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Original Research Article

Profile of Non-Neoplastic and Neoplastic Thyroid Lesions by Fine Needle Aspiration Cytology and their Correlation with Histopathology-A One Year Prospective Study in a Teaching Hospital

Dr. Vanita Pandey, Dr. V. Hari Shanker, Dr. V. Indira, Dr. K. Mahesh Kumar
Department of Pathology, Malla Reddy Institute of Medical Sciences, Suraram, Hyderabad, Telangana state, India

***Corresponding author**
Dr. Kandukuri Mahesh Kumar
Email: doctormaheshgoud@gmail.com

Abstract: FNAC is highly cost effective, patient friendly out-patient procedure with minimal discomfort and gives basic to accurate information regarding the lesions. It is considered as first line investigative technique as it gives quick results with good sensitivity and specificity. It also stratifies cases requiring further investigations, surgical intervention or just clinical follow-up. Present study is about the profile of non-neoplastic and neoplastic thyroid lesions by Fine needle aspiration cytology and correlates the FNAC findings with the histopathology. This study was undertaken in the Department of Pathology, Malla Reddy Institute of Medical Sciences, Suraram, Hyderabad, Telangana state, India, between January 2015 and December 2015. Minimum age of the patient in the study was 10 years and the maximum age of the patient was 79 years. Total numbers of cases were 212, and the study duration was 1 year. In our study of 212 cases, we encountered 178 cases (83.9 %) of Non-Neoplastic lesions and 34 cases (16.1 %) of neoplastic lesions. 189 cases (89.1%) were reported in females, 23 cases (10.9 %) were reported in male patients. Highest incidence was noted in the age group 30- 39 years (69 cases) and least incidence of thyroid lesions was noted in 70-79 age groups (4 cases). Most of the thyroid lesions we came across in the present study were benign. The neoplastic and malignant lesions were few and they were correlated well with histopathology examination. FNAC is accurate and is used as first line of investigation in the thyroid lesions; it also avoids unnecessary surgical interventions.
Keywords: Fine Needle Aspiration Cytology, Thyroid lesions, Neoplastic, Non-Neoplastic, Follicular Neoplasm, Papillary Carcinoma Thyroid, Medullary carcinoma thyroid

INTRODUCTION

The use of fine needle aspiration cytology (FNAC) in the investigation of thyroid lesions has become an acceptable and widely practiced minimally invasive technique, which is safe, simple, rapid and relatively pain-free. FNAC is highly cost effective, patient friendly out-patient procedure with minimal discomfort and gives basic to accurate information regarding the lesions. It is considered as first line investigative technique as it gives quick results with good sensitivity and specificity. It also stratifies cases requiring further investigations, surgical intervention or just clinical follow-up. It mainly rules out the unnecessary explorative surgical procedures. Fine needle aspiration cytology (FNAC) of thyroid was documented in the Martin and Ellis paper of 1934 [1]. FNAC is now recognized to be the first line investigation for solitary thyroid lesions, has a valuable role in the diagnosis of the diffuse non – toxic goiter and can be used to confirm the diagnosis of clinically obvious malignancies [1]. The purpose of aspiration cytology is to obtain diagnostic material for cytology study from organs that do not shed cells spontaneously. The bone marrow, spleen, liver, breast, thyroid gland and lymph nodes are common sites where FNAC is suitable and gives good diagnostic results. Diffuse thyroid gland enlargements or solitary thyroid nodules are common clinical findings in day to day practice. Most of the lesions are common in women and vast majority of these lesions are non neoplastic. However distinction of these benign lesions from a malignancy cannot be based reliably on the clinical presentation only. Several diagnostic tests have been used for diagnosis of these lesions. Recent studies have demonstrated that among all the diagnostic modalities, FNAC is most accurate and simplest screening test for rapid diagnosis of thyroid lesions. We present our study of 212 cases of thyroid lesions reported on FNAC and their correlation with histopathology (HPE) findings in our institute for a period of one year.

OBJECTIVE OF THE STUDY

To study the profile of non-neoplastic and neoplastic thyroid lesions by Fine needle aspiration cytology and correlate the FNAC findings with the histopathology.

MATERIALS AND METHODS

This study was undertaken in the Department of Pathology, Malla Reddy Institute of Medical Sciences, Suraram, Hyderabad, Telangana state, India, between January 2015 and December 2015. Approval from the institutional ethical committee was taken before commencing the study. Patients with palpable thyroid mass were included in the study. Minimum age of the patient in the study was 10 years and the maximum age of the patient was 79 years. Total numbers of cases were 212, and the study duration was 1 year. Aspiration was carried out using 5 or 10 ml disposable syringe with 22-25 gauze needle attached. Then, the material was fixed in 95% ethyl alcohol and routinely stained with hematoxylin and eosin (H&E) stains. The cytomorphological features were studied and final diagnoses were given. The correlation was done with histopathological examination. The received postoperative biopsy or surgical excised specimen were fixed in 10% buffered formalin and subjected to gross examination, processing, paraffin embedding, and section cutting, staining by H&E and mounted. The histomorphological features of various diseases thyroid lesions were studied. FNAC and histopathological examination of the same lesions were correlated where required. Special stains were used wherever needed.

RESULTS

In our study of 212 cases, we encountered 178 cases (83.9 %) of Non-Neoplastic lesions and 34 cases (16.1 %) of neoplastic lesions. 189 cases (89.1%) were reported in females, 23 cases (10.9 %) were reported in male patients. Highest incidence was noted in the age group 30- 39 years (69 cases) and least incidence of thyroid lesions was noted in 70-79 age groups (4 cases)**(Table 1)**.

Table 1: Age and Sex Distribution of the Thyroid lesions

AGE	No. of Cases	MALES	FEMALES
10-19	10	03	07
20-29	60	06	54
30-39	69	04	65
40-49	38	02	36
50-59	20	05	15
60-69	11	02	09
70-79	04	01	03
TOTAL	**212**	**23**	**189**

In our study, the most common non-neoplastic lesion was Multinodular goiter (78 cases) followed by Hashimoto's thyroiditis (64 cases) (Figure 1); least common being thyroglossal cyst and subacute thyroiditis (Figure 2). Similarly the most common neoplastic lesion was follicular adenoma (21 cases) followed by papillary carcinoma (Figure 3 & 4) and other carcinomas are least common.

Table 2: Incidence of Non-Neoplastic lesions

LESION	Number of Cases	Percentage (%)
Thyroglossal cyst	03	1.70
Subacute thyroiditis	03	1.70
Hashimoto's thyroiditis	64	36.0
Colloid goiter	20	11.3
Multinodular goiter	78	44.0
Colloid cyst	10	5.30
TOTAL	**178**	

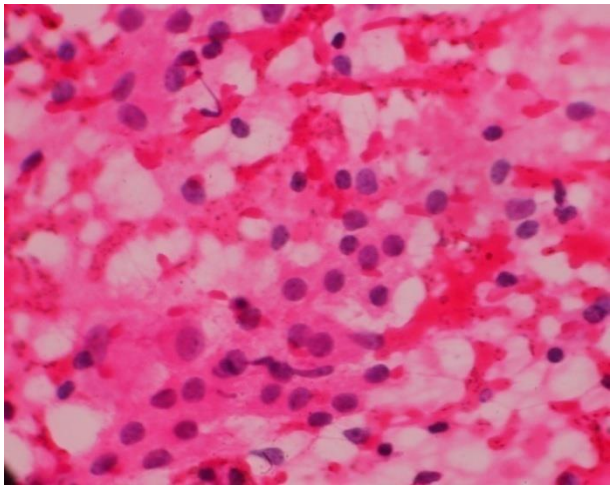

Fig 1: Cytosmears showing Hurthle cell change in Hashimoto's Thyroiditis with few impinging lymphocytes seen

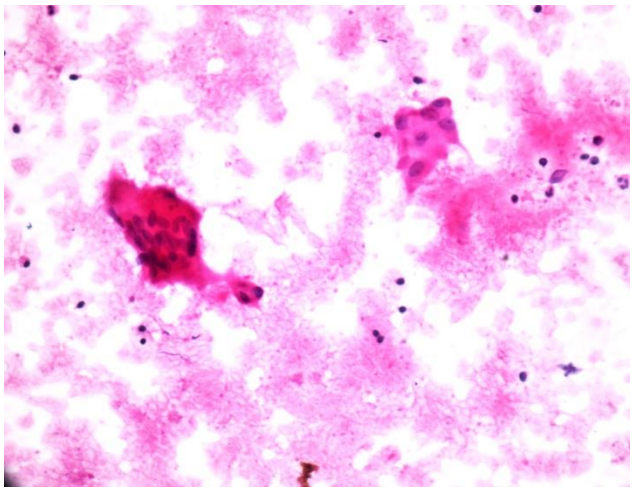

Fig 2: Multinucleate Giant cells in subacute thyroiditis

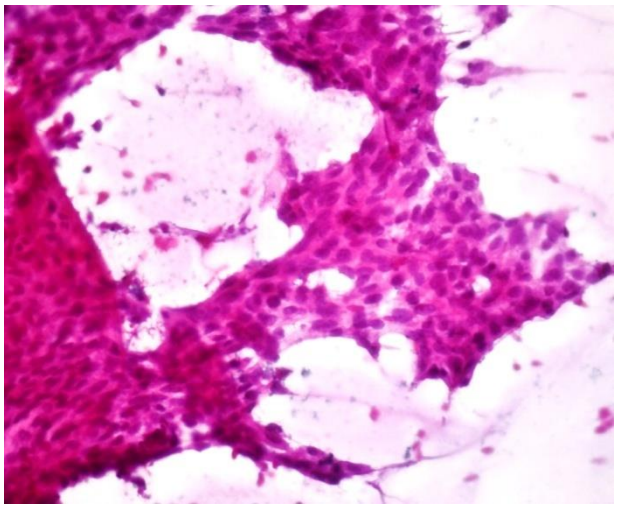

Fig 3: Sheets of oval cells in papillary carcinoma thyroid

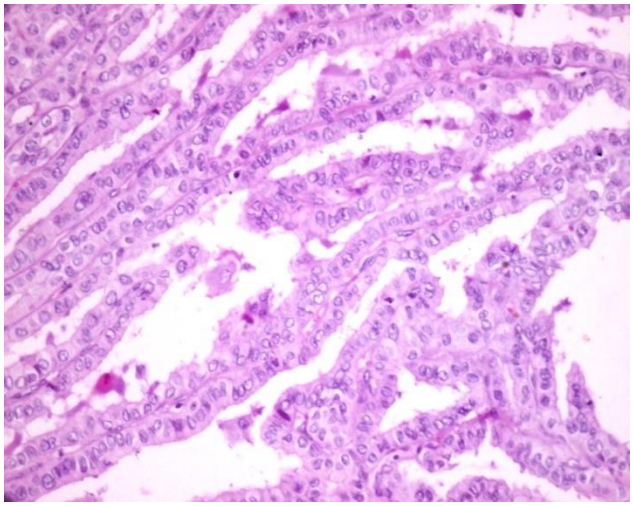

Fig 4: Histopathology image of papillary carcinoma of the Thyroid

Table 3: Incidence of Neoplastic lesions

LESION	Number of Cases	Percentage (%)
Follicular Adenoma	21	61.8
Hurthle Cell Adenoma	01	2.94
Papillary Carcinoma	09	26.4
Medullary Carcinoma	01	2.94
Anaplastic Carcinoma	01	2.94
Follicular Adenoma with Follicular variant of Papillary Carcinoma	01	2.94
TOTAL	**34**	

DISCUSSION

Thyroid lesions are common clinical findings and have a reported prevalence of 4–7% in adult population [2]. Fine needle aspiration (FNAC) is an ideal first line diagnostic test in evaluating thyroid nodules [3]. The procedure is regarded as a valuable method of diagnosing various thyroid lesions and distinguishing between malignant lesions from those with benign lesions that can be followed clinically [4]. It has been proposed as a pre-operative screening method to reduce the number of patients with benign nodules for surgery [4, 5].

Thyroglossal cyst is a fibrous cyst that forms from a persistent thyroglossal duct. Thyroglossal cysts can be defined as an irregular neck mass or a lump which had developed from cells and tissues left over after the formation of the thyroid gland during developmental stages. Thyroglossal cysts are the most common cause of midline neck masses and are generally located substandard to the hyoid bone, yet these neck masses can occur anywhere along the path of the thyroid gland from the base of the tongue to the suprasternal notch. Microscopically, these cysts contain serous fluid or colloid mixed hemorrhagic fluid with or without cyst macrophages and few thyroid follicular cells.

Subacute thyroiditis is a self-limited thyroid condition associated with a triphasic clinical course of hyperthyroidism, hypothyroidism, and return to normal thyroid function. Subacute thyroiditis may be responsible for 15-20% of patients presenting with thyrotoxicosis and 10% of patients presenting with hypothyroidism. Recognizing this condition is important; because it is self-limiting, no specific treatment, such as anti-thyroid or thyroid hormone replacement therapy, is necessary in most patients. High thyroid hormone levels result from the destruction of the thyroid follicle and the release of preformed thyroid hormone into the circulation, with thyrotoxicosis consequently developing. This phase lasts 4-10 weeks. The disease undergoes remission in 2-4 months. At this time, the thyroid is depleted of colloid and is now incapable of producing thyroid hormone, resulting in hypothyroidism. The hypothyroid phase may last up to 2 months. Often, the hypothyroidism is mild, and no thyroid hormone therapy is required unless the patient has signs or symptoms of hypothyroidism. As the follicles regenerate, the euthyroid state is restored. 90 to 95% of patients return to normal thyroid function. The key cytological characteristics for subacute thyroiditis are i) A high number of Multinucleate giant cells, (ii) epithelioid cells with a tendency for clustering, (iii) epithelioid cell granulomas, (iv) lymphocytes, macrophages and neutrophils, (v) frequently degenerated follicular epithelial cells displaying mild-moderate cellularity, and (vi) a dirty background that is composed of cellular debris, naked, degenerated nuclei and thick colloids.

Hashimoto thyroiditis is part of the spectrum of autoimmune thyroid diseases and is characterized by the destruction of thyroid cells by various cells and antibody-mediated immune processes. This condition is the most common cause of hypothyroidism. Hypothyroidism typically has an insidious onset with subtle signs and symptoms that may progress to more advanced or even florid signs and symptoms over months to years. The presentation of patients with hypothyroidism may also be subclinical, diagnosed based on routine screening of thyroid function. Such patients may have nonspecific symptoms that are difficult to attribute to thyroid dysfunction. They frequently do not improve with thyroid hormone supplementation. Microscopy shows pleomorphic Hurthle cells with moderate to abundant cytoplasm, central to peripheral nucleus, increased nuclear-cytoplasmic ratio and sometimes binucleate forms. These cells can be seen arranged in crowded three-dimensional aggregates, sheets, and in micro-follicular pattern. Background showed sparse lymphocytes, scant colloid, and erythrocytes.

Colloid nodular goiter is the enlargement of an otherwise normal thyroid gland. Colloid nodular goiters are also known as endemic goiters. They are usually caused by not getting enough iodine in the diet. Colloid nodular goiters tend to occur in certain areas with iodine-poor soil. Risk factors for colloid nodular goiters include-being over age 40, being female, having a family history of goiter, living in an area where there is endemic iodine deficiency, not getting enough iodine in your diet. On cytology ,aspirate contains abundant colloid, scant follicular cells -follicular cells may be dispersed or grouped into follicles and small monolayer sheets -the cells are small, uniform with central nucleus; cytoplasm pale and containing abundant para vacuolar granules; inconspicuous nucleoli -may have Hurthle cells, isolated or in monolayers.

Toxic multinodular goiter also known as toxic nodular goiter, toxic nodular struma, or Plummer's disease is a multinodular goiter associated with a hyperthyroidism. It is a common cause of hyperthyroidism [6, 7] in which there is excess production of thyroid hormones from functionally autonomous thyroid nodules, which do not require stimulation from thyroid stimulating hormone (TSH) [8]. It is the second most common cause of hyperthyroidism (after Graves' disease) in the developed world. In countries where the population is iodine-deficient i.e. the developing world, iodine deficiency is the most common cause of hypothyroidism. (Decreased iodine leads to decreased thyroid hormone.) However, iodine deficiency can cause goiter (thyroid enlargement); within a goiter, nodules can develop. Risk factors for toxic multinodular goiter include individuals over 60 years of age and being female [9].Cytosmears usually show variable amount of colloid -numerous follicular cells arranged mainly in monolayers, follicles and tissue fragments -large monolayered honeycoombed sheets representing macro follicles with evenly distributed nuclei without overlapping is an indicator of benignity -true papillae with fibro vascular cores can be seen. Pseudo papillary structures are not uncommon -usually short and non-branching. There should not be significant overlapping or crowding of nuclei -occasional micro follicles are present. Increased numbers of micro follicles may be seen in a cellular hyperplastic nodule. Predominance of micro follicles is suspicious for follicular neoplasm.

Follicular adenoma is a benign encapsulated tumor that shows evidence of follicular differentiation. Generally it is a solitary cold nodule that corresponds to a lesion that can reach 10 cm in diameter. Follicular adenomas often have central involuted areas similar to those seen in goiters [10]. Cellular smears comprising of sheet like, numerous layered cell aggregates of different patterns of varying cell types in colloid and hyperplastic nodules. Clusters made up of small acini with a central lumen may contain small amount of colloid representing the micro follicles. These micro follicles, otherwise referred to as fetal follicles are the characteristic of follicular neoplasm but may be found focally in multinodular goiter. Rosette like groupings without a lumen suggests a more solid growth patterns (embryonal). A trabecular pattern is appreciated if the epithelial cells are arranged in rows and elongated structures made up of cells attaching themselves to the strands of vascular stroma and mimicking a papillary structure. Small blood vessel with adherent epithelial cells can be found in any type of follicular neoplasm [11, 12]. The cytological diagnosis of follicular tumors is difficult because the criterion does not rest fundamentally on cellular characteristics but on other aspects, such as capsular or vascular invasion and metastases at a distance.

Papillary carcinoma of thyroid is a malignant epithelial tumor that forms papillary and follicular structures and exhibits characteristic nuclear changes [13]. Papillary carcinoma is the most common histological variant of thyroid carcinoma and it is the thyroid tumor most often associated with irradiation of the head and neck. Female patients are affected 3 times more than male. They are often multicentric with the proportion being 20 to 80%. The tumor has a notable propensity to lymphatic dissemination. In more than 50% of patients, regional cervical lymph nodes are affected at the time of surgery. Aspirations of papillary carcinoma has cytological picture as hypercellular smears, cells arranged in to papillary structures or monolayers with digitiform projections or in syncytial aggregates or are dispersed. The papillary structures can have varied morphology and dimensions with or without fibro vascular core. The sheets of cells may have distinct anatomical border, nuclear crowding or overlapping [11, 12]. Individually, papillary carcinoma

cells are larger than those of follicular proliferation; they have a polygonal contour with well defined margins and a central nucleus. The cytoplasm generally abundant can be of variable density, sometimes it is dense and homogeneous or it is granular as in oncocytic transformation. At other times, particular in cystic forms, it contains numerous vacuoles [11, 12].

The nuclei are oval, moderately pleomorphic and the nucleolus is generally small. The optically clear or ground glass (orphan Annie) so characteristic of the histological sections is not noted in smear. Nonetheless, nuclear cytoplasmic inclusions and longitudinal folds are often identified. Nuclear cytoplasmic inclusions are present in more than 5% of 90% of cases. They are characterized by precise contour and a density and texture similar to that of cytoplasm. The longitudinal nuclear folds, which are particularly prominent with pap technique, can appear as multiple longitudinal furrows or superficial notches, giving the nucleus a lobed appearance [14].

This is a malignant tumor consisting of cells that have Para follicular differentiation. Its incidence ranges from 12 to 17% of all thyroid carcinomas. In contrast to other carcinomas, medullary carcinoma does not show any predilection for sex or age. It can appear sporadically or as a familial disease with a dominant autosomal inheritance. In the familial form it can appear as an isolated lesion or in conjunction with other endocrinal neoplasms constituting multiple endocrinal neoplasm syndromes (MEN) [11, 15]. The cytological picture varies from case to case. The classic polygonal and fusiform cells varieties are the most common and those most easily recognized. The aspiration generally contains abundant blood and numerous dispersed cells. Loose monolayers or 3-dimensional cells clusters are seen less often. The isolated cells have well defined margins and vary notably in form and size. Marked cellular polymorphism is usually evident, with round, oval, triangular, polygonal and a fusiform cell the cytoplasm is moderate dense and eosinophilic and occasional contains granules. Although these cytoplasmic granules have diagnostic value, they are not pathognomonic, having been described in follicular tumors, anaplastic carcinoma and metastatic carcinoma of the breast. Nuclei are usually oval, moderately pleomorphic with coarse granular chromatin and one or two small nucleoli. Binucleate and multinucleate cells are sometimes seen. In some cases, a dense amorphous material is found that stains similarly to colloid; it demonstrates a characteristic birefringence of the amyloid when stained with Congo red and examined under polarized light [11, 12, 15].

Anaplastic carcinoma represents 10% of all thyroid carcinomas; and is the most aggressive tumor of this gland. More than 85% of patients die within one year of diagnosis. This carcinoma occurs above all in older women with the average being 65years [14, 16]. In 80% of case a previous history of goiter due to follicular hyperplasia, follicular adenoma, papillary carcinoma, and follicular carcinoma is evident. The disease is usually manifested by rapid thyroid enlargement, regional lymphadenopathy, dyspnoea, dysphonia, dysphagia and pain. Visceral metastases are common primarily to lung and liver [15].

Aspiration usually yields large malignant cells with bizzare appearance either spindle, or epithelial, undifferentiated small cells, with marked nuclear pleomorphism, multinucleation, mitotic figures, against a background showing necrotic cell fragments, debris, sometimes inflammatory [12,13].

Our study is in correlation with the study done by N kukar *et al.;* [17], where the age of presentation of various thyroid lesions ranged from 11 years to 80 years with maximum patients falling in the age group of 31-50 years.

Thyroid lesions are more prevalent in females than males. In our study 89.1% of cases were females and 10.9% males. Male to female ratio was 1:8.2. Similar findings were reported by N kukar *et al.;* and Dorairagen N *et al.;* [18].

In our study ,our incidence of non-neoplastic lesions correlating with the analysis of 1344 cases of thyroid lesions conducted by Hyang Mi KO *et al.;* [19] 83.4% cases were nonneoplastic 1.6% follicular neoplasm, 7.3% malignant, 2.7%indeterminate & 5% unsatisfactory. We have reported 89.1 % of thyroid lesions as non-neoplastic and remaining 10.9 % as neoplastic lesions.

CONCLUSION

FNAC is highly cost effective, patient friendly out-patient procedure with minimal discomfort and gives basic to accurate information regarding the lesions with good sensitivity and specificity. Most of the thyroid lesions we came across in the present study were benign. The neoplastic and malignant lesions were few and they were correlated well with histopathology examination. FNAC is accurate and is used as first line of investigation in the thyroid lesions; it also avoids unnecessary surgical interventions.

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