International Journal of Basic and Applied Medical Sciences ISSN: 2277-2103 (Online)
An Open Access, Online International Journal Available at http://www.cibtech.org/jms.htm
2015 Vol. 5 (1) January-April, pp. 152-157/Shashi and Sharma
Research Article

GOITROUS THYROIDITIS: CLINICAL AND PATHOLOGICAL IMPLICATIONS

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ABSTRACT
The present investigation evaluates the clinico-pathological features of different syndromes of thyroiditis. Eighty nine patients with clinical diagnosis of thyroiditis in the age group of 32-56, coming for treatment in Govt. Rajindra Prasad Medical College and Hospital Kangra, Himachal Pradesh, India were included in the study. It incorporates subacute and chronic categories of thyroiditis. Sixty five cases of chronic thyroiditis were diagnosed. Subacute granulomatous "De Quervain's" thyroditis was diagnosed in twenty patients. The thyroid function hormones TSH, T3 and T4 of the patients were analyzed by enzyme immune assay technique. All the patients with Hashimoto's and lymphocytic thyroiditis were affected with hypothyroidism, while patients of subacute granulomatous thyroiditis were hyperthyroid. The smears of diagnosed cases revealed presence of scant colloid with diffuse lymphoid infiltration, fibrosis, atrophy of follicular cells and oncocytic changes viz hurthal cell transformations in some follicular cells in patients of Hashimoto's thyroiditis. The FNACs of lymphocytic thyroiditis patients were characterized by presence of numerous lymphoid cells at different stages of maturation, including mature and immature lymphoid cells and a few plasma cells. Aggregates of paravacuolar granulomas with degenerative and proliferative changes of the follicular cells in filtered by lymphocytes were visible in smears of subacute granulomatous thyroiditis. Our results suggest that the mean age of subacute thyroiditis is significantly lower than that of those with chronic thyroiditis. There was a tendency towards hypothyroidism associated with chronic thyroiditis and towards hyperthyroidism associated with subacute thyroiditis.

***Keywords*:** *Hashimoto's Thyroiditis, Lymphocytic Thyroiditis, Subacute Thyroiditis, TSH, T3, T4*

INTRODUCTION
Thyroiditis is an inflammation of the thyroid gland that may be painful and tender when caused by infection, radiation, trauma, or painless when caused by autoimmune conditions, medications, and an idiopathic fibrotic process. The most common forms are Hashimoto's disease, subacute granulomatous thyroiditis, postpartum thyroiditis, subacute lymphocytic thyroiditis, and drug-induced thyroiditis (Bindra and Braunstein, 2006). Subacute thyroiditis is a seasonal disorder that generally affects middle aged women. It is characterized by neck pain and generalized malaise, fatigue, fever and chills following an upper respiratory infection, usually of viral etiology.

Fine needle aspiration specimens contain acute inflammatory cells on a background of mixed inflammatory cells and multinucleated giant cells with degenerated thyroid follicular epithelial cells (Thompson and Heffess, 2002).

In chronic lymphocytic thyroiditis, the cytological markers include lymphocytic infilteration of the interfollicular space, invasion of follicles by the lymphocytes giving a fire-flare appearance characterized by eosinophilic vacuolated cytoplasm and later total destruction of follicles (Cabay and Salem, 2008). Chronic Hashimoto's thyroiditis is a female predominant autoimmune disease, characterized clinically by a diffuse and nontender goiter, hypothyroidism, and antibodies against thyroid microsomal antigens (Siriweera and Ratnatunga, 2010) and presence of diffuse lymphcytic infilterates, lymphoid follicles with reactive germinal centres, hurthal cell change of the follicular epithelial cells, parenchymal atrophy, and fibrosis have been reported (Bhatia *et al.*, 2007).

The present investigation assessed the clinico-pathological features of the different syndromes of thyroiditis in Kangra valley, Himachal Pradesh, India.

MATERIALS AND METHODS

Patients and Methods

Study Population

Eighty nine patients (women 60, men 20) aged 32-56 (mean age 47 ± 11.45 years) affected with clinical thyroiditis, were selected.

Clinical Evaluation

All patients were subjected to thorough history taking and complete clinical examination with special emphasis on manifestations of hypo- or hyperthyroidism and clinical criteria of the goiter and its association with pain.

Laboratory Tests

Serum levels of thyroid stimulating hormone, triiodothyronin and thyroxine were estimated by enzyme immune assay tests on ELISA reader.

Pathological Investigations

Preoperative fine needle aspiration cytology was done in all patients. The smears were air dried, fixed in methanol and stained with May- Grunwald Giemsa and Papanicolau stains. The cytopathological results were correlated with clinical features and thyroid function.

RESULTS AND DISCUSSION

Results

Eighty nine patients with clinical diagnosis of thyroiditis in the age group of 32-56 years were included. The mean age of patients with subacute thyroiditis was significantly lower than that of those with chronic thyriditis (37.43 ± 4.49 vs 45.49 ± 7.34 years, $p<0.0001$). Sixty five cases of chronic thyroiditis were diagnosed, out of which forty five patients have Hashimoto's thyroiditis. Lymphocytic thyroiditis was diagnosed in twenty four goitrous patients. Subacute granulomatous "De Quervain's" thyroditis was diagnosed in twenty patients (Table 1).

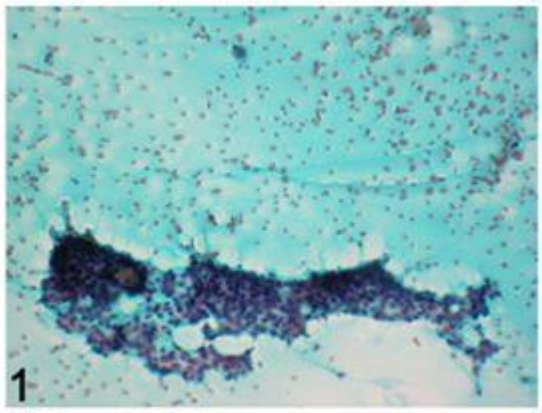
Table 1: Frequency of thyroiditis syndromes in the present series (Singer's Classification, 1965)

Thyroiditis	No. of Patients (n=89)	%age
Chronic Thyroiditis	(69)	
- Hashimoto's thyroiditis	45	50.56
- Lymphocytic thyroiditis	24	26.97
Subacute thyroiditis	20	22.47

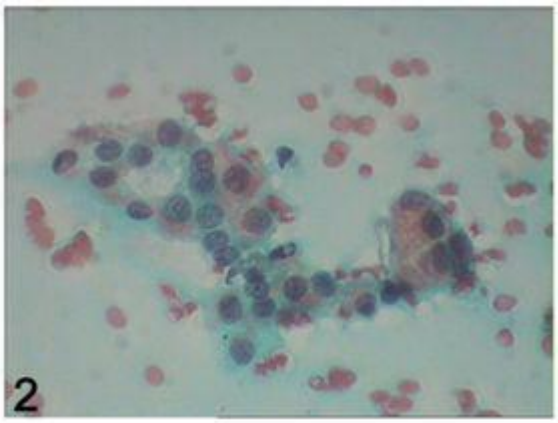
The thyroid hormonal tests revealed that TSH was significantly ($p<0.0001$) elevated and T3 and T4 were declined in Hashimoto's and lymphocytic thyroiditis patients. Subacute thyroiditis patients exhibited significant ($p<0.0001$) decrease in the concentration of TSH and increase in T3 and T4 levels. There was a significant association between hypothyroidism and chronic thyroiditis and between hyperthyroidism and subacute thyroiditis (Table 2).

Table 2: Hormonal profile of the studied thyroiditis patients

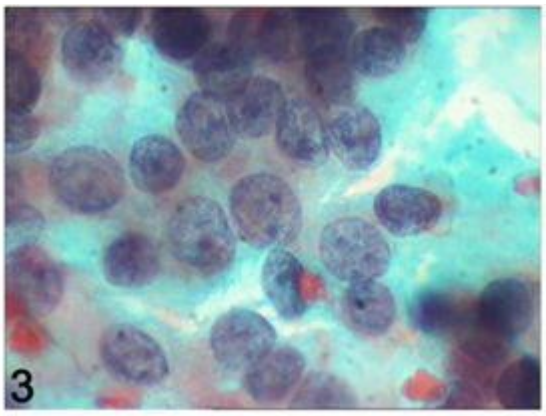
Laboratory Test	Normal Range	Hashimoto's thyroditis	Lymphocytic thyroditis	Sub acute thyroiditis	
		Mean ± SD	Mean ± SD	Mean ± SD	P- Value
TSH (µIU/ml)	0.4 – 4.2	12.56 ± 2.56	9.56 ± 3.60	0.23 ± 0.05	
T3 (ng/ml)	0.8 - 1.9	0.34 ± 0.04	0.42 ± 0.04	3.65 ± 1.39	p<0.0001
T4 (µg/dl)	4.8 – 12	2.62 ± 1.49	2.89 ± 1.05	14.69 ± 4.05	



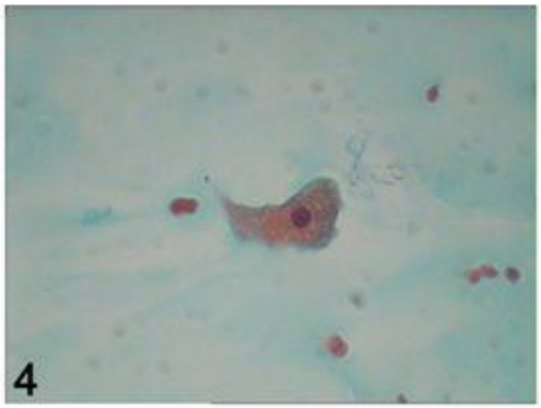
Photom 1: Hashimoto's thyroiditis: a synacium of benign follicular epithelial cells with nuclear crowding and overlapping. PAP stain, X100



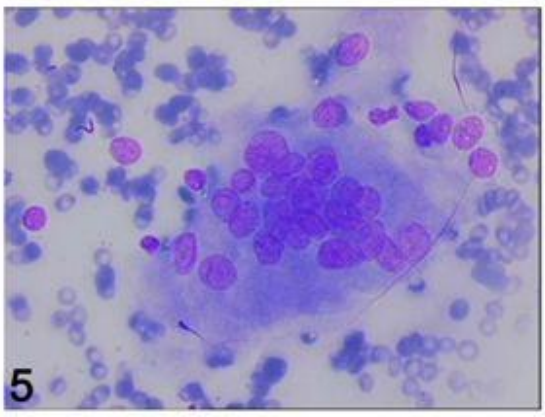
Photom 2: Hashimoto's thyroiditis: Sheet of monomorphic Hürthal cells. PAP stain, X400



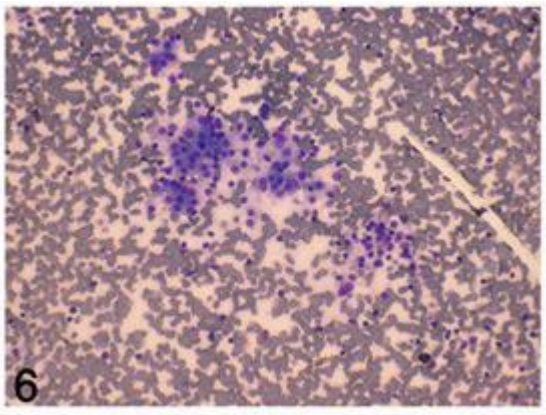
Photom 3: Magnified view of cohesive group of Hürthle cells with granular cytoplasm in Hashimito's thyroiditis. PAP stain, X1000



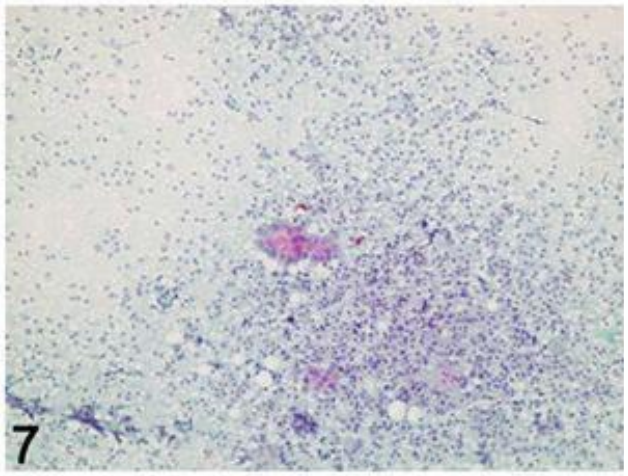
Photom 4: Hemosederine macrophage in Hashimoto's thyroiditis. PAP stain, X400



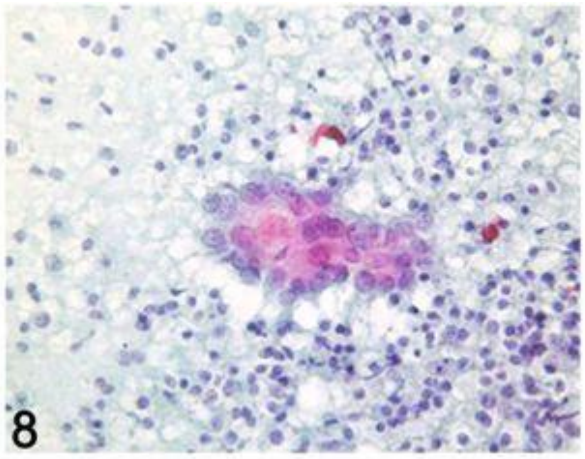
Photom 5: Hashimoto's thyroiditis: a multinucleated giant cell. MGG stain, X600



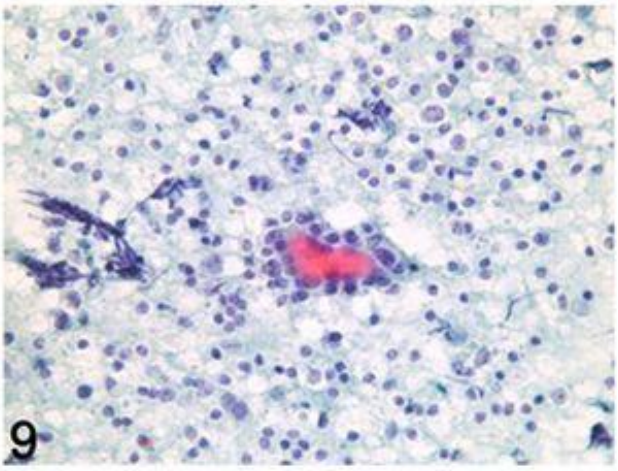
Photom 6: Lymphocytic thyroiditis showing monolayered clusters of follicular cells surrounded by lymphocytic infilterate. MGG stain, X100



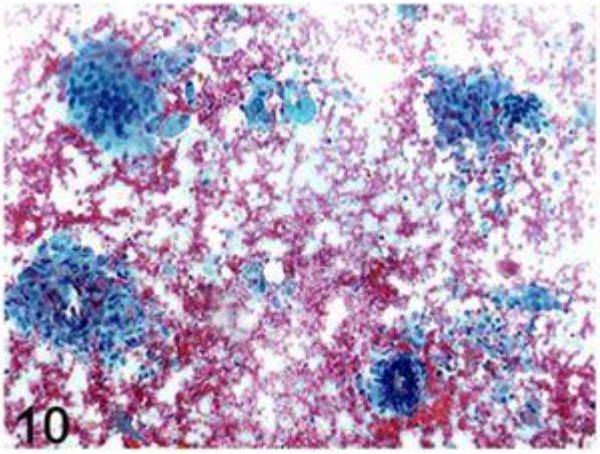
Photom 7: Lymphocytic thyroiditis: cluster of hyperplastic follicular cells with lymphocytic infiltration. PAP stain, X100



Photom 8: Magnified view of photom. 6, showing a cluster of hyperplastic follicular cells surrounded and partially infiltrated by lymphocytes. PAP stain, X400



Photom 9: Lymphocytic thyroiditis: a colloid filled follicle. PAP stain, X400



Photom 10: Subacute thyroiditis: Clusters of follicular cells arranged in granuloma pattern. PAP stain, X400

Hashimoto's thyroiditis was diagnosed in forty five patients. The smears revealed presence of scant colloid, and abundant cells predominantly lymphoid and epithelial. Synanciums of benign follicular epithelial with nuclear crowding and overlapping were visible. The transformed cells have vasicular nuclei with one or two nucleoli and scant cytoplasm (Figure 1).

Most of the follicular cells formed hurthal cells transformations. Monolayered sheets of hurthal cells with granulated cytoplasm were prominent (Figure 2). On high magnification, classic hurthal cells with well defined margins, fine granular eosinophilic cytoplasm and a large, hyperchromatic and pleomorphic nucleus were seen (Figure 3). Aside from lymphoid and epithelial cells, aspirations from thyroiditis patients also revealed presence of hemosederin-ladan macrophages. These were macrophages, which phagocytised ruptured red cells and leads to transformation of hemoglobin into brown colored hemosederin (Figure 4). Smears of a few patients showed presence of multinucleated giant cells with 20-30 nuclei and colloid containing cytoplasm (Figure 5).

Lymphocytic thyroiditis was diagnosed in twenty six goitrous patients. The FNAC of the lymphocytic thyroiditis patients were moderately cellular smears comprised of benign follicular epithelial cells admixed with an abundant polymorphous benign lymphoid infilterate in a colloidal and hemorrhagic background. Most of the lymphoid cells were lymphocytes and plasmacytes (Figure 6). There were small groups of follicular epithelial cells in aciner or ball like clusters with vasicular nuclei and scant cytoplasm. The follicular cells were varying in number and morphology. Clusters of transformed oncocytic cells surrounded and in filtered by lymphocytes were also visible. The oncocytic cells have abundant eosinophilic and granular cytoplasm and large bizarre nuclei (Figures 7, 8). In a female patient aged 52 years a colloid containing follicle surrounded by a polymorphic lymphoid population was also noted. The colloid material was dense and deeply eosinophilic (Figure 9).

Subacute granulomatous thyroiditis was found in twenty patients. The smears were highly cellular with scant colloid material in the background. The cell population mostly contains nacrotic follicular cells, neutrophils, fibroblasts, lymphocytes, macrophages and multinucleated giant cells. Aggregates of paravacuolar granules with degenerative and proliferative changes of the follicular cells infiltered by lymphocytes were visible in FNAC smears of almost all the patients with sub acute thyroiditis (Figure 10). Presence of multinucleated giant cells was a key feature of subacute thyroiditis. Multinucleated cells with more than 50 nuclei were present in almost all patients. In some cases carrot shaped nuclei were seen in synacial clusters.

Discussion

The present study reported that the patients with subacute granulomatous thyroiditis were significantly younger than those that chronic thyroiditis. Most patients were women aged 40-50 years. All the patients with Hashimoto's and lymphocytic thyroiditis were affected with hypothyroidism, while patients of subacute granulomatous thyroiditis were hyperthyroid. Similar findings were reported by many authors (Bhatia *et al.,* 2007; Peter, 1991). Khlil *et al.,* (2004) documented that the mean age of the subacute granulomatous thyroiditis patients was significantly lower than that of those with chronic thyroiditis patients. Patients with chronic thyroiditis revealed subclinical thyroidism, on the other hand a transient elevation in thyroid hormones and reduction in TSH level was noted the subacute granulomatous thyroiditis patients.

During present study Hashimoto's thyroiditis patients revealed presence of scant colloid with diffuse lymphoid infilteration, fibrosis, atrophy of follicular cells and oncocytic changes in some follicular cells, hurthal cell transformation. Hemorragic nacrosis, which is characterized by abundant hemosiderin- laden macrophages, was also noted. Nguyun *et al.,* (1996) reported presence of numerous lymphoid cells and sheets of hurthal cells with abundant, granular and eosinophilic cytoplasm and slightly or marked nuclear polymorphism in the smears of diagnostic cases. Multinucleated cells and hemosiderin-laden macrophages were noted only in one case. Handa *et al.,* (2008) reported lymphocytic infilteration destroying follicular epithelial cells, hurthal cell changes, lymphoid tangles, epithloid cells and multinucleated cells in patients with thyroiditis.

The FNAC of the lymphocytic thyroiditis patients were moderately cellular smears comprised of benign follicular epithelial cells admixed with an abundant polymorphous benign lymphoid infilterate in a colloidal and hemorrhagic background. Most of the lymphoid cells were lymphocytes and plasmacytes. Cabay and Salem (2008) noted a few groups of benign follicular cells scattered within an filteration of mature lymphocytes in smear of the aspiraes of a 21 year old woman presented with chronic lymphocytic thyroiditis. Aggregates of paravacuolar granules with degenerative and proliferative changes of the follicular cells infiltered by lymphocytes were visible in FNAC smears of almost all the patients with sub acute thyroiditis. The smears were highly cellular with scant colloid material in the background. The cell population mostly contains nacrotic follicular cells, neutrophils, fibroblasts, lymphocytes, macrophages and multinucleated giant cells. Shabb and Salti (2006) documented salient cytologic features included cellular smears, multinucleated giant cells in 100% of cases, some ingesting colloid or neutrophils, fibrous fragments with enmeshed inflammatory cells were a constant feature; follicular cells were scant to

absent in most cases. Granulomas were rare. Colloid, when present was thick, with central cracks and frayed edges.

ACKNOWLEDGEMENT
We thank the Pathology Department of Rajendra Prasad Medical College, Kangra, H.P., India for providing cytologic and histologic follow up and University Grant Commission, Govt. of India for providing financial assistance.

Conflict of Interest
We declare that we have no conflict of interest.

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