Surgical Indications for Goiter with Background Hashimoto's Thyroiditis: Institutional Experience

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Abstract Hashimoto's thyroiditis (HT) is usually treated conservatively with thyroxine. Its incidence is higher in Iodine sufficient areas and may require surgery for associated nodularity or complications. A retrospective study on surgically treated HT cases was conducted in a tertiary care teaching hospital in an Iodine sufficient area of Southern India. 34 cases of goiter with associated HT, who underwent thyroidectomy between 2007 and 2010 were analysed for indications of surgery. Minimum follow-up period was 6 months. F:M ratio was 31:3 with mean age of 41.3 years. Goiter was diffuse in 41% and nodular in 59%. 16 (47%) of patients were hypothyroid. Autoimmune association was found in 35%. Commonest surgery done was hemithyroidectomy in 12 (35%) followed by subtotal thyroidectomy in 10 cases. Most frequent indication for surgery was nodular goiter in 12 (35%) followed by associated malignancy, persistent goiter, pressure symptoms and painful thyroiditis. Histopathology showed diffuse HT alone in 12 (35%) and rest of the cases had HT as a component synchronous with other pathologies. Associated pathologies were benign multinodular goiter (6), colloid nodule (6), papillary cancer (5), follicular adenoma (4), cyst (1). Surgery for HT is primarily indicated for associated

pathologies like dominant nodule, suspicious or proven malignancy, persistent goiter, painful thyroiditis, pressure symptoms and rarely for HT perse. Rate of surgery for HT associated goiter appears to be higher in Iodine sufficient areas, the cause of which needs to be studied further.

Keywords Hashimoto's thyroiditis · Thyroxine · Surgery

Introduction

Hashimoto's thyroiditis (HT) is traditionally considered a medical disease managed either by long-term surveillance for development of thyroid failure in case of small euthyroid goiters or by full-dose thyroxine replacement/suppressive therapy in case of large hypothyroid goiters [1]. The incidence of HT is higher in iodine-sufficient areas [2]. Surgery is required in very few patients with associated complications, nodules or suspicion of malignancy [3]. Increasing experience and reports of surgical intervention for newer indications are challenging this traditional view of HT as a medical disease. In the present study, we attempt to enlist all the indications for surgery in HT-associated goiter on the basis of our own experience from an iodine-sufficient area and review of the literature.

Materials and Methods

The study was conducted combinedly by the departments of General Surgery and Endocrine Surgery in a tertiary care institute hospital catering to three districts of an iodine-sufficient area in Southern India. It is a retrospective observational study of thyroid cases treated at the institute hospital. All the patients with thyroid

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disease who underwent surgery between 2007 and 2010 provided the clinical material. Clinicopathological data were collected from case records and registers and were cross checked with the pathology department. Of the 149 patients with fully available data, 34 patients, forming our study cohort, had HT on final histopathology. According to our institutional protocol, the size criterion for surgery in a benign nodular goiter is a largest nodule more than 3 cm.

Inclusion criteria for the cases were as follows: 1) Thyroidectomy with final histopathology report of HT, either as a sole finding or associated with other pathology, 2) HT diagnostic criteria as lymphoplasmocytic infiltrate, focal follicular disruption, Hurthle cell metaplasia with or without fibrotic element and 3) Age >30 years. Exclusion criteria were as follows: 1) Cytologically diagnosed HT, but histopathology showing no focus of HT; irrespective of anti-thyroid peroxidase (anti-TPO) titer. Thyroid stimulating hormone (TSH) range used for functional assessment was 0.4–5.5 mIU/L.

At a minimum follow-up period of 6 months, patient's clinical and health status with regard to symptomatic relief, psychological well-being and residual/recurrent goiter were recorded. Review of the literature was done using Medline and Google search. Statistical analysis was done with descriptive statistics using SPSS 12.0 version.

Results

The study period spanned over 36 months with a mean follow-up period of 17.4 months. Thirty-four of 149 (22.8%) patients who underwent operation had HT on final histopathology. The mean age of patients was 41.3 years, and female to male ratio was 31:3 (91.2%), reflecting female preponderance. The palpable nature of the goiter was diffuse in 41% of the cases with or without fine nodularity and another 59% had well-defined nodule(s). Two-fourths of the cases of large multinodular goiter (MNG) had retrosternal extension. Hypothyroidism was present in 16 (47%) of patients. Autoimmune associations in the form of diabetes mellitus was present in 4 (11.7%), vitiligo in 2 (5.9%), both diabetes and vitiligo in 2 (5.9%), Addison's disease in 2 (5.9%) and rheumatoid arthritis in 2 (5.9%). Preoperative diagnosis of HT on fine-needle aspiration cytology (FNAC) was possible in 8 (32%) cases. Anti-TPO titer was assayed only in 10 cases and was positive in 9 of them. All the clinicopathological data are depicted in Table 1.

Table 2 displays the details of surgical intervention and indications for surgery. Commonest procedure done was hemithyroidectomy in 12 (35%) cases followed by subtotal thyroidectomy in 10. Therapeutic neck dissection was done

Table 1 Clinicopathological pProfile of the HT cases

Variables	Frequency
Period of study (months)	36
Period of follow-up (months)	17.4 (6–36)
Mean age (years)	41.3 (30–60)
Sex (F:M)	31:3
Nature of goiter	
-Diffuse	14
-STN	11
-MNG	9
Functional status	
-Euthyroid	14
-Subclinically hypothyroid	6
-Hypothyroid	10
-Hyperthyroid	4
Autoimmune association (n%)	12 (35%)
Fnac findings	
-Hashimoto's thyroiditis	11
-Colloid nodule	12
-Malignancy	3
-Suspicious for malignancy	2
-Adenomatous goiter	6
Anti-TPO positivity ^a	100%
TSH (mIU/L)	3.9 (0.05–13.2)

^a Anti-TPO titer was done only in 10 patients

along with total thyroidectomy in 3 cases of papillary thyroid cancer, who presented with thyroid nodule and jugular lymphadenopathy. Most frequent indication for surgery was nodular goiter in the form of either solitary thyroid nodule (STN) or MNG in 16/34 (47%) of cases. Other indications were associated malignancy, persistent goiter, pressure symptoms and painful thyroiditis. None of the patients had operative mortality. Morbidity in the form of recurrent laryngeal nerve palsy and persistent hypocalcaemia did not occur in any case, although four patients had transient hypocalcaemia and one had transient unilateral recurrent laryngeal nerve palsy that improved within 4 months.

Histopathological details are shown in Table 3. Macroscopically, diffuse goiter was the most frequent finding followed by solitary and multinodular forms. HT was diffusely present throughout the gland only in 12/34 (35%) cases and rest of the cases had HT as a component synchronous with other pathologies. Two of 5 cases of papillary thyroid cancer had incidentally detected papillary microcarcinoma and 1 case, which was suspicious for malignancy on FNAC, turned out to be follicular adenoma. We did not attempt to characterise the pathological subvariants of HT.

Table 2 Details of surgical intervention

Variable	Number (n=)	Percentage (%)
HT operated (n)	34	
Type of surgery		
-Hemithyroidectomy	12	35
-Subtotal thyroidectomy	10	29.5
-Near total thyroidectomy	2	6
-Total thyroidectomy	7	20.5
-TT+neck dissection	3	9
Indications for surgery		
-Dominant nodule/STN	9	26
-Large MNG	7	20.5
-Pressure symptoms	4	12
-Suspicious/proven malignancy	6	17.5
-Persistent goiter on LT4 Rx ^a	4	12
-Recurrent painful thyroiditis	4	12

^a LT4 Rx=On replacement thyroxine therapy

Discussion

HT is the commonest form of thyroiditis. It is a chronic autoimmune thyroiditis and occurs predominantly in women between 30 and 50 years and its incidence increases with age [4]. The incidence of HT varies from 0.1% to 5% and is more commonly seen in iodine-sufficient areas of the world [2]. Many areas of Southern India are iodine sufficient compared with sub-Himalayan Northern India, and prevalence of HT was 7.5% among female goitrous students in the postiodisation era [5]. Its onset is mostly insidious and asymptomatic, but occasionally sudden and painful. Neck pain and tenderness are rare and usually suggests the alternative diagnosis of de Quervain's thyroiditis responsive

to steroids [6]. Although hyperthyroidism is found in few cases in earlier stages, most of the cases have variable degrees of hypothyroidism in later stages. HT can coexist with a plethora of other pathologies, such as colloid nodule, papillary carcinoma, Graves' disease, follicular adenoma, etc., in the same gland.

FNAC with or without anti-TPO antibody titer is diagnostic in majority of the cases [7]. Although the commonest finding on physical examination is a diffuse, firm goiter, in few cases it can present as a large, nodular goiter with/without compressive symptoms.

Treatment of HT is conservative in majority of cases, as it is traditionally considered to be a medical disease. Treatment is long-term surveillance with periodic examination in small, euthyroid goiter till thyroid failure occurs and full-dose thyroxine replacement for thyroid failure or TSH suppressive therapy to regress a large, symptomatic goiter [1]. HT as a pathological entity is rarely an indication for surgical intervention, but surgery is indicated for many clinicopathological conditions associated with HT, such as large nodules, malignancy, pressure symptoms, etc., in the same gland. There are very few articles comprehensively addressing the indications for surgery in HT. Majority of the studies addressed one or few indications for surgery. HT-associated malignancy as a surgical indication has been addressed in many studies [8–10], but end up concluding that malignancy is largely coincidental and surgery is required for suspicious or proven malignancy and not for HT per se. Painful thyroiditis as the surgical indication for HT is rare and exists in the form few case reports. Kon and DeGroot [11] reported largest series of 7 patients with this condition undergoing surgery. We had 4 such patients, 3 of them had episodic pain and 1 had persistent pain with variable degrees of tender thyroid.

The inclusion criterion of >30 years was chosen to avoid overlap with HT, which might have developed in childhood and adolescence. This is because in our experience childhood and adolescent HT have a different clinical behaviour of more frequent lymphadenopathy, less frequent surgery, etc.; studies on which are underway. The mean age of our patient group was 41.3 years with 91% comprising women. Around 41% of the goiters were diffuse and firm on clinical examination and 47% were either subclinically or overtly hypothyroid. Both diffuse goiter and high rate of hypothyroidism [12] are common features associated with HT. High anti-TPO antibody titer is present in more than 90% of cases and serves as a non-specific diagnostic marker for HT [13]. However, we cannot comment on its impact in the role of surgery, as only 10 patients underwent this test and all of them were positive for it. We used a TSH range of 0.3–5.0 mIU/L, to categorise

Table 3 Histopathological profile of the patients

Variable	Number (N)	Percentage (%)
Macroscopic appearance		
-Solitary nodule	11	32
-MNG	7	21
-Diffuse	16	47
Microscopic		
-Benign MNG ^a	6	17.5
-Colloid nodule ^a	6	17.5
-Papillary cancer ^a	5	15
-Follicular adenoma ^a	4	12
-Cyst ^a	1	3
-Only HT ^b	12	35

^a All these cases had pathological component of Hashimoto's thyroiditis associated with the mentioned pathology

^b Hashimoto's thyroiditis was present diffusely throughout the gland

functional status of thyroid. Although recent studies point to an upper normal limit of 2.5–3.0 mIU/L [14, 15], it is not universally implemented. Moreover, our upper limit of 5.0 mIU/L justified for our cohort, as none of the patients with TSH between 2.5 and 5.0 mIU/L had features of hypothyroidism. Only 32% of patients were positive for HT on FNAC, and all of those were diffuse goiters. FNAC was not used as inclusion criterion in the study, as the diagnostic sensitivity in HT varies from 78% to 98.7% [16, 17].

One or more thyroid nodules measuring ≥ 3 cm was our definition for a large thyroid nodule and was an indication for surgery even in the absence of pressure symptoms. Many studies on the natural history of thyroid nodules show that larger nodules grow or evolve into toxic nodules with time. In a German study, there was steady increase in nodular size in up to 50% of 109 consecutive patients in a 3-year follow-up study [18], although this rate may be lower in traditionally iodine-sufficient areas [19]. Accordingly, we operate a nodular goiter of 3 cm even in the absence of pressure symptoms. Extent of surgery was based on the pattern of nodularity and possibility of malignancy. However, recommendations on the extent of surgery for HT were not possible with the available data and results. Long-standing HT can form the substratum for lymphoma with a relative risk of 66 compared with a normal gland that may require surgical biopsy for diagnosis [20]. None of our patients required it, although longer follow-up is needed to address this issue.

HT is associated with a plethora of pathologies as can be seen in our histopathological profile. The coexistence of malignancy with HT has been intriguing since long, with evidence for [21] and against causal association [22]. In the absence of proper evidence, it has to be treated similar to thyroid cancer without HT. Various subtypes of HT have been described [23], although their clinical implication is an enigma. Technically, our surgical experience with the operated cases of HT taught us that an HT-afflicted thyroid is easier to handle and retract due to firm rubbery consistency, especially in diffuse goiter with better visualisation of vascular pedicles. On the contrary, it makes the dissection from surrounding visceral structures difficult due to fibrous adhesions. Although this depends on the extent of fibrous/glandular component and whether it is a focal or diffuse variant.

We had no reliable reference for role of surgery in HT from Indian experience. Similar study was conducted by Thomas and Rutledge [24] who reported a 3% incidence of HT in their case series operated for nodular goiter and in whom the indications of surgery for HT were narrower. The comprehensive list of indications for surgery in HT based on this study and related review of the literature is as follows:

- 1) Dominant nodule or large solitary thyroid nodule (>3 cm)
- 2) Large MNG (>3 cm/retrosternal extension)
- 3) Compressive symptoms
- 4) Proven or suspicious associated malignancy
- 5) Persistent goiter not responsive to full-dose thyroxine replacement
- 6) Associated Graves' disease (Hashitoxicosis)
- 7) Painful thyroiditis
- 8) Incisional biopsy for suspicious lymphoma
- 9) Cosmetic reasons
- 10) Patient's wishes

We had high HT incidence of 22.8% among cases operated for goiter compared with many surgical series, which range from 3% to 33% [21, 24, 25]. Schlicke [21] reported a similar incidence of 23% of HT amongst 713 operated cases of nodular goiter, although from a different geographic zone. Okayasu et al. [26] highlighted the geographical and regional differences in prevalence of HT, even amongst iodine-sufficient areas. Still, the cause of apparently high rate of surgery for HT in our area and few other geographical areas is intriguing. Although largely hypothetical, proposed mechanisms for high rate of surgery in HT in few areas are as follows: 1) HT in certain iodine-sufficient areas have different natural history; 2) Non-iodine environmental factors; 3) Long standing HT leading to more frequent nodule formation requiring surgery; 4) Its just coincidental as both thyroid nodules and HT are common ailments in community; 5) Other pathologies such as nodules, malignancy triggering HT in the thyroid gland or 6) different pathological variant of HT. Nevertheless, we opine that these assumptions are worth investigating to clear the cloud on the role of surgery in HT, especially in iodine-sufficient areas. HT is an interestingly complex disease and the issue of surgery furthers its complexity. We need long-term prospective studies and focussed studies addressing each issue to resolve these issues.

Conclusions

Surgery for HT is primarily indicated for associated pathologies such as dominant nodule, suspicious or proven malignancy, persistent goiter, painful thyroiditis, pressure symptoms and rarely for HT per se. Rate of surgery for HT-associated goiter appears to be higher in iodine-sufficient areas, the cause of which needs to be studied further.

Disclosure Statement There are no conflicts of interest between the authors.

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