and fewer than 5% of them are actually malignant [2]. The presence of solitary or dominant nodule in a multinodular goiter should be investigated to exclude carcinoma. Of all patients with Graves disease, approximately 30% presents with palpable or radiological nodules [3, 4] out of which malignant potential is present in 17% as compared to incidence of 5% usually found in the general population. Some literatures showed increased malignant rate upto 10% in graves disease as compared to general population [5, 6].

Many cases treated as Hashimoto's thyroiditis may have an associated malignancy. Papillary thyroid carcinoma (PTC) is the most prevalent and the one with the best prognosis among all malignant thyroid neoplasm [7]. In areas with adequate iodine intake, most common cause of hypothyroidism is Hashimoto's thyroiditis (HT) which is a type of chronic lymphocytic thyroiditis [8]. Studies across the world has shown the positive association between papillary thyroid cancer and hashimoto thyroiditis [9, 10, 11].

Though FNAC has revolutionized the management of thyroid nodule, the accuracy of cytological diagnosis is highly dependent on the person performing the aspiration and the person interpreting it.

Correspondence
Harshwardhan D Pokharkar
Associate Consultant,
Kokilaben Dhirubhai Ambani
Hospital, Mumbai,
Maharashtra, India

The sensitivity and specificity ratios for FNAC in published series range between 65% and 98% for sensitivity and 73–100% for specificity [12, 13]. Studies show that 2–15% of FNAC are insufficient to diagnose, 50–70% benign, 15–30% suspicious and 5–10% malignant [14, 15, 16]. More often patient whose sample lacks a specific diagnosis, requires the need for further procedure. Indications of total thyroidectomy are very limited and it is occasionally performed for non malignant conditions [17]. to treat small carcinomas, moicrocarcinomas and some benign thyroid disease with total thyroidectomy is controversial [18]. Furthermore, it has been shown that the complication rates of permanent recurrent laryngeal nerve palsy (0–1.3%) and permanent hypoparathyroidism (1%) following subtotal thyroidectomy are similar to those following total thyroidectomy [19].

There is always a clinical dilemma when FNAC is benign or inconclusive. We studied patients with presence of thyroid nodules whose FNAC is benign or inconclusive and undergone total thyroidectomy in view of clinical suspicion.

Materials and methods

This is a hospital based analysis of all thyroid surgeries performed in a thyroid service unit over a period of 4 years between 2006 to 2009. The total number of thyroid surgeries during this period was 277. We have 30 patients who underwent completion thyroidectomy following

confirmation after hemi thyroidectomies which were done outside. Fine needle aspiration cytology was the guiding investigation to surgery in all the remaining 247 patients. The cytologists were able to identify papillary carcinoma in 132 patients, Hashimoto's thyroiditis in 42, benign nodules (colloid goiter, adenomatous nodule, nodular goiter, Hashimoto's thyroiditis, follicular neoplasm) in 64 patients. Ultrasonography was attempted in the patients with thyroiditis and benign nodules, after fine needle aspiration cytology. The information from ultrasonography was suspicious but not satisfactory and hence we planned surgery for all the patients. The proposed surgery was total thyroidectomy for confirmed papillary carcinoma and in the intermediate group; decision was taken for total thyroidectomy depending on the presence of nodules in the other lobe during exploration. Those cases where hemithyroidectomy was done were excluded from the analysis.

Results

FNAC was done for 247 patients. Cytopathological analysis showed 132 cases of papillary thyroid cancer, 7 cases of MTC and 2 cases of ATC. Remaining 106 cases were benign in which 42 cases of Hashimoto's thyroiditis, 14 cases of follicular neoplasm and 50 cases were reported as benign colloid goiter, adenomatous hyperplasia and multinodular goiter.

Table 1: Fine needle aspiration cytology report

FNAC Diagnosis	Number of patients
Papillary thyroid cancer	132
Hashimoto's thyroiditis	42
Colloid goiter, adenomatous nodule, nodular goiter	50
Medullary thyroid cancer	07
Follicular neoplasm	14
Anaplastic thyroid cancer	02
Total	247

Out of 277 patients, all underwent surgery in our institution. 30 patients had undergone completion thyroidectomy for malignancy in hemithyroidectomy specimen. Total 231 patients had undergone total thyroidectomy in which 141 cases for FNAC proven thyroid malignancy, 42 cases for Hashimoto's thyroiditis. Remaining 48 cases of total thyroidectomy was done for intraoperative finding of nodule in opposite lobe. Neck dissection was done in 21 patients with FNAC proven malignancy in which 7 were medullary and 14 were papillary thyroid cancer with neck nodes. Remaining 16 benign cases underwent hemithyroidectomy.

Table 2: Surgical procedure executed.

Surgical procedure	Number of patients
Hemi thyroidectomy	16
Total thyroidectomy	210
Total thyroidectomy + neck dissection	21
Completion thyroidectomy	30

Out of 106 FNAC proven benign cases, 90 cases that had undergone total thyroidectomy, 51 cases were found

malignant in final HPR. Out of 51 cases, most common HPR was papillary thyroid cancer (n=37), 10 follicular thyroid cancer and only 4 cases of follicular variant of papillary thyroid cancer.

Table 3: Malignancy in cytological benign lesions (n=106)

Type of malignancy	Number of patients
Papillary thyroid cancer	37
Follicular variant of papillary thyroid cancer	4
Follicular thyroid cancer	10

In 106 cases of benign cytopathology, the most common variant was Hashimoto's thyroiditis [39%] followed by adenomatous hyperplasia [26%], follicular neoplasm, colloid goiter and multinodular goiter in the decreasing order. The incidence of malignancy was 48% in overall benign thyroid lesions in which association of malignancy was highest for follicular neoplasm [71%] followed by adenomatous hyperplasia [57%]. 19 out of 42 cases of hashimoto's thyroiditis were found malignant in final HPR.

Table 4: Incidence of malignancy in benign nodule (n=106)

Type of benign lesion	N	Number of patients with malignancy [final HPR]
Colloid goiter	12	02
Adenomatous nodule	28	16
Nodular goiter	10	04
Hashimoto's thyroiditis	42	19
Follicular neoplasm	14	10
Total	106	51

Mixed histopathologies of thyroid cancer with lymphocytic thyroiditis were found in 55 cases. 19/42 patients operated for hashimoto's thyroiditis having foci of papillary cancer in their final HPR. 18% cases of proven papillary thyroid

cancer showed mixed picture of PTC with hashimoto's thyroiditis. 48 cases of benign thyroid lesions who underwent total thyroidectomy, 12 cases were positive for PTC with foci of lymphocytic thyroiditis.

Table 5: Association of hashimoto's thyroiditis with benign and malignant thyroid lesions.

FNAC	HPR	Number of patients
Hashimoto's thyroiditis (n=42)	Predominantly Hashimoto's thyroiditis + Papillary thyroid cancer	19
Papillary thyroid cancer (n=132)	Predominantly Papillary thyroid cancer + Hashimoto's thyroiditis	24

Discussion

Though thyroid gland is a superficial organ easily identifiable in the neck, at times it will be difficult to differentiate a malignant gland from a benign thyroid gland. There is a possibility of malignancy associated with benign disorders. Multinodular goiter, nodules in hypothyroid patient, cystic thyroid nodule may all possess a focus of papillary carcinoma and by cytology alone, it may not be possible to differentiate these nodules into benign and malignant. It becomes difficult for the surgeon to make a correct decision on treatment modality, thus making the role of surgery important in doubtful thyroid swellings. On the other hand, if patients not diagnosable by FNAC are treated medically, it is possible the tumor in them may progress leading to delay in the management of thyroid cancer. Current indications of total thyroidectomy are toxic and nontoxic multinodular goiter, Hashimoto's thyroiditis, Graves's disease and malignancies either with a less aggressive clinical course (e.g., papillary thyroid carcinoma) or a rapidly progressive course (e.g. anaplastic thyroid cancer) [20, 21].

In PubMed based data search we found various articles in favor of total thyroidectomy for benign cytology. A retrospective analysis was performed by Pezzolla A *et al.*, on 240 patients submitted to surgical intervention in order to establish the incidence of the carcinoma. One hundred sixty five patients (68.75%) were affected by benign disease (132 multinodular goiter, 30 uninodular goiter, 2 Plummer and 1 Basedow) and 75 (31.25%) by carcinoma. In 30 of 165 patients (18.2%), affected by benign disease, occurred a histological diagnosis of thyroid carcinoma, (18 papillary carcinoma, 6 follicular carcinoma, 5 papillary carcinoma follicular variant and 1 oncocytic carcinoma) [22]. In other study done by Heydar Ali Esmailia *et al.*, 96 cases of benign category underwent surgery and 4 of them had malignancy on histopathological examination (3 papillary Ca and one follicular Ca) [23]. Gul K *et al.*, showed in his study cytologically 87.7% of nodule are benign, out of which, in 13 patients with benign cytology and in 3 Graves patients without any nodule ultrasonographically, incidental thyroid carcinoma was found (5.7%) [24]. A meta analysis showed that the HT incidence is 2.77 higher in patients with PTC when compared to patients with benign thyroid diseases. In addition, in patients with thyroid carcinoma, the association of HT is 1.99 times higher among those with PTC than in

patients with other pathological types of thyroid cancer [11]. There is a rate of 26.8% of patients with the HT PTC association, however without statistical significance with tumor size [25].

In a study on role of total thyroidectomy in benign thyroid diseases done by Pietro Accetta *et al.*, the most common preoperative diagnosis was nontoxic multinodular goiter, followed by autoimmune thyroiditis; recurrent goiter occurred in 11 cases. On final HPR, multinodular goiter was found in 37 (56.1%) patients, autoimmune thyroiditis in 22 (33.3%), follicular adenoma isolated in five (7.6%), Hurthle cell adenoma in two (3.0%). Sixteen patients (24.2%) had more than one histopathological diagnosis [26]. It is known that non-toxic multinodular goiter is the most frequent indication for total thyroidectomy in benign diseases of the gland. However in our study we found hashimoto's thyroiditis as the most common indication of TT in benign thyroid lesions indicating lesser incidence of multinodular goiter in southern India. Total thyroidectomy remains the procedure of choice in various groups of surgeons for cases of thyroid malignancy with involvement of both lobes, regardless of the size of the nodules and large goiters [27].

The autoimmune thyroiditis, also known as Hashimoto's thyroiditis, is an always-evolving clinical disease and the main cause of primary hypothyroidism. Besides the blood tests that bring the suspicion of the disease, ultrasound usually shows an enlarged gland, with heterogeneous texture and pseudo nodules, in several cases displaying well-defined nodules, which characterize the nodular thyroiditis. Some researchers have observed a higher incidence of cancer in autoimmune thyroiditis, suggesting that this association is not just casual. Di Pasquale [28], on an extensive review of 23 cases of thyroiditis spanning 16 years, found 20 papillary carcinomas and three follicular associated. In the period that includes the present study, we performed thyroidectomy in 42 patients with autoimmune thyroiditis, of which 19 (45%) had concomitant carcinoma, all papillary. Once defined the surgical approach, we consider TT as the best option, as in 42 of our cases.

The postoperative diagnosis of follicular carcinoma almost always results in a new operation to total thyroidectomy, regardless of prognostic factors. Thus, without definitive diagnosis, and knowing that about a third of follicular neoplasm may be malignant, TT is a valid option for those with bilateral nodules and those who do not accept the

possibility of reoperation [26]. In our study, about 71% cases of follicular neoplasm were found as malignant in final HPR [10-14].

In our analysis, we had papillary carcinoma in cytology diagnosed hashimoto's thyroiditis (45%), cytology diagnosed benign nodules has papillary carcinoma (44%) and hashimoto's thyroiditis (18%) in a pure papillary thyroid carcinoma diagnosed cytologically. The overall incidence of hashimoto's thyroiditis in this series is 24%. The associated malignancy in hashimoto's thyroiditis is 25%. Association of PTC with hashimoto's thyroiditis may be more as ours is a referral hospital and most of the cases referred to our institute are suspicious cases only.

Conclusion

The incidence of association of papillary thyroid cancer in hashimoto's thyroiditis and other benign thyroid nodules are high in our series. Hence the clinician should look into other aspects especially when FNAC is inconclusive and in benign lesion when suspicion is high, one should not hesitate to perform surgery. Since the preference is total thyroidectomy even for some of the benign thyroid nodules, the same can be opted in patients who have diffuse enlargement or multinodular goiter where FNAC diagnosis is not certain. If this principle was followed, we could have avoided the 2nd surgery (completion thyroidectomy) in 30 patients in our series. The complications following total thyroidectomy has definitely come down with meticulous surgical technique and one should not hesitate to perform total thyroidectomy whenever necessary. Total thyroidectomy for benign thyroid disease can avoid reoperation for nodular goiter and hyperthyroidism and eliminate any subsequent risk of malignant change in thyroid glands.

Finally, our results had indicated the significant prevalence of thyroid micro carcinomas among benign thyroid diseases; this prevalence would suggest TT as the preferred treatment in benign thyroid diseases for which surgery is indicated. In conclusion, total thyroidectomy can be safely performed, with low incidence of permanent complications. Safe thyroid surgeries not only increases its indications but also avoids future recurrences and reoperations with permanent cure.

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Abbreviations

Papillary thyroid cancer [PTC], medullary thyroid cancer [MTC]. Fine needle aspiration cytology [FNAC], Total thyroidectomy [TT], Hashimoto thyroiditis [HT], Histopathology report [HPR], Anaplastic thyroid cancer [ATC].

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

The department of surgical oncology was involved in the diagnosis, management and post-operative recovery of the patients. The Pathology department was responsible for

pathological diagnosis. All authors have contributed with the literature review and with the preparation of this manuscript. All authors read and approved the final manuscript.

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