MULTINODULAR GOITER AND RISK OF MALIGNANCY, SURGERY OR FOLLOW UP?

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Abstract

Nodular goiter is one of the most common presentation of thyroid gland diseases. The risk of development of thyroid cancer is relatively rare (1%) of all types of tumors, however, it is the most common endocrine malignancy, and usually presented as multinodular goiter. Fine needle aspiration cytology (FNAC) considered as the golden tool in the diagnosis of thyroid nodule though, it still has false negative rate which is variable depending on the experience and the technique being used. This means that even if the FNAC done prior to surgery shows negative finding, this doesn't exclude the presence of carcinoma, especially in multinodular goiter where it is possible not to sample the involved area.

In this prospective study which was done in Almawanee Teaching Hospital between 2012-2018, 69 patients with Multinodular goiter where considered for the risk of harboring an incidental malignancy.

The results of patients with multinodular goiter of benign origin was 57 patients (82.86%) while multinodular goiter which has an incidental malignancy was 12 patients (17.14%).

Conclusion: due to relatively high risk of malignancy in multinodular goiter especially with non-compliance for follow-up from patients and risk of missing incidental malignancy by FNAC in multinodular goiter, it is preferable to do total or near total thyroidectomy.

Key words: Goiter, Malignancy, FNAC, Surgery, Incidence

Introduction

Nodular goiter is one of the most common presentation of thyroid gland diseases. The frequency of thyroid nodularity is found to be increasing throughout the life with an incidence of about 4%-7% in the whole population based on clinical examination and 30%-50% of population by ultrasound examination.

Nodular goiter is endemic in areas with low iodine level in the diet. The low iodine diet will result in diffuse goiter, but normal follicular cells show a difference in growth potential and variable response to TSH. This will lead to growth of micro and macrofollicules and development of nodular goiter.

Thyroid nodularity can be found either as solitary nodule, in many times as dominant nodule "this usually being part of multiple nodules of different sizes but the dominant is the most prominent one" or as multiple thyroid nodules with different sizes with no dominant nodule.

The risk of developing thyroid cancer is relatively rare and estimated to be around 1% among all types of tumors. However, it is the most common endocrine malignancy, therefore it is very important to think about this risk in multinodular goiter.

Although it is usually thought that solitary thyroid nodules are more likely to harbor malignancy, recent studies have shown an increase in the incidence of malignancy in multinodular goiter to the degree that in some studies the incidence of malignancy in multinodular goiter becomes comparable to that in solitary nodules.

Rapid increase in the size of the nodules, hard texture on palpation, voice changes and presence of cervical lymphadenopathy are features of prediction of malignancy.
However, not all thyroid cancer has such features on presentation. Fine needle aspiration cytology (FNAC) is considered as the golden tool in the diagnosis of thyroid nodule. It is found that FNAC reduces the number of patients undergoing thyroidectomy for benign conditions. However, fine needle aspirate cytology still has a false negative rate which is variable depending on the experience of the histopathologist and the technique being used. This means that even if the FNAC being carried out prior to surgery and shows a negative finding, this doesn't exclude the presence of carcinoma, especially in multinodular goiter where it is possible not to sample the involved area.

This study aimed to evaluate the risk of presence of an incidental malignancy in multinodular goiter.

**Patient and method**

This is a prospective study carried out in Almawanee Teaching Hospital in the period from June 2012 to June 2018. In this study, 69 patients with multinodular goiter were studied for the risk of harboring an occult malignancy. All patients included in this study were assessed thoroughly by; history: duration of goiter, features of thyrotoxicity, features goes with malignancy like hoarseness of voice. examination: nodularity, consistency of nodules (whether hard or not), presence of palpable lymph nodes. investigations: thyroid function test (TSH, T3, T4), ultrasound examination, Fine needle aspiration cytology, and some patients CT-scan was also done.

The Patients included in this study are all with multinodular goiter, in euthyroid or toxic status with no features suggestive of malignancy in history, examination or by fine needle aspiration cytology. Patients who were scheduled to undergo surgery were offered an option of either to undergo surgery or to be kept on follow up. Informed consent was taken from those patient who accept to have surgery. Patients who are to be operated upon were assessed by full pre-operative evaluation and ENT exam. Under general anesthesia and endotracheal tube, total thyroidectomy was performed for all patients and specimen was sent for histopathological examination. Thyroxin was started for all patients. Patients with specimen showing to have incidental malignancy were sent to oncologist for further management.

Data were collected, arranged in tables or figures and analyzed statistically.

**Results**

In this study, 69 patients with multinodular goiter have been included. Figure 1, show the percentage of patients with multinodular goiter of benign origin which is 57 patients (82.86%) while multinodular goiter which has an incidental malignancy found in 12 patients (17.14%).

**Figure 1: Ratio of incidental malignancy to benign etiology of multinodular goiter (n=69)**
Table I shows the distribution of multinodular goiter between males and females. Male to female ratio is 1:2. Multinodular goiter of both benign causes or that which has malignant nodules are more common in females than in males.

### Table I: Gender distribution

| Gender   | Benign | Malignant | Total |
|----------|--------|-----------|-------|
| Male     | 16     | 5         | 21    |
| Female   | 41     | 7         | 48*   |
| **Total**| **57** | **12**    | **69**|

Table II represents the distribution of multinodular goiter by age. It is mostly seen through the 5th decade of life for both benign and malignant causes (32 patients 46.37%). The lowest prevalence is seen in the 3rd decade of life (2 patients 2.89%).

### Table II: Age distribution

| Age   | Benign | Malignant | Total   |
|-------|--------|-----------|---------|
| 20-29 | 2      | 0         | 2(2.89%)|
| 30-39 | 11     | 3         | 14      |
| 40-49 | 26     | 6         | 32(46.37%)*|
| 50-59 | 13     | 2         | 15      |
| 60+   | 5      | 1         | 6       |
| **Total**| **57** | **12**    | **69(100%)**|

Table III shows the percentage of histopathological types of incidental malignancy found after thyroidectomy for multinodular goiter. The most common type was the papillary thyroid cancer (50%). Non Hodgkin lymphoma has the lowest prevalence (8.33%).

### Table III: Types of malignancy

| Type                              | Number of patients |
|-----------------------------------|--------------------|
| Papillary thyroid carcinoma       | 6 (50.0%)*         |
| Follicular thyroid carcinoma      | 3 (25.0%)          |
| Hurthle cell carcinoma            | 2 (16.67%)         |
| Non Hodgkin lymphoma              | 1 (8.33%)          |
| **Total**                         | **12 (100%)**      |

Table IV shows the histopathological types of benign multinodular goiter. The most common cause is the colloid variety (71.92%).

### Table IV: Benign etiologies of multinodular goiter

| Type       | Number of patients |
|------------|--------------------|
| Colloid    | 41 (71.92%)*      |
| Hashimoto's| 10 (17.55%)       |
| Follicular adenoma | 4 (7.02%)  |
| Hyperplasia| 2 (3.51%)         |
| **Total**  | **57 (100%)**     |
Discussion

Although thyroid tumors are rare, however, still the best prognostic type (papillary carcinoma) can present as an aggressive tumor.

In our study, the incidence of multinodular goiter found to be higher in the 5th decade of life, both for the benign type and for the malignant one. The study done by Rozan et al\textsuperscript{10} found to have same results while the study done by D. Shrestha et al\textsuperscript{1} has shown the higher rate in the 4th decade of life. Many studies showed that nodules appeared in early life only in endemic areas of goiter, while it appears late in sporadic goiter. Patients are usually unaware of the nodular goiter until they reach their 40s or 50s\textsuperscript{4}.

Gender distribution shows female to male ratio of about 2:1. In most of the studies, thyroid diseases including multinodular goiter and those who has malignant thyroid condition were found to be more common in females. These studies showed the same ratio that we found in our study\textsuperscript{1,7}. Despite the fact that male gender increasing the suspicion in malignancy, still most studies show higher incidence of thyroid malignancy in females\textsuperscript{1,6,7}.

The incidence of incidental thyroid malignancy in our study found to be (17.14%). This percentage is about the same as in a study done by Smith J.J.\textsuperscript{11} and by Ullah I. et al\textsuperscript{12}. Such an incidence can't be ignored in a patient thought to have a benign disorder. There was no malignancy detected preoperatively in all the cases included in this study. The preoperative detection of malignancy in our study was depending basically on FNAC. The problem with FNAC is that it concentrates mainly on palpable nodule. Even if the impalpable nodules were examined under ultrasound guide, it can't assess all the nodules and might miss many other nodules which in many instances might harbor malignant cells.

In our society, there is a common patient's non-compliance\textsuperscript{1} large number of patients won't be restricted to the follow-up, especially in cases with multinodular goiter, add to that many of the malignant nodules have unpredicted course of growth which might extend locally to the trachea or nearby structures and won't be diagnosed until they become fixed to nearby structures.

Patients with thyroid cancer usually presented with multinodular goiter. That's why surgical excision is an option to eliminate the risk of missing an aggressive tumors and minimize the requirement to operate on an advanced tumor. However, still there is a debate on whether performing total or subtotal thyroidectomy. The opponents of total thyroidectomy argue that it's not worthy doing such approach for a benign condition, especially there is no documented malignancy, beside that patient will be rendered hypothyroid and will need replacement therapy for the rest of his life. Also hypoparathyroidism, whether temporary or permanent, seen more with total or near total thyroidectomy than with subtotal thyroidectomy\textsuperscript{13}. Actually as an argument to all that, it's found that on performing subtotal thyroidectomy, the remaining tissue may harbor residual malignancy in 11\%, and its detected in 10\% of specimen from recurrent goiter. Besides that, its proved that re-operating on previously operated thyroid has higher risk of complications than the 1st operation with more extensive resection\textsuperscript{14}.

Conclusion; due to relatively high risk of malignancy in multinodular goiter especially with non-compliance for follow up from patients and risk of missing incidental malignancy by FNAC in multinodular goiter, it is preferable to do total or near total thyroidectomy.
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