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ORIGINAL ARTICLE

Completion Thyroidectomy for Differentiated Thyroid Cancers: Predicting Contralateral Disease

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Abstract
About 12% of the Indian population present with a thyroid nodule to the surgeon, who is then faced with a clinical dilemma if the fine needle aspiration cytology (FNAC) is inconclusive or indeterminate, and the ultrasonogram of the neck is also not contributory. The extent of surgery and the need for a second surgery always weighs on the mind of the surgeon and the patient. We attempt, in our study, to identify a few pathological features in a hemithyroidectomy specimen which would predict the occurrence of malignancy in the opposite lobe. To determine the pathologic predictors of malignancy in the contralateral thyroid lobe, in patients of differentiated thyroid cancer (DTC) who underwent hemithyroidectomy. A retrospective review of the case records of all patients who underwent thyroid surgery in our Institute between January 2010 and December 2014 was undertaken. Various pathologic parameters were analyzed with respect to their predictive power regarding the occurrence of malignancy in the opposite lobe. Three hundred eighty-nine patients underwent thyroid surgery during the above period, of which 91 patients underwent completion thyroidectomy, as they were found to have malignancy in the hemithyroidectomy specimen. The effect of age, gender, and tumor size on bilaterality could not be established statistically. Other variables such as perithyroidal spread and perineural invasion also did not demonstrate statistical significance. Multifocality of the tumor in the hemithyroidectomy specimen, lymphovascular invasion, and capsular invasion were the pathologically significant factors determining the presence of malignancy in the contralateral lobe. Multifocality, lymphovascular invasion, and capsular invasion can be used as additional markers to decide on performing a completion thyroidectomy in a patient of differentiated thyroid cancer.

Keywords Completion thyroidectomy · Differentiated thyroid cancer · Tall cell variant · Multifocality · Capsular invasion · Lymphovascular invasion

Introduction

Thyroid nodules are common in clinical practice and are seen in about 12.2% of the Indian population [1]. However, the age adjusted incidence rates of thyroid cancer vary from 0.6 (in males) to 1.6 in 100,000 (for females) [1]. So, the majority of thyroid nodules, which are clinically palpable and come to the surgeon's notice, are benign. Even so, studies have demonstrated a 5 to 9% incidence of cancer in these nodules [2].

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The 2015 revised American Thyroid Association (ATA) guidelines still recommend ultrasonography of the neck followed by fine needle aspiration cytology (FNAC) as the preferred modalities for establishing a working diagnosis in the management of thyroid nodules [3]. However, in about 15–30% of patients, the FNAC will be indeterminate or inconclusive, which leaves the patient and the surgeon uncertain about the risk of malignancy, the need for surgery, and also the extent of surgery to be performed.

Studies have reported a 15 to 42% rate of malignancy in FNACs reported as indeterminate or Bethesda Class III (atypical follicular lesion of unknown significance AFLUS) [3]. Taking this into account, the ATA guidelines recommend a diagnostic thyroid lobectomy for nodules with indeterminate FNAC, as the initial surgical approach. A completion thyroidectomy is suggested as a follow up procedure *unless* the lesion

is < 1 cm in size, unifocal, and intrathyroidal, with no lymph node metastases and is a low risk tumor.

The advantages of doing a completion thyroidectomy include the possibility of performing a postoperative I-131 whole body scan, radio iodine ablation if necessary, and the use of serum thyroglobulin as a tumor marker for follow-up. The reported complications of recurrent laryngeal nerve paresis or palsy (up to 5%) and transient or permanent hypoparathyroidism (0.5–33%) should not deter the surgeon from performing a necessary surgery [4]. Histopathologic examination of the resected hemithyroidectomy specimen forms the basis for the decision to perform a completion thyroidectomy.

Aim of the Study

This study aims to determine the incidence of malignancy in the contralateral lobe, after performance of a completion thyroidectomy and to identify the histopathologic factors which would predict the presence of malignancy in the opposite lobe.

Patients and Methods

A retrospective review of the case records of all patients who underwent thyroidectomy (for all causes) between January 2010 and December 2014, a period of 60 months, was undertaken, after obtaining the necessary approval from our Institute Ethical Committee. Out of a total of 389 patients who underwent thyroid surgery, 91 patients were subjected to a completion thyroidectomy.

Data Collection

The clinical data of all the patients including age, sex, presenting complaints, and examination findings were collected. The histopathologic factors which were analyzed included the type of malignancy in the ipsilateral lobe, tumor size, capsular invasion, perithyroidal spread (strap muscle and recurrent laryngeal nerve invasion), lymphovascular invasion, perineural invasion, multifocality of the tumor, and nodal positivity in the central compartment (level 6).

Statistical Analysis

A two-tailed Fisher's test was used to determine the correlation between the various clinicopathologic factors and the chances of occurrence of malignancy in the contralateral lobe. Odds ratio was used to calculate the statistical significance.

Results

Demographic Data

Out of 91 patients who underwent completion thyroidectomy, 75 (82.4%) were females and 16 (17.5%) were males. Twenty-eight patients (30.7%) had a malignancy in the contralateral lobe on final histopathologic examination. Twenty of these patients were female (i.e., 26.6% of the entire female cohort) and eight were male (50% of the entire male cohort). There was no significant age difference between the patient cohort with a malignant contralateral lobe and those with a benign lobe (52.6 + 11.9 vs 50.8 + 13.6).

The gap between the first and second surgeries in both the groups was also not significantly different varying from 60.3 + 15.4 days (malignant contralateral lobe) versus 71.6 + 12.8 days in the patients without cancer in the contralateral lobe (Table 1).

Tumor Histopathology

Forty-four patients (48.3%) were reported to have the classic variant of papillary thyroid carcinoma (PTC), 28 (30.7%) follicular variant of papillary thyroid carcinoma, 2 (2.1%) had follicular carcinoma, 3 patients (3.2%) tall cell variant of papillary carcinoma, and 2 patients (2.1%)

Table 1 Demographic data of the patient population

	No malignancy in the contralateral lobe $n = 63$	Presence of malignancy in the contralateral lobe $n = 28$	*P* value
Gender			
Males	8 (12.6%)	8 (28.5%)	NS
Females	55 (87.3%)	20 (71.4%)	
Age at surgery	50.8 ± 13.6 years	52.6 ± 11.9 years	NS
Interval between the two surgeries	71.6 ± 12.8 days	60.3 ± 15.4 days	NS

NS not significant

Table 2 Correlation between the histologic variant and malignancy in the contralateral lobe

Histologic variant $N = 91$	Absence of tumor $n = 63$	Presence of tumor $n = 28$
Classic variant of papillary carcinoma	32 (72.7%)	12 (27.2%)
Follicular variant of papillary carcinoma	21 (75%)	7 (25%)
Tall cell variant of papillary carcinoma	0 (0)	3 (100%)
Micro papillary carcinoma	8 (66.6%)	4 (33.3%)
Medullary carcinoma	0 (0)	2 (100%)
Follicular carcinoma	2 (100%)	0 (0)

medullary cancer. Twelve patients (13.1%) were diagnosed to have micropapillary carcinoma.

Out of the 91 completion thyroidectomy specimens, 28 (30.7%) showed malignancy in the contralateral lobe. 27.2% of patients with the classic variant of papillary carcinoma, 25% of patients with the follicular variant, 33.3% of patients with micropapillary carcinoma, and 100% of patients with the tall cell variant were found to have cancer in the opposite lobe (Table 2).

Capsular invasion was present in 10 out of the 28 patients (35.7%), extra thyroidal spread in 7 (25%), lymphovascular invasion in 10 (35.7%), multifocality in 21 patients (75%), and level 6 nodal positivity in 11 patients (39.2%) (Table 3).

Pathologic Parameters Predicting Bilaterality

On applying the Fisher's two-tailed test to analyze the various pathologic variables, we found that multifocality of the primary tumor in the thyroid lobe was highly predictive of the presence of cancer in the opposite lobe. Statistical significance was also found between lymphovascular invasion and capsular invasion and the presence of malignancy in the contralateral lobe ($p < 0.003$) (Table 4).

Tumor size, stage, extrathyroidal spread, perineural invasion, and nodal positivity had no bearing on the occurrence of malignancy in the opposite lobe. High-risk histologic variants such as the tall cell variant all had cancer in the opposite lobe.

Table 3 Pathologic parameters analyzed in the patient cohort

Variable	Absence of tumor $n = 63$	Presence of tumor $n = 28$
Capsular invasion	9 (14.2%)	10 (35.7%)
Extra thyroidal spread	9 (14.2%)	7 (25%)
Lymphovascular invasion	14 (22.2%)	10 (35.7%)
Multifocality	8 (12.7%)	21 (75%)
Level 6 nodal positivity	14 (22.2%)	11 (39.2%)
Perineural spread	8 (12.7%)	8 (28.5%)

Discussion

We conducted a retrospective review of the case records of all patients of thyroid cancer who underwent surgery at our center, in order to determine the pathologic factors which could predict the occurrence of malignancy in the contralateral lobe after a hemithyroidectomy.

The rate of contralateral malignancy in our series was 30.7%, and the most common histologic variant was the classic variant of papillary thyroid carcinoma (48.3%). The median size of the primary tumor was 2.2 cm, and 79% of the tumors were between 2 and 3 cm in size. All patients with the tall cell variant of papillary carcinoma and medullary

Table 4 Statistical analysis of the clinicopathologic factors in the patient cohort

Variable	Malignancy present in the contralateral lobe		*P* value
	Yes ($n = 28$)	No ($n = 63$)	
Tumor stage			
T2	14	29	NS
T3	13	26	
T4	1	8	
Capsular invasion			
Present	10	9	*P < 0.001*
Absent	18	54	
Extrathyroidal disease			
Present	7	9	NS
Absent	21	54	
Lymphovascular invasion			
Present	10	14	*P < 0.04*
Absent	18	49	
Perineural spread			
Present	8	8	NS
Absent	20	55	
Multifocality of tumor			
Present	21	8	*P < 0.02*
Absent	7	55	
Nodal positivity			
Present	11	14	NS
Absent	17	49	

NS not significant

thyroid carcinoma had cancer in the contralateral lobe. Papillary microcarcinomas were detected in 14.2% of the patients with cancer in the contralateral lobe and did not have any statistical significance.

The incidence of contralateral cancer has varied from 29 to 56.3% in different studies, and our 30.7% rate falls within this range [5, 6]. Our data revealed that the size of the primary tumor did not correlate with the occurrence of bilateral disease. In addition, pathologic variables like extrathyroidal spread or perineural invasion also had no statistical correlation with bilaterality of disease. This correlates well with the published literature [7].

Even though 39.2% of the patients with bilateral malignancy had level 6 nodal positivity, this particular parameter was not found to have any significant predictive value in determining the occurrence of malignancy in the opposite lobe. However, Pacini et al. demonstrated that 73.3% of patients with central compartment nodal involvement at surgery had bilateral malignancy [8]. It is also well established that in the presence of lymph nodal positivity, a total thyroidectomy may be warranted to help in radio iodine ablation and in follow-up [9, 10]. In our Institute, we use frozen section analysis of the lymph nodes to take an intraoperative decision on completing the thyroidectomy. Frozen section of the primary thyroid lobe has been shown to be unreliable in helping the surgeon take a decision on doing a total thyroidectomy [11].

High-risk variants such as the tall cell variant of papillary carcinoma and the diffuse sclerosing variant are thought to progress to anaplastic carcinoma and are associated with a higher disease specific mortality rate [12]. In our series, all patients of tall cell papillary carcinoma were found to have malignancy in the contralateral lobe. Hence, we suggest that irrespective of other factors such as size, age, or gender, the finding of a high-risk variant of papillary carcinoma should prompt the performance of a total thyroidectomy.

Our data revealed a statistically significant predictive value for lymphovascular invasion and capsular invasion. This finding is contrary to existing literature, which does not demonstrate any such value for these factors [13–15].

Multifocality of the primary tumor was the most important predictive factor with an odds ratio of 2.76 ($p < 0.02$). This holds especially true for papillary thyroid carcinoma. In fact, if multifocality of the tumor alone is analyzed, the rate of bilateral malignancies rises to 68.2%in our series compared to 30.7%for the entire cohort, as a whole.

There is a debate in literature whether multifocal carcinomas arise as a result of true multicentricity or due to intrathyroidal spread of the tumor [16, 17]. A few studies have shown that even when the primary tumor was of follicular or Hurthle cell origin, 99% of the contralateral cancers was papillary carcinomas [18]. This indirectly shows that true multicentricity is probably more common than intrathyroidal spread of the tumor.

This study is one of the few Indian papers attempting to determine the factors which would predict malignancy in the contralateral thyroid lobe [19, 20]. Our data reaches statistical significance for multifocality, capsular invasion, and lymphovascular invasion, and these parameters can hence be used as aids in the decision-making process.

Conclusion

Multifocality of the tumor, capsular, and lymphovascular invasion were found to be strongly predictive of malignancy in the contralateral lobe. These factors which can be easily assessed on routine histopathologic examination can therefore be used as aids in the decision-making process by the surgeon.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have conflict of interest.

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