Original Research Article

Indian Journal of Pathology: Research and Practice
Volume 6 Number 3, July - September 2017 (Part-I)
DOI: http://dx.doi.org/10.21088/ijprp.2278.148X.6317.8

Significance of Hurthle Cells in Thyroid Cytology and its Correlation with Histopathology

E. Aruna*, Suratha Siva Jyothsna*, Durga K.**

*Assistant Professor, Department of Pathology, NRIIMS, Visakhapatnam, Andhra Pradesh-531163, India. **Professor, Department of Pathology, TB Chest Hospital, Osmania Medical College, Hyderabad, Telangana 500095, India.

Abstract

Introduction: Thyroid gland is very often subjected to FNAC as thyroid enlargement is a common clinical problem and also due to its easy accessibility for the procedure. Hurthle cells are commonly encountered in thyroid aspirates from varied etiology. *Aim of the Study:* To find the significance of Hurthle cells in thyroid cytology and to note the cytological features that would differentiate reliably between different lesions containing Hurthle cells. *Materials and Methods:* This was a two yearstudy conducted in the Department of Pathology, at NRI Institute of Medical Sciences, Visakhapatnam. A total of 858 thyroid aspirates were done of which 240 cases showed Hurthle cells. These 240 cases consisted of the study group in which histopathology examination was done in 107 cases. There were 229 female and 11 male patients in the age groups of 10 to 70 years. *Observations and Results:* Hurthle cells were seen in 240 (11.6%) cases. Non neoplastic and neoplastic Hurthle cell lesions comprised 222 (92.5%) and 18 (7.5%) cases respectively.There was a female predominance with the male to female ratio being 1:20. There were 201 cases (83.7%) with non neoplastic and 39 (16.2%) with neoplastic etiology. Hashimoto's thyroiditis, nodular goiter and follicular adenomas commonly showed Hurthle cells. For Hurthle cell lesions, important cytological features were predominantly monomorphic Hurthle cell population, macronucleoli and absence of inflammatory cells. There was good agreement between the cytology and histopathological examination. *Conclusion:* Hurthle cells are seen in various lesions of thyroid. The presence of>50% of Hurthlecells in an aspirate indicates a Hurthle cell neoplasm.Aspiration cytology in Hurthle cell lesions can differentiate non neoplastic lesions from neoplastic lesions with high accuracy, but differentiation between benign and malignant neoplasms is less reliable.

Keywords: Thyroid FNAC; Hurthle Cells; Hashimoto's Thyroiditis; Thyroid Histopathology.

Introduction

Thyroid gland is unique among endocrine organs. Because of its superficial location, it is amenable to direct physical, cytological and histopathological examination. The diagnosis of thyroid lesions using aspiration cytology was first reported by Martin and Ellis in 1930 [1]. Fine needle aspiration cytology (FNAC) of thyroid gland is now a well-established first line diagnostic test for the evaluation of thyroid lesions for confirming benign lesions and thereby, reducing unnecessary surgery [2]. FNAC of thyroid has dominant role in determining the management of patients with thyroid nodules [3,4].

Different imaging techniques are now used for preoperative diagnosis of thyroid nodules, like radio nucleotide scanning, high resolution ultrasonography, etc. However, FNAC is still regarded as the single most accurate and cost effective procedure, particularly if ultra sound is used as a guide for better sample collection especially for cystic lesions.

The success of FNAC is dependent on several factors like experience of the aspirator, skillful cytological interpretation and rational analysis based upon cytological and clinical correlation [5]. The technique is relatively painless, gives quicker results, is cost effective and less complicated than surgical

Corresponding Author: Dr E. Aruna C/o E. Koteshwara Rao, H.No: 15-5: Near Anganwadi School, Prabhu Nagar, Poranki (post), Penamaluru (mandal), Krishna District, Andhra pradesh-521137.

E-mail: drearuna@gmail.com

(Received on 05.05.2017, **Accepted on** 27.05.2017)

© Red Flower Publication Pvt. Ltd.

biopsy.It is an out-patient procedure with low risk of complications, hence, suitable for practice in countries with limited resources.

The main indications for FNA are diagnosis of diffuse nontoxic goiter, or solitary/dominant thyroid nodule, confirmation of a clinically obvious thyroid malignancy and to obtain material for special laboratory investigations [2].

There has been renewed interest in the diagnosis and treatment of Hurthle cell lesions because of the increasing use of FNAC in the preoperative diagnosis of thyroid nodules. Hurthle cells are of uncertain significance in thyroid disease and this study tries to clarify the significance of Hurthle cells in FNAC of thyroidlesions.

Aims and Objectives

1. To find the significance of Hurthle cells in thyroid cytology.
2. To note the cytological features that would differentiate reliably between lesions containing Hurthle cells.
3. To aid in the decision of therapeutic management of patients with Hurthle cells in cytology.

Material and Methods

This was a prospective study done in the Department of Pathology, at NRI Institute of Medical Sciences, Visakhapatnam, over a period of two years.A total of 858 patients underwent thyroid FNAC in the study period, of which 240 cases showed Hurthle cells. The study group consisted of these 240 cases. There were 229 female and 11 male patients and their age ranged from 10 to 70 years.

Procedure

Informed written consent was taken from all the patients for the FNAC procedure. The procedure was performed by cytopathologists in all the cases. Prior to the aspiration, detailed clinical history, biochemical investigations and ultrasound findingswere noted. The procedure was explained to the patient. Physical examination of the thyroid and for cervical lymphnodes was done. The nodule(s) to be aspirated was identified. The patient was placed supine with the neck hyper-extended to expose the thyroid. For support a pillow was placed under the shoulders. The patient was asked not to swallow, talk or move during the procedure. A 23/24 gauge needle attached to 10/20 ml disposable syringe was used either with or without aspiration. Three or five passes were made in each case. In case of cystic nodules, the cyst content was aspirated, centrifuged, and slides were made from the sediment for cytological analysis. The slides from all the cases were stained with hematoxylin and eosin stain, Papanicolaou stain and May Grunwald Giemsa stain. After aspiration, firm pressure was maintained at the procedure site. The patient was asked to sit for a few minutes. No major complications like penetration into the trachea, laryngeal nerve palsy, or hematoma were recorded. Only slight pain and occasional dizziness was recorded in a few patients.

Of the 240 cases, 107 patients underwent surgery and histopathology specimens were studied in these 107 patients. The tissue specimens were fixed in 10 % neutral buffered formalin and were submitted for routine histopathological processing. After paraffin embedding 4 microns thick sections were made and stained with hematoxylin and eosin.

The cytology and histopathology results were compared.

Inclusion Criteria

1. All thyroid aspirates including ultrasound guided aspirates.
2. Smears with well-fixed and well-preserved morphology

Exclusion Criteria

1. Cases with incomplete clinical details
2. Inadequate smears containing less than 5 or 6 groups of well-preserved cells; each group consisting of at least 10-15 cells.
3. Non-diagnostic smears with only blood or too few follicular cells or with only degenerative foam cells.

Observations and Results

The total number of thyroid aspirates was 858 and total number of aspirates with Hurthle cells was 240 (11.6%). Non neoplastic and neoplastic Hurthle cell lesions comprised 222 (92.5 %) and 18 (7.5 %) cases.

Gender Wise Distribution of the 240 Cases

There were 11 males (4.5 %) and 229 females (95.5 %). The male to female ratio was 1:20.8

Functionalactivity: Euthyroid status was observed

Table 1: Age wise distribution of cases containing Hurthle cells (n=240)

Age (years)	No. of Cases	Percentage
<10	02	0.8
10-20	73	30.4
21-30	76	31.7
31-40	53	22.1
41-50	20	8.4
51-60	08	3.3
61-70	08	3.3
Total	240	100

Table 2: Conditions showing predominance of Hurthle cells

Non – neoplastic (201)	No. of cases	%
Hashimoto's thyroiditis	133	55.4
Nodular goiter	59	24.5
Toxic goiter	09	3.8
Neoplastic (39)		
Papillary carcinoma	06	2.5
Follicular neoplasm	24	10
Hurthle cell neoplasm	09	3.8
Total	240	100

in 184 (76.6%) cases. Hypothyroidism and hyperthyroidism were observed in 49 (20.4%) and 7 (3.0 %) cases respectively.

Clinical Presentation

Diffuse thyroidswelling was present in 175 (73.0%) cases. Solitary thyroid nodule and multinodular presentations were observed in 54 (22.5%) and 11 (4.5 %) cases respectively.

There were 201 cases (83.7%) of nonneoplastic etiology and 39 (16.2%) with neoplastic etiology.

The study of the cytological smears was based on the presence and distribution, and proportion of Hurthle cells to thyrocytes, individual cytomorphology, nuclear features, cohesiveness, associated cells and the background in which Hurthle cells were distributed.

Of the 240 cases which showed Hurthle cells, surgery was done in 107 cases. As many cases were diagnosed as Hashimoto's thyroiditis and colloid goiter which did not require surgical intervention, we had histopathological correlation only for 107 cases.

Table 3: Cytology and histopathology results in cases with prominent Hurthle cells (n=240)

Cytological Diagnosis	Histopathological Diagnosis	No. of Cases
Hashimoto's thyroiditis	Hashimoto's thyroiditis	35
Hashimoto's thyroiditis	Papillary carcinoma with Hashimoto's thyroiditis	1
Nodular goiter	Nodular goiter	30
Nodular goiter with thyroiditis	Follicular adenoma with thyroiditis	1
Nodular goiter with thyroiditis	Nodular goiter	1
Hurthle cell neoplasm	Hurthle cell adenoma	09
Follicular neoplasm	Follicular adenoma	22
Follicular neoplasm	Adenomatous goiter	1
Papillary carcinoma	Papillary carcinoma	06
Follicular neoplasm with thyroiditis	Follicular carcinoma	1
Total		107

Clinical follow up was done for rest of the cases. Cases diagnosed as Hashimoto's thyroiditis underwent antithyroid antibody test which came positive in all cases of Hashimoto's thyroiditis.

Cytological picture of Lymphocytic Thyroiditis

Cellular smears showed mixed populations of lymphocytes, and few Hurthle cells and scanty or no colloid.

Hashimoto's Thyroiditis

Smears showed variable cellularity from mild to moderate with lymphocytic infiltrate being mild-

moderate. The colloid was scanty in majority of the smears, with occasional smears showing moderate amount of colloid. There was an admixture of epithelial cells, lymphocytes and plasma cells. Some smears also showed giant cells, epithelioid cells. Epithelial cells were arranged in monolayered sheets, clusters, groups and few lying singly. Hurthle cells were also arranged in monolayered sheets, clusters and groups. Hurthle cells were larger with abundant eosinophilic granular cytoplasm and large mostly nuclei with little pleomorphism. Some showed prominent nucleoli.

Nodular Goiter

Smears showed thyroid follicular epithelial cells and Hurthle cells in honey comb pattern with scanty colloid.

Toxic Goiter

Moderately cellular smears with thyroid follicular cells in monolayered sheets, groups with fire flare appearance. Hurthle cell were mild to moderate in number and arranged in honeycomb pattern, and clusters. No lymhocytes were seen.

Hurthle Cell Neoplasm

Smears showed increased cellularity and were composed predominantly of Hurthle cells with abundant pink granular cytoplasm and round bland nucleus. No pleomorphism was noted. No colloid or inflammatory cells noted.

Papillary Carcinoma

Increased cellularity, papillary arrangement of thyroid follicular cells showing optically clear nucleus with nuclear grooves and inclusions. Hurthle cells were few in number.

Follicular Neoplasm

Aspirates showed increased cellularity with thyroid follicular cells arranged in follicles on a background of Hurthle cells and lymphocytes.

Table 4: Comparison of clinical and laboratory features in Hashimoto's thyroiditiswith Jayaram et al study [9]

Clinicopathological features of Hshimoto thyroiditis	Chinese [n=21(%)]	Indian [n=50(%)]	Malay [n=17(%)]	Present study [N=36(%)]
Nodular presentation	10 (47.5)	12 (24)	7 (41)	7(5.3)
Hurthle cells	15 (71.5)	26 (52)	8 (47)	All cases
Lymphoid follicles	16 (76)	31 (62)	12 (70.5)	Occasional
Follicular/Hurthle cell infiltration by lymphoid cells	15 (71.5)	38 (76)	8 (47)	All cases
Thyroid function	[n=17(%)]	[n=39(%)]	[n=12(%)]	[n=133(%)]
Hypothyroid	8 (47)	15 (38.5)	4 (33)	41 (30.8%)
Euthyroid	8 (47)	18 (46.1)	7 (59)	89 (66.9%)
Hyperthyroid	1 (6)	6 (15.4)	1 (8)	3 (2.3%)

Table 5: Comparison of cytological features of Hashimoto's thyroiditis in various studies

Cytologic feature	Jayaram et al(1987)[15]	Friedman et al(1981)[10]	Kini et al (1981)[11]	Bhalotra et al (1990)[12]	Jayram G et al (2006)[9]	Present series
Number of cases	40	40	87	68	88	133
Nodular presentation	few	80%	22%	Not recorded	33%	5.3%
Hurthle cells	many	98%	variable	rare	56%	97%
Follicular cell atypia	Mild-moderate	Present	Often	Some cases	44%	Rare
Lymphoid follicles	Not recorded	Present	Present	Not recorded	Present (67%)	Occasional
Follicular cells infiltrated by lymphocytes	Present	Not recorded	Present	Present	69%	Present
Plasma cells	Not recorded	Present	Present	Present	23%	Present
L:E ratio	High	High	High	High	High	High
Giant cells	33%	Infrequent	Rare	25%	39%	Rare
Granuloma	8%	Not recorded	Not recorded	50%	16%	Rare
Fireflares	25%	Not recorded	Not recorded	Most cases	23%	Rare

The Differentiating Features of Hurthle Cells in Neoplastic and Non-Neoplastic Lesions of the Thyroid

In neoplastic lesions a high percentage of Hurthle cells mostly isolated or in loose cohesive sheets as monomorphic cell population were seen. Cells were oval-polygonal with abundant granular eosinophilic cytoplasm, eccentric nucleus with finely granular chromatin and prominent macronucleoli were observed. In nonneoplastic lesions, Hurthle cells were seen in flat sheets and clusters with a few single cells.The nuclear chromatin even and bland and had identifiable nucleoli. Inflammatory cells in the background were present in most of the cases.

Discussion

Fine needle aspiration of the thyroid is a reliable, relatively non-invasive method for identifying Hurthle cell nodules likely to be neoplastic and requiring surgical excision for careful histological evaluation. Hurthle cell nodules of the thyroid can result from non-neoplastic as well as neoplastic conditions. Non-neoplastic Hurthle cell lesions are more common than neoplastic lesions. Thyroid nodules that are predominantly composed of Hurthle cells are called Hurthle cell neoplasms, and they represent approximately 5% of thyroid neoplasms [6]. In our study, on FNA smears, Hurthle cell neoplasm constituted 3.7% of Hurthle cell containing lesions.

The various nonneoplasticHurthle cell containing lesions arelymphocytic thyroiditis, Hashimoto's thyroiditis, toxic goiter, multi-nodular goiter and Reidle'sthyroidits.

The variousneoplastic lesions that can have Hurthle cells are Hurthle cell adenoma or carcinoma, follicular adenoma or carcinoma, papillary carcinoma and medullary carcinoma

Other conditions that may also show Hurthle cells are old age, post radiation, post chemotheraphy [7].

The diagnosis of Hashimoto's thyroiditis on FNAC samples is made when lymphoid and Hurthle cell components are present in varying proportion. Problems may arise when the proportion of these two cell components shows marked deviation.

Smears rich in lymphocytes or mixed population of lymphocytes with few Hurthle cells is Lymphocytic thyroiditis, which is the initial stage in evolution of Hashimoto's Thyroiditis. These patients are usually young age [2]. In our study we had most of the patients in the 10-20 years age group.

According to Laurie Mac Donald, a diagnosis of lymphocytic thyroiditis should not be made when only a few lymphocytes are present [8].

In our study majority of Hashimoto's thyroiditis patients were between the age group of 30-50 years, and most of the patients were females, and the clinical presentation was diffuse enlargement of the thyroid gland. Our findings correlate with other studies.

According to Jayaram et al, nodular presentation was noted in one third of cases (33%). They also noted transformation of diffuse to nodular goiter in 3/8 cases with follow-up, which could possibly be due to the cycle of regeneration and regression [9].

In our study high lymphocyteto epithelial cell ratio was noted in Hashimoto's thyroiditis. In florid cases the smears mimicked reactive lymphoid hyperplasia. Few cases also showed multinucleated giant cells and epithelioid cell granulomas. Similar findings were also noted by Jayaram et al, Friedman et al, Kini et al and Bhalotra et al [9-12].

Out of 133 Hashimoto's thyroiditis diagnosed on FNAC, 27 cases underwent surgery, out of which 26 proved to be Hashimoto's thyroiditis. One case which was diagnosed as Hashimoto's thyroiditis on FNAC proved to be papillary carcinoma with Hashimoto's thyroiditis on histopathology. Papillary carcinoma was missed on FNAC possibly due to sampling error. So aspiration from multiple sites will help to overcome this problem. Papillary carcinoma can occur in the background of Hashimoto's thyroiditis [13].

Jayaramet al have suggested careful evaluation of cases that show pleomorphic Hurthle cells in the presence of scant number of lymphocytes [14].

Most of the Cases Presented as Diffuse Goiter

Nine cases diagnosed as toxic goiter on FNAC proved to be toxic goiter on histopathology also. FNAC was successful in diagnosing toxic goiter in all patients. Toxic goiter showed moderately increased cellularity, thyroid follicular cells arranged in honey comb pattern and follicular pattern. Typical fire flare appearance was also observed. Hurthle cells were arranged in honey comb clusters having abundant pink granular cytoplasm with round mildly pleomorphic nucleus. No nucleoli were seen. Background showed hemorrhage, but no lymphocytes were seen.

The aspirates from non-neoplastic Hurthle cell nodules of nodular goiter tend to exhibit tissue fragments of Hurthle cells that display a 'honey comb' pattern. This is in contrast to Hurthle cell neoplasm in which a dissociated pattern is seen. Also in non-

neoplastic lesions, the Hurthle cells less commonly display the characteristic nuclear morphology. Macro nucleolus is infrequently seen. Other features that may help in differentiation are the admixture of regular follicular epithelial cells and the frequent occurrence of pyknotic nuclei in Hurthle cells.

On FNAC we could correctly diagnose nodular goiter in almost all cases. In a few cases of nodular goiter, smears showed Hurthle cells associated with ordinary follicular cells arranged as honey comb with abundant colloid. However the amount of colloid is not a statistically significant parameter [16].

One case of nodular goiter with thyroiditis turned out to be nodular goiter on histopathology. One case of nodular goiter with tyroiditis turned out to be follicular adenoma with thyroiditis. Here small population of lymphocytes from peripheral blood was considered as the source of the cells causing misinterpretation [8].

In our study, nine cases were diagnosed as Hurthle cell neoplasm on FNAC, which subsequently proved to be Hurthle cell adenomas on histopathology. We could accurately diagnose Hurthle cell neoplasm on FNAC.

The presence of >50% of Hurthle cell in FNAC indicates Hurthle cell neoplasm. Non-neoplastic lesions have <50% of Hurthle cells. Hurthle cell carcinomas have >90 % Hurthle cells in FNAC. Pure Hurthle cell neoplasm do not exhibit inflammatory cells and colloid in the background [17].

These two findings were observed in our study. In our study,Hurthle cell adenomas presented as solitary nodules.Hurthle cell adenomas are usually unilateral and carcinomas are usually bilateral. Hurthle cell adenomas behave in a benign fashion, whereas,the carcinomas pursue a more aggressive course. Unequivocal capsular/ vascular invasion is a pre-requisite for the diagnosis of Hurthle cell carcinoma. [3]

Hurthle cells were also encountered in follicular neoplasms and papillary carcinomas on FNAC. Jayaram et al have encountered Hurthle cells in thyrotoxic goiter, follicular neoplasm and also in papillary carcinomas. However, the presence of other specific features will point to the correct diagnosis [14].

In case of follicular neoplasm, the thyroid follicular epithelial cells are seen in micro acinar groupings, clusters with colloid. Hurthle cells are seen in small groups and in cohesive sheets. Histologically well encapsulated follicular adenoma with Hurthle cell component is obvuious. We had 24 cases of follicular neoplasm of which 22 proved to be follicular adenomas on histopathology. One case turned out to be adenomatous goiter and one case which was diagnosed as follicular neoplasm with thyroiditis turned out to be follicular adenoma. Here lymphocytes from the peripheral blood were mistaken as lesional lymphocytes. We have noted that peripheral blood lymphocytes are slightly smaller than lesional lymphocytes and they will be very few in number. So thyroiditis should not be considered when there are very few lymphocytes

In our study we had six cases of papillary carcinoma on cytology. The smears typically showed thyroid follicular cells arranged in papillary pattern, clusters and as follicles showing nuclear cytoplasmic inclusions and other features of papillary carcinoma. Hurthle cells were many, with slight nuclear pleomorphism. Hurthlecells were arranged in papillae and clusters. Smears also showed mild to moderate amount of fibrous tissue and lot of hemorrhage in the background.

Several studies report a high rate of papillary carcinoma in patients with Hashimoto's thyroiditis indicating a possible correlation between the two diseases. Increased incidence of papillary carcinoma in Hashimoto's thyroiditis patients might therefore indicate that Hashimoto's thyroiditis is a precursor of thyroid cancer [13].

Female patients with Hashimoto's thyroiditis undergoing thyroidectomy are 30% more likely to have papillary carcinoma [18]. Also Hashimoto's thyroiditis and papillary carcinoma of thyroid share same gene derangement of RET/PTC [19].

Recently two studies reported a 95 % prevalence of RET/PTC gene derangements in histologically benign tissue affected by Hashimoto's Thyroiditis, suggesting that multiple occult tumors exist in patients of Hashimoto's Thyroiditis with high frequency [20]. Hence, some workers suggest total thyroidectomy as the surgical procedure of choice, especially in young female patients with Hashimoto's thyroiditis [21].

The presence of Hurthle cells in papillary carcinoma does not change its usual behavior. The architectural pattern rather the cell type predicts the behaviour of the tumour [22].

The accurate diagnosis of Hurthle cell tumour by FNA is very important. The aspirates from Hurthle cell lesion show monomorphic cells with loosely cohesive tissue fragments as well as single cells. The nuclear chromatin is finely granular with prominent nucleoli. There were no inflammatory cells in the background. The accurate diagnosis based on FNA will help to plan the further management of the patient.

Conclusion

The presence of Hurthle cells doesnot always indicate a diagnosis of Hashimoto's thyroiditis or lymphocytic thyroiditisbecauseHurthle cells are also seen in various other lesions of thyroid. The presence of >50% of Hurthlecells in an aspiration indicates aHurthle cell neoplasm.Aspiration cytology in Hurthle cell lesions can differentiate non neoplastic lesions from neoplastic lesions with high accuracy, but differentiation between benign andmalignant neoplasms is less reliable.

References

1. HandaU, Garg S, Mohan H, Nagarkart N. Role of FNAC in primary diagnosis and management of thyroid lesions: A study on 434 patients.Journal of cytology 2008;25:13.
2. Orell SR In:Orell SR , Sterrett GF, Walters MN, Whitakar D, editors- Manual & atlas of FNAC , 4th edition. New Delhi; Churchill- Living Stone; 2005.p.125-64.
3. Burch HB. Fine needle aspiration of thyroid nodules: determination of insufficiency rates and malignancy yield at thyroidectomy. ActaCyto 1996;40;1176-83.
4. Kini U. Role of fine needle aspiration in the medical management of minimally enlarged thyroid. Diagcytopathol 2006;34:196-200.
5. Guhamallick M, Sengupta S, Bhattacharya NK, Basu N, Roy S, Ghosh AK, et al. Cytodiagnosis of thyroid lesions—usefulness and pitfalls: A study of 288 cases. J Cytol 2008;25:6-9.
6. Sippel RD, Elaraj DM, Khanafshar E, Zarnegar R, Kebebew E,Duh QY & Clark OH. Tumor size predicts malignant potential inHurthle cell neoplasms of the thyroid. World Journal of Surgery 2008;32:702–707.
7. Monogram on Thyroid –Virginia A. Livolsi Surgical pathology of the thyroid vol 22 in series major problems in pathology by James L.Bennington, Saunders, 1990.p.3.
8. MacDonald L,YazdiHM. Fine needle aspiration biopsy of Hashimoto's Thyroiditis: Sources of Diagnostic error. Acta cytological 1999;43(3):400-406.
9. Jayaram G. Iyengar KR, Sthaneshwar P, Hayati JN. Hashimoto's Thyroiditis – A Malaysian perspective. Cyto. J. 2007;24;119-24.
10. Friedman M, Shimaoka K, Rao U, Tsukada Y, Gavigan M, Tamura K. Diagnosis of chronic lymphocytic thyroiditis (nodular presentation) by needle aspiration. ActaCytol 1981;25:513-22.
11. Kini SR, Miller JM, Hamburger JI. Problems in the cytologic diagnosis of the "cold" thyroid nodule in patients with lymphocytic thyroiditis ActaCytol 1981;25:506-12.
12. Bhalotra R, Jayaram G. Overlapping morphology in thyroiditis (Hashimoto's and subacute) and Grave's disease. Cytopathology1990;1:371-2.
13. Matesa-Anic D, Matesa N, Dabelic N, Kusic Z. Coexistence of papillary carcinoma and Hashimoto's thyroiditis. ActaClin Croat 2009;48:9-12.
14. Jayaram G. "Problems in the interpretation of Hurthle cell populations in fine needle aspirates from the thyroid". ActaCytologica 1983;27:84-85.
15. Jayaram G, Marwaha RK, Gupta RK, Sharma SK. Cytomorphologic aspects of thyroiditis – A study of 51 caseswith functional, immunologic and ultrasonographic data. ActaCytol 1987;31:687-93.
16. Gonzalez JL. Fine needle aspiration of Hurthle cell lesions: A cytomorphologic approach to diagnosis.Am. J. Clinical pathology 1993;100:231-235.
17. Kauffmann PR, Dejax C, de Latour M. The meaning andpredictivity of Hurthle cells in FNAC for Thyroid nodular Diseases. Eup.J. of Surg Oncology 2004;7: 786-89.
18. Repplinger D, Bargren A, Zhang YW, Adler JT, Haymart M, Chen H. Is Hashimoto's Thyroiditis a risk factor for papillary thyroid cancer? J.Surg.Res. 2008;150(1): 49-52.
19. Robbins andCotran Pathologic basis of disease . Vinay Kumar, Abbas AK, Fausto N. 'The Endocrine System', 7th edition 2004, Saunders, p1164-1165.
20. Nikiforova MN, Caudill CM, Biddinger P, Nikiforova YE. Prevalance of RET/PTC rearrangement in Hashimoto's Thyroiditis and Papillary thyroid carcinoma. Int.J. Surg. Pathol 2002;10(1):15-22.
21. Kurukahueciogiu O, Taneri F, Yuksel O, Aydin A, Tezel E, Onuk E. Total thyroidectomy for the treatment of Hashimoto's Thyroiditis coexisting with Papillary thyroid cancer. Actacyto. 2007;24(3):510.
22. Kini SR. Cytopathology of Hurthle cell lesions of the thyroid gland by fine needle aspiration. Acta cytological 1981;25(6):647-652.