CYTOMORPHOLOGICAL GRADING IN HASHIMOTO'S THYROIDITIS - A PIONEER STUDY

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ABSTRACT

BACKGROUND

Hashimoto's Thyroiditis is a leading cause of hypothyroidism results due to immune mediated destruction of follicles and is characterised by infiltration of lymphoid cells. The aim of the present study is to categorise cytomorphology in to various grades and understand the spectrum of lesion and its complications.

MATERIALS AND METHODS

Fine needle aspiration cytology was done on patients with diffuse and nodular enlargement of thyroid in the Department of Pathology, Osmania Medical College over a period of one and half year from January 2015 to June 2016. Smears were made and stained by pap staining and H & E and diagnosis is based on characteristic cytomorphology of thyroid lesion.

RESULTS

A total number of 363 cases were received in the Department of Pathology of which 246 cases presented with diffuse enlargement and rest were nodular with varied cytological features. A total number of 177 cases of Hashimoto's thyroiditis were diagnosed of which 171 cases presented with diffuse enlargement and 6 cases as nodular are the subjects of present study.

CONCLUSION

Fine needle aspiration is a simple and reliable diagnostic procedure in the evaluation of Hashimoto's thyroiditis. The present study emphasises that cytomorphologic grading of HT is useful in deciding the line of treatment, its followup and complications.

KEYWORDS

Hashimoto's Thyroiditis, Hypothyroidism, Cytomorphology.

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INTRODUCTION: The first report of chronic lymphocytic thyroiditis (Struma lymphomatosa) was described by Hakaru Hashimoto in 1912. The disease is now popularly known as Hashimoto's Thyroiditis (HT).(1) It is an autoimmune disorder which is more prevalent in Asians and its incidence is increasing which is thought to be due to increased iodine intake especially people living in coastal areas. It is more common in females with peak age incidence 30-50 years.(2) HT was thought to be an uncommon disease in the past, and the diagnosis was often made by Histopathological examination of the resected thyroids or biopsied thyroid tissue. Increased diagnostic modalities lead to more recognition of disease by fine needle aspiration.(3) It is important to diagnose Hashimoto's thyroiditis as it is leading cause of hypothyroidism and requires lifelong supplementation with thyroxine.(4) It is usually associated with raised antithyroid peroxidase antibody; however, 10-15% of patients may be antibody negative.(5)

Clinically, it presents as diffuse enlargement of thyroid more or less being usually asymptomatic, less frequently as nodular. Gradually, patient develops hypothyroidism in the usual clinical course. It has a risk of transforming into malignancy with increased risk of extranodal marginal B cell lymphoma.(6) and Papillary carcinoma.(7) Hence patients diagnosed as HT need followup. Fine needle aspiration cytology is a simple, safe, cost effective procedure performed in outpatient clinic and a reliable tool in the evaluation of thyroid lesions. Hashimoto's Thyroiditis is the second most common lesion next to colloid goitre and is associated with hypothyroidism.(8) FNAC is accurate in diagnosing HT in most of the cases with few exceptions, necessitating medical treatment, thus avoiding surgical excisions. The efficacy of FNAC in HT has led medical management in most of the cases. Clinically suspected cases of Hashimoto's Thyroiditis when missed on cytology are due to technical limitations and inadequate material i.e., sparse cellularity. Hence, an integrated approach with ultrasonography, T3, T4, TSH and anti TPO antibodies in conjunction with cytologic evaluation improves diagnostic accuracy of HT. An attempt is made to grade the cytomorphology of HT to decide the line of treatment, followup and to assess its complications.

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MATERIALS AND METHODS: It is a prospective and observational study in patients attending as fresh cases from medical, surgical and endocrinology department which were referred to the Department of Pathology for aspiration cytology. FNA also performed on patients with HT on treatment for followup. A total number of 363 cases were received in the department of cytology with diffuse and nodular enlargement of Thyroid for FNAC. Majority of the cases, 332 were female and remaining 31 were males. Most of the cases belong to 3rd and 4th decade. 246 cases out of 363 cases presented with diffuse enlargement and 117 cases presented with nodular enlargement. Total number of cases are 363, males 31 and females were 332.

Age	Males	Females
1-10	1	3
11-20	9	56
21-30	3	120
31-40	9	87
41-50	4	34
51-60	2	19
61-70	0	10
71-80	3	3
Total	**31**	**332**

Table 1: Showing Age and Gender Distribution of Various Thyroid Lesions

Aspiration/non-aspiration technique was performed under aseptic precautions after taking written consent. 23-25 gauge needle with 5 mL syringe of Dispovan was preferred. 2-4 passes were given from different sites to unearth combined lesions if at all present. The amount of resistance that is offered by the lesion while aspiration is also observed. Nature of aspirate smeared on slides was documented. When fluid was obtained a direct smear was made and simultaneously centrifuged smears were studied. In case, when straw coloured/colourless fluid was obtained, the lesion was completely drained and repeat aspiration was done with a view of not missing papillary carcinomas which are known to occur with cystic change. Unstained smears were viewed under microscope to assess cellularity. When found inadequate, repeat aspiration was done in the same setting and under ultrasonographic guidance selectively. Staining was done by routine H & E and PAP stains. In suspected cases of HT with NHL, aspirate can be sent for Flow cytometry for further evaluation.

Detailed clinical history with respect to age, gender, clinical presentation as diffuse or nodular enlargement, radiological finding, hormone status and antithyroid antibodies were noted wherever available. Cell blocks are prepared when aspirates were fluid and haemorrhagic selectively with 10% Formalin. Surgical specimens of thyroid were fixed in 10% Formalin and routine processing done and IHC with TTF-1, CK19, CD56, HBME-1 and galectin-3 were done in cases of neoplastic lesions when occurred as a co-lesion.

RESULTS: Fine needle aspiration was done in 363 cases, out of which 246 cases presented as diffuse enlargement of thyroid and rest 117 cases as a solitary nodule. And 69/363 cases presented with clinical manifestations of either hypothyroidism, toxicity or pressure symptoms. (Table 2). Cytosmears were studied and various thyroid lesions were evaluated by their characteristic cytomorphology. Patients with HT on treatment with Thyroxine and combined cases associated with neoplastic lesions are excluded from the study for the sake of grading cytological features of HT. Patients presenting with diffuse thyroid enlargement were analysed cytologically. 171/246 cases were diagnosed as HT, 58 cases were as simple colloid goitre and rest 15 cases were diagnosed as neoplastic lesion predominantly Papillary carcinoma of Thyroid. Patients presenting as a solitary nodule were evaluated and 86/117 cases were diagnosed as nodular goitre and 6 cases were labelled as Nodular HT. (Table 3).

	Male	Female	Sub total
Nodular Enlargement	20	97	117
Diffuse enlargement	11	235	246
Total	**31**	**332**	**363**
Symptomatic	11	58	69
Asymptomatic	20	274	294
Total			**363**

Table 2: Showing Gender Wise Distribution of Clinical Presentation in Thyroid Lesions

Diffuse		Nodular	
Simple colloid goitre	58	Nodular goitre	86
Hashimoto's thyroiditis	171	Papillary with cystic change	8
Papillary	12	Follicular neoplasm	9
Papillary with HT	3	Medullary	2
Lymphoma with HT	2	Anaplastic	1
		Hashimoto thyroiditis	6
		Follicular neoplasm with HT	2
		Medullary with HT	1
Total	**246**		**117**

Table 3: Cytomorphological Diagnosis of Diffuse and Nodular Enlargement

HT was predominantly seen in 3rd and 4th decades ranging from 9 years to 68 years as shown in the table 1. Cytological features of 177 cases of Hashimoto's thyroiditis including diffuse and nodular enlargement along with 2 cases of HT with lymphoma are the subjects for grading. Other combined lesions with HT and patients on treatment are excluded for the grading. (Table 4).

Age	Total HT	Female		Male	
		Diffuse	Nodular	Diffuse	Nodular
1-10	2	2			
11-20	38	34		4	
21-30	71	67	4		
31-40	39	39			
41-50	16	14	1	1	
51-60	11	9		1	1
61-70	2	2			
71-80	0	0			
Total	**179**	**167**	**5**	**6**	**1**

Table 4: Distribution of Cases of HT With Respect to Age, Gender and Clinical Presentation

Cellularity was assessed by two different pathologists. Criteria for diagnosis of HT was presence of follicular cells, impingement of lymphocytes in thyroid follicles, Hurthle cells, Lymphocytes in various stages of maturation, colloid, fibroblasts, histiocytes, giant cells, plasma cells, eosinophils, epithelioid cells, follicular cells with nuclear grooving, metaplastic squamoid cells and atypical lymphoid cells. Based on the above cytologic components, a grading system is attempted which occurs as a spectrum of lesion and grouped into grades I to VI. (Table 5).

Grade I	Groups of follicular cells of uniform size and shape, lymphocytes infiltrating follicular cells. Background shows colloid, lymphocytes and blood elements.
Grade II	Groups of follicular cells of uniform size and shape, lymphocytes infiltrating follicular cells, occasional Hurthle cells on search. Background shows colloid, lymphocytes and blood elements.
Grade III	Group of follicular epithelial cells loosely arranged cells, groups of Hurthle cells with nuclear atypia, lymphocytes infiltrating follicular cells, reactive lymphocytes, fibroblasts. Scant colloid in the background.
Grade IV	Groups and individual follicular epithelial cells, Hurthle cells in clusters with pleomorphism, lymphoplasma cells, histiocytes, epithelioid cells, reactive lymphocytes, increase in fibroblasts.
Grade V	Scant follicular cells, few Hurthle cells in groups with pleomorphism with prominent nucleoli mimicking malignancy. Occasional squamoid cells. Background shows lymphoplasma cells, reactive lymphocytes.
Grade VI	Scant follicular cells, occasional Hurthle cells, plenty of lymphocytes, centrocytes, centroblasts with increased mitosis mimicking Lymphoma.

Table 5: Cytomorphological Grading System from Grade I to Grade VI:

Total analysis of 179 cases of HT were graded based on the above cellular criteria as mentioned in the Table 6. 40 cases belonged to grade I with sparse to plenty of lymphocytes. Majority of the cases of 69 and 53 cases were in the grades II and III respectively. 10 cases were reported under grade IV with hypocellular smears, Hurthle cell clusters with nuclear atypia and increased fibroblasts. 5 cases were grouped in grade V, showed scant follicular cells, few Hurthle cells in groups with pleomorphism with some of the cells showing prominent nucleoli mimicking malignancy along with presence of squamoid cells at times. 2 out of 179 cases were grouped in grade VI, showed numerous atypical lymphoid cells with increased mitosis mimicking NHL.

Grading	No. of Cases
I	40
II	69
III	53
IV	10
V	5
VI	2
Total	**179 cases of HT**

Table 6: Showing Number of Cases in Various Grades

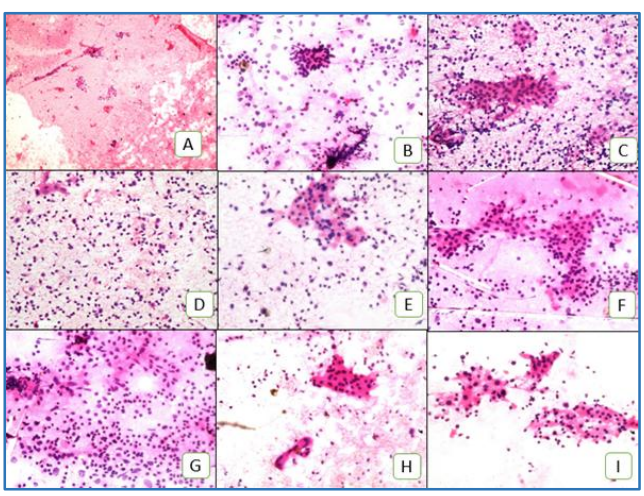

Figure 1: Grade I: A-C. A shows follicular cells in clusters and sparse lymphocytes and colloid in the background. **B** shows clusters of follicular cells with lymphocytes impinging. **C** shows clusters of follicular cells with florid lymphocytes. **Grade II: D- E. D** shows follicular cells, occasional Hurthle cells and plenty of lymphocytes. E and F shows clusters of follicular cells infiltrated by lymphocytes with mild Hurthle cell change and lymphocytes in the background. **Grade III: G-I. G, H** and **I** shows clusters of follicular cells, Hurthle cell change with mild atypia and lymphocytes in the background.

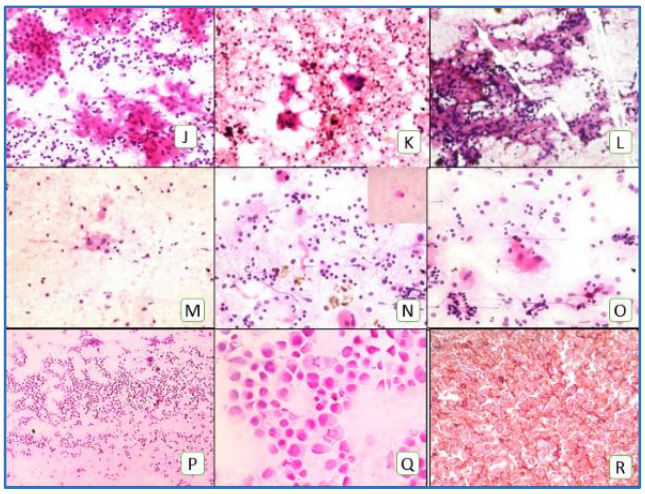

Figure 2: Grade IV: J-L. J and K shows clusters and sheets of Hurthle cells with atypia, lymphoid cells in the background and epithelioids in J. **L** shows clusters of follicular cells, Hurthle cells, increased fibroblasts and few lymphocytes in the background. **Grade V: M-O.** M, N and O shows follicular cells, squamoid cells, fibroblasts and few lymphoplasma cells. **Grade VI: P-R:** P shows follicular cells and plenty of lymphoid cells giving lymph node picture. Q shows lymphoid cells with plasmacytoid appearance and nuclear atypia. Mitotic figures are seen suggestive of lymphoma. R shows histopathology biopsy positive for CD 20 antibody, suggestive of B cell lymphoma.

DISCUSSION: HT is an autoimmune disorder characterised by lymphocytic infiltration of thyroid follicles resulting in immune mediated destruction with fibrosis. Genetic and environmental factors are responsible for the causation of the disease.[4] It is more common in middle age and young females in our study in 3rd and 4th decade similar to S Shirish et al 2014.[2] Usually, it presents as a diffuse enlargement of thyroid gland firm in consistency, moves with deglutition and less frequently as nodular.[8] Similarly, we also noticed 173 cases of HT with diffuse enlargement and 6 cases presented as nodular. HT was the most commonly encountered thyroid lesion in our study constituting 49.3% cases followed by goitre 39.6% cases in contrast to Kumar N et al[9] where goitrous lesions were more common. Majority are hypothyroid with raised TSH levels and positive for anti-TPO antibodies.

On ultrasonography, diffuse echogenicity along with irregular echo pattern is an early marker of HT, but not specific as seen in other conditions like Grave's disease and drug-induced thyroiditis.[10] Grade I lesions with minimal thyroid enlargement showing sparse lymphocyte infiltration poses diagnostic difficulty which may need ultrasonography and estimations of anti-TPO antibody. However, few number of the cases were anti-TPO negative in grade I category. Most of such cases on repeat aspiration resolved uncertainty. During postpartum period, thyroiditis can occur with raised anti-TPO antibodies. Such cases are diagnosed as postpartum thyroiditis. We had one such case included under this study. A false positive diagnosis of Hashimoto's Thyroiditis can be made when lymph node in pretracheal fascia is aspirated, hence presence of follicular cells is mandatory. In cases with sparse cellularity, cytologic clues to increase the sensitivity of diagnosis are needed. It is observed that eosinophilic infiltration has higher association with HT.[7]

Lymphocytic infiltration, impinging of lymphocytes with follicular cells with scant colloid and Hurthle cell change is the hallmark of HT.[9] Grade II and grade III lesions shows the hallmark features which are the predominant forms diagnosed in our study. Increased number of histiocytes, epithelioids with fibroblasts are categorised in grade IV. Grade I to grade IV lesions of HT are sufficed with replacement therapy and followup. Few cases of grade IV HT when show increased fibroblasts with clinical presentation of firm diffuse enlargement of the gland with pressure symptoms, underwent surgical excision and proved to be fibrous variant of HT as supported by Lannaci G et al.[11] Fibrous variant of HT clinically mimics a malignant lesion. Kanaya H et al[12] reported a case of fibrous variant of HT, its cytology revealed clusters of large multinucleated cells suggestive of anaplastic carcinoma, a misdiagnosis. Histology proved no malignant change.

Clusters of Hurthle cells in smears lead to mistaken diagnosis of Hurthle cell adenoma and presence of nuclear atypia in Hurthle cells mimic a neoplastic lesion. Hurtle cell nodules and nuclear atypia is part and parcel of HT. Presence of squamoid cells in the smears lead to mistaken consideration of primary squamous cell carcinoma of thyroid.[13] categorised in grade V. But such cases are fore runners of a malignant lesion and should be followed up. Smear with few follicular cells and many lymphoid cells with atypical nuclear features and increased mitotic figures raised suspicion of lymphoma.[14] in two of our cases which were proved as Non-Hodgkin's B cell lymphoma, grouped in Grade VI. Cases with such cellularity on FNAC should be evaluated with ancillary technique like Flow cytometry.

Such cases can be managed medically and surgical intervention for diagnosis is avoided. Bhatia et al 2007.[15] graded cytology smears in to Grade I (Mild) characterised by lymphoid cells infiltrating the follicles with increased number of lymphocytes in the background. Grade II (Moderate) with mild-to-moderate lymphocytic infiltration with Hurthle cell change. Grade III (Severe) with florid lymphocytic infiltration with germinal centre formation and few follicular cells. Bhatia et al did not mention about complications of HT which can be diagnosed cytologically.

We encountered 6 cases of nodular HT which resulted due to increased fibrosis. Nodular form of HT presents as differential diagnosis of solitary nodule which needs surgical excision for Histopathological diagnosis. It has to be differentiated from Hurthle cell adenoma, papillary thyroid carcinoma.,[16] primary thyroidal NHL, which are associated with complications of HT, needs surgical excision. In the present study, a total number of 40 cases of neoplastic lesion are diagnosed by FNAC out of which 12 cases presented as diffuse enlargement and 20 cases as nodular and 8 cases of Neoplastic lesions were associated with HT as co-lesion.

Several authors have reported association of Hashimoto's Thyroiditis with Follicular Adenoma.,[17] Papillary carcinoma.,[18] Medullary carcinoma.,[19] Hurthle cell adenoma.[20] and Hurthle cell carcinoma. There is an increased risk of PTC with HT or can coexist.[21] The role of HT in causation of PTC is not well understood and is under study. Follicular cells with nuclear grooving in HT can be mistaken for PTC. Oncocytic metaplasia is known to occur in HT. Smears with more than 75% Hurthle cells is characteristic of Hurthle cell neoplasm. High proportion of cells more than 90% with cellular discohesiveness, nuclear pleomorphism, large nucleoli and lack of accompanying inflammatory cells favour Hurthle cell carcinoma.

Known case of Hashimoto thyroiditis with increased serum calcitonin levels are suggestive of Medullary carcinoma as a co-lesion even though FNAC is nondiagnostic. Serum calcitonin is a tumour marker used in diagnosis and followup of medullary carcinoma of thyroid. Usha M et al[14] reported a case of a 52-year-old suffering from HT since 10 years with primary thyroid lymphoma diagnosed by FNAC, as DLBCL. The main cytological differential diagnosis to be kept in mind is Anaplastic carcinoma. Diagnosis by FNA can avoid surgery. Squamous metaplasia is known to occur with HT and presents as a nodule. Tetsuro Kobayashi et al[13] described in a 59-year-old Japanese female, diagnosed histologically a nodule which showed clusters of squamous cells without mitosis surrounded by dense connective tissue. Primary squamous cell carcinoma is a rare malignant lesion, accounts for less than 1% of total malignant lesions. Chavan RK et al[22] reported in a female patient a case of primary squamous cell carcinoma histologically.

FNAC misdiagnosed it as papillary carcinoma of thyroid. Extensive investigations ruled out primary elsewhere in the head and neck. Metastasis from primary squamous cell carcinoma to thyroid gland is known to occur.[23] A cytomorphologist while dealing with HT should be aware of the cellular features occurring as a spectrum, and its complications, its association with the various neoplastic lesions which are known to exist as a co-lesion as described in our study.

CONCLUSION: FNAC is safe, simple cost effective outpatient procedure serves as an important diagnostic tool in evaluation of thyroid lesions. FNAC is accurate in diagnosis of HT with higher sensitivity and specificity. FNAC is a first line diagnostic tool in evaluation of HT. In comparison to Anti-TPO antibody, ultrasonography is useful to assess the degree of immune mediated glandular destruction, fibrosis and ongoing complications. Based on cellular compositions, HT is described in 6 different grades based on which line of treatment, medical and surgical excision and followup is decided. Due to early and accurate diagnosis of HT by FNAC and integrated approach, patients are subjected to medical treatment and kept on followup. Surgical excision has become rarity in recent times, exceptionally done when associated with complications.

REFERENCES

1. Nguyen GK, Ginsberg J, Crockford PM, et al. Hashimoto's thyroiditis: cytodiagnostic accuracy and pitfalls. Diagnostic cytopathology 1997;16(6):531-536.
2. Chandanwale SS, Gore CR, Bamanikar SA, et al. Cytomorphologic spectrum of Hashimoto's thyroiditis and its clinical correlation: a retrospective study of 52 patients. Cyto Journal 2014;11(1):9.
3. Staii A, Mirocha S, Todorova-Koteva K, et al. Hashimoto thyroiditis is more frequent than expected when diagnosed by cytology which uncovers a pre-clinical state. Thyroid Research 2010;3(1):11.
4. Kudva R, Kishore M. Hashimoto's thyroiditis: a correlation of cytomorphology with clinical, biochemical & radiological findings. International Journal of Science and Research 2015;4(2):1771-1774.
5. Noureldine SI, Tufano RP. Association of Hashimoto's thyroiditis and thyroid cancer. Current Opinion in Oncology 2015;27(1):21-25.
6. Ekambaram M, Kumar B, Chowdhary N, et al. Significance of eosinophils in diagnosing Hashimoto's thyroiditis on fine-needle aspiration cytology. Indian Journal of Pathology and Microbiology 2010;53(3):476.
7. Caleo A, Vigliar E, Vitale M, et al. Cytological diagnosis of thyroid nodules in Hashimoto thyroiditis in elderly patients. BMC surgery 2013;13(Suppl 2):S2-S41.
8. Gayathri BN, Kalyani R, Kumar MLH, et al. Fine needle aspiration cytology of Hashimoto's thyroiditis-a diagnostic pitfall with review of literature. Journal of Cytology. 2011;28(4):210-213.
9. Kumar N, Ray C, Jain S. Aspiration cytology of Hashimoto's thyroiditis in an endemic area. Cytopathology 2002;13(1):31-39.
10. Grani G, Carbotta G, Nesca A, et al. A comprehensive score to diagnose Hashimoto's thyroiditis: a proposal. Endocrine 2015;49(2):361-365.
11. Iannaci G, Luise R, Sapere P, et al. Fibrous variant of Hashimoto's thyroiditis as a diagnostic pitfall in thyroid pathology. Case Reports in Endocrinology Article ID-308908, 2013;2013(4):p.5.
12. Kanaya H, Konno W, Fukami S, et al. Acute exacerbation of Hashimoto thyroiditis mimicking anaplastic carcinoma of the thyroid: a complicated case. Ear Nose Throat J 2014;93(12):E18-21.
13. Kobayashi T, Okamoto S, Maruyama H, et al. Squamous metaplasia with Hashimoto's thyroiditis presenting as a thyroid nodule. Journal of Surgical Oncology 1989;40(2):139-142.
14. Usha M, Kamath S, Sridhar M, et al. Primary thyroid lymphoma in the background of Hashimoto thyroiditis. Clinical Cancer Investigation Journal 2015;4(3):362-364.

15. Bhatia A, Rajwanshi A, Dash RJ, et al. Lymphocytic thyroiditis–is cytological grading significant? A correlation of grades with clinical, biochemical, ultrasonographic and radionuclide parameters. Cyto Journal 2007;4(1):10.
16. Carson HJ, Castelli MJ, Gattuso P. Incidence of neoplasia in Hashimoto's thyroiditis: a fine-needle aspiration study. Diagnostic Cytopathology 1996;14(1):38-42.
17. Kollur SM, El Sayed S, El Hag IA. Follicular thyroid lesions coexisting with Hashimoto's thyroiditis: incidence and possible sources of diagnostic errors. Diagnostic Cytopathology 2003;28(1):35-38.
18. Jankovic B, Le KT, Hershman JM. Clinical Review: Hashimoto's thyroiditis and papillary thyroid carcinoma: is there a correlation? The Journal of Clinical Endocrinology & Metabolism 2013;98(2):474-482.
19. Mousa U, Gursoy A, Ozdemir H, et al. Medullary thyroid carcinoma in a patient with Hashimoto's thyroiditis diagnosed by calcitonin washout from a thyroid nodule. Diagnostic Cytopathology 2013;41(7):644-646.
20. Mehdi G, Siddiqui FA, Ansari HA, et al. Hurthle cell adenoma as an incidental finding in Hashimoto's thyroiditis-case report and short review of literature. Internet J Pathol 2009;8(1):7.
21. Mazokopakis EE, Tzortzinis AA, Dalieraki-Ott EI, et al. Coexistence of Hashimoto's thyroiditis with papillary thyroid carcinoma. A retrospective study. Hormones 2010;9(4):312-317.
22. Chavan RN, Chikkala B, Biswas C, et al. Primary squamous cell carcinoma of thyroid: a rare entity. Case Reports in Pathology Article ID- 838079, 2015;2015:pgs. 3.
23. Vamsy M, Dattatreya PS, Sarma LY, et al. Metastatic squamous cell carcinoma thyroid from functionally cured cancer cervix. Indian Journal of Nuclear Medicine 2013;28(2):112-114.