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THYROIDITIS: A DISEASE WITH MANY FACES

By

Mohamed R. Khalil[1], Mervat A. Hamza[2], Mohamed M. Moussa[1], Wessam M. Algendi[3], Mahmoud F. Sakr[1], Yasser M. Hamza[1], Hatem F. Alwagih[1]

[1]Departments of Surgery, [2]Pathology, and [3]Clinical Pathology, Faculty of Medicine, University of Alexandria, Egypt

Background: ***Diagnosis of thyroiditis is rather difficult since it can simulate any other thyroid disease. This study was conducted to determine the clinico-pathological features of thyroiditis and to evaluate the efficacy of the various modalities utilized for diagnosis of the disease.***

Patients and Methods: ***The study included 59 patients with the clinical diagnosis of thyroiditis. Ten patients had subacute thyroiditis (SAT) and 49 had chronic thyroiditis (CHT). Investigations included serum levels of T3, T4 and TSH, anti-chromosomal antibodies (AMA), anti-thyroglobulin antibodies (ATGA), Ultrasonography for the thyroid gland and FNAC. Twenty-four patients improved by conservative treatment while 35 needed thyroidectomy where histopathology for the excised glands confirmed the diagnosis of thyroiditis.***

Results: ***The mean age of patients with SAT was significantly lower than that of those with CHT (28.13±5.82 years vs 44.1±8.36 years, respectively) (t= 5.62, p=0.002). Seventy one percent of patients with CHT had concomitant autoimmune disease, and nine of the 10 patients with SAT had history of recent upper respiratory tract infection. There was an obvious tendency towards hypo-thyroidism associated with CHT and towards hyperthyroidism associated with SAT. Both AMA and ATGA were significantly higher in patients with CHT as compared to those with SAT (P<0.05). Hypoechoic sonographic pattern of the goiters formed the majority in both groups (33/49 and 8/10 for CHT and SAT respectively) (X^2=26.612, P<0.001). FNAC could diagnose 30 out of 49 cases of CHT with a sensitivity of 59.2% a specificity of 90%, a positive predictive value of 96.7% and a negative predictive value of 31%. It did not diagnose any of the ten SAT. Conclusions: Diagnosis of thyroiditis requires a high index of suspicion. A history of concomitant autoimmune disease could associate CHT. An upper respiratory tract infection may well precede a SAT. CHT is associated with a significant rise of AMA and ATGA. Hypoechoic sonographic pattern is found in a significant number of patients with thyroiditis. FNAC is specific yet insensitive test for the diagnosis of thyroiditis.***

Key Words: Thyroiditis, Hashimoto, De Quervain's, Riedel's.

INTRODUCTION

The term thyroiditis refers to infiltration of the thyroid gland by inflammatory cells, caused by a diverse group of inflammatory disorders.(1) The scheme, which reflects the current understanding of this disorder, was introduced by Singer.(2) It incorporates acute, subacute and chronic categories. Subacute disease includes granulomatous "De Quervain's" thyroiditis and silent or painless thyroiditis. The chronic group includes lymphocytic "Hashimoto's" thyroiditis and invasive fibrous "Riedel's" thyroiditis". Thyroiditis may mimic other thyroid diseases and may present with features compatible with one or more of the thyroiditis syndromes.(3) Recognition of the various thyroiditis syndromes, and in particular the various presentations that may be encountered as these diseases evolve, is essential for proper diagnosis and treatment.

The present study was conducted to determine the clinico-pathological features of the different syndromes of thyroiditis and to evaluate the efficacy of the various modalities utilized for diagnosis of the disease.

PATIENTS AND METHODS

Study Population

The present study included 59 patients with clinically suspicious thyroiditis, admitted to the Head and Neck Surgery Unit, Alexandria Main University Hospital, during 2001. There were 50(84.75%) women and 9(16.25%) men. Their ages ranged from 18 to 65 years, with a mean of 41.5±23.5 years. None of the patients had acute suppurative thyroiditis in the present series. Patients were categorized into two groups; those with chronic thyroiditis (n=49, group I) and those with subacute thyroiditis (n=10, group II) (Table 1). This diagnosis was confirmed by histopathology in the 35 patients who were operated upon. The remaining 24 patients improved clinically on medical treatment and did not have an operation.

Clinical Evaluation

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

Laboratory Tests

Laboratory tests included complete blood picture, liver function tests, and blood urea and serum creatinine; in addition to serum levels of T3, T4 and TSH (ELISA),[4] as well as anti-chromosomal antibodies (AMA) and anti-thyroglobulin antibodies (ATGA) (ELISA).[5]

Imaging Studies

Patients were also subjected to plain X-ray of the neck and ultrasonography of the thyroid gland. Lesions of the thyroid were divided by ultrasonography into dominantly hyper-echoic, dominantly hypo-echoic and mixed or hetero-echoic.

Pathological Investigations:

Preoperative fine needle aspiration cytology (FNAC) was done for all patients, and postoperative tissue examination of the excised specimen in patients operated upon (n =35).

RESULTS

The mean age of patients with subacute thyroiditis was significantly lower than that of those with chronic thyroiditis (28.13±5.82 years vs 44.1±8.36 years, respectively) (t= 5.62, p=0.002). Thirty-five (71.4%) of the 49 patients with chronic thyroiditis had concomitant autoimmune disease, and nine (90%) of the 10 patients with subacute thyroiditis had history of recent upper respiratory tract infection (Table 2). Thirty patients of the chronic group had a family history of autoimmune phenomenon, namely, diabetes mellitus (n=26) and vitilligo (n=4). Seven more patients had a family history of goiter the type of which was not pathologically proven. Twenty-seven (55.1%) patients of the chronic group had a bilateral nodular goiter, while four patients (40%) of the subacute group had a bilateral diffuse goiter.

There was a significant association between hypo-thyroidism and chronic thyroiditis and between hyperthyroidism and subacute thyroiditis (Table 3). Both AMA and ATGA were significantly higher in patients with chronic thyroiditis as compared to those with subacute thyroiditis (Table 4).

The ultrasonic pattern of the goiters of the both studied groups showed that hypo-echoic lesions formed the majority in both groups (33/49 and 8/10 in groups I and II, respectively). None of the lesions in patients with subacute thyroiditis was hyper-echoic. There was significant association between hypoechogenicity of the thyroid gland and thyroiditis (X^2 =26.612, P<0.001).

All the studied patients (n=59) were subjected to FNAC. This diagnosis was compared to histopathology in the 35 patients who were operated upon and to clinical diagnosis in the remaining 24 patients (Table 5). FNAC could diagnose 29 out of 48 cases of Hashimoto thyroiditis (Figs 1-3). It has therefore a sensitivity of 60.4% a specificity of 81.8% a positive predictive value of 93.5% and a negative predictive value of 32.1%. FNAC could not diagnose any of the ten patients with subacute thyroiditis.

Table 1: ***Frequency of thyroiditis syndromes in the present series (Singer's classification).***

Thyroiditis	***N***	***%***
Chronic Thyroiditis (Group I):		
- Hashimoto's disease.	48	81.35
- Riedle's thyroiditis.	1	1.70
Subacute Thyroiditis (Group II)		
- De Quervain's thyroiditis	9	15.25
- Painless (silent) thyroiditis.	1	1.70
Total	59	100

Table 2: ***Associated general diseases in the studied patients***

Associated Disease	*Group I (n=49) Chronic thyroiditis*	*Group II (n=10) Subacute thyroiditis*
- Upper respiratory tract infection	0	9
- Diabetes mellitus (DM)	13	0
- Rheumatoid arthritis (RA)	7	0
- RA + DM	5	0
- Rheumatic heart disease	6	0
- Vitilligo	4	0
- Total	35	9

Table 3:. ***Hormonal profile of the studied patients***

Laboratory test	*Normal range*	*Group I (n = 49)*	*Group II (n = 10)*	*t-test*
T3 (pg/dl)				
- Range	1.5 – 4.5	0.2 – 7.1	1.6 – 10.64	t = 3.26
- X ± SD		1.36 ± 1.92	4.72 ± 3.68	P = 0.043
T4 (µg/dl)				
- Range	4.5 – 12.5	2.8 – 16	7.5 – 16.8	t = 6.42
- X ± SD		6.31 ± 4.18	14.60 ± 3.61	P = 0.004
TSH.(µIU/ml)				
- Range	0.35 – 5.5	0.2 – 6.6	0.01 – 0.5	t = 5.88
- X ± SD		3.32 ± 1.48	0.14 ± 0.18	P = 0.003

Table 4:. ***Profile of antithyroid antibodies in the studied patients.***

Laboratory test	*Group I (n= 49)*	*Group II (n=10)*	*t-test*
AMA(IU/ml)			
- Range	120 – 3600	1.1 – 7.3	t = 3.44
- X ± SD	988.22 ± 917.30	29.66 ± 24.64	P = 0.006)
ATGA: (IU/ml)			
- Range	175 – 1220	0.44	t = 3.36
- X ± SD	694.2 ± 428.45	6.15 ± 9.31	P = 0.004

AMA = anti-chromosomal antibodies
Anti TG = Antithyroglobulin antibody

Table 5: ***the results of FNAC versus the final diagnosis***

Histopathology$	*N*	*FNAC*	*N*
Hashimoto thyroiditis	27	Hashimoto thyroiditis	19
		Proleferative follicular lesion	6
		Colloid goiter	2
Riedel's thyroiditis	1	Riedel's thyroiditis	1
De Quervain thyroiditis	6	Hashimoto thyroiditis	2
		Proleferative follicular lesion	2
		Colloid goiter	2
Silent thyroiditis	1	Hashimoto thyroiditis	1
Subtotal	35	Subtotal	35
Clinical Diagnosis*			
Hashimoto thyroiditis	21	Hashimoto thyroiditis	10
		Proliferative follicular lesion	5
		Colloid goiter	6
De Quervain thyroiditis	3	Hashimoto thyroiditis	1
		Proliferative follicular lesion	1
		Colloid goiter	1
Subtotal	24	Subtotal	24
Total	59		

$ Those are the 35 patients who had thyroidectomy.

* those are the 24 patients who did not require an operation.

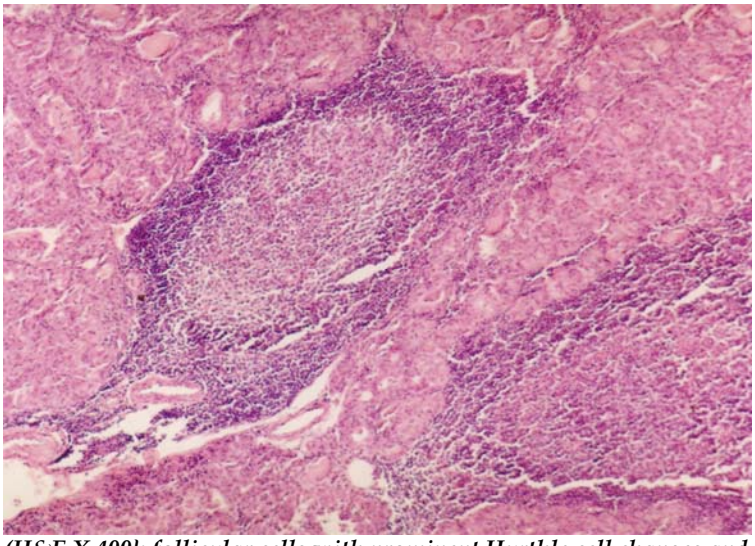

Figure 1*: A tissue section (H&E X 400}: follicular cells with prominent Hurthle cell changes and stromal lymphocytic infiltrate. Note also the tendency to form germinal center. A case of Hashimoto thyroiditis.*

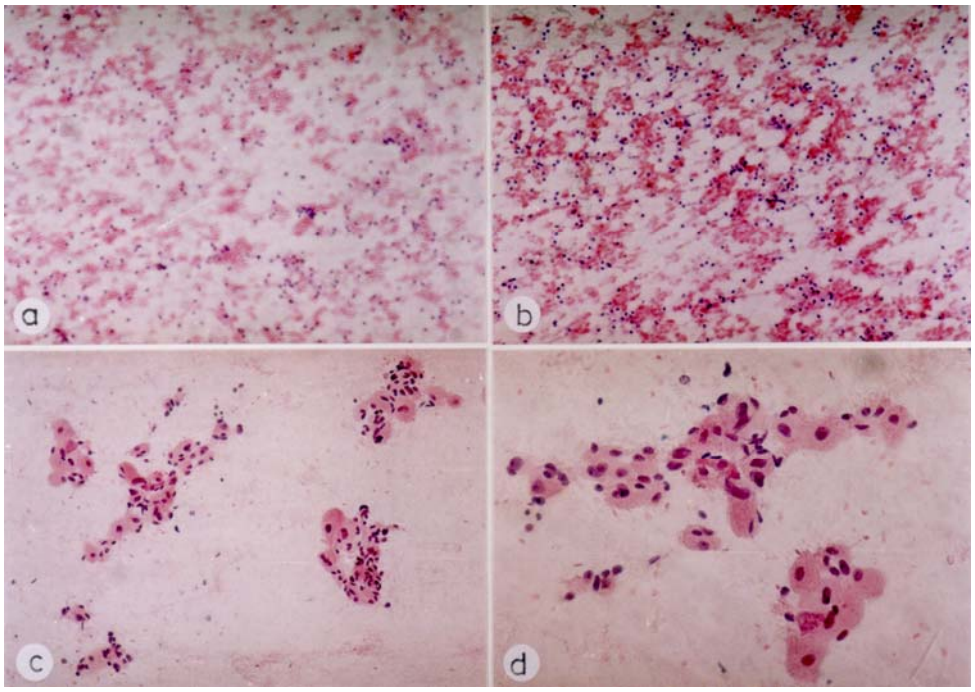

Figure 2:

Fig. (2a): FNAC with numerous scattered pleomorphic benign looking lymphocytes: Hashimoto thyroiditis. {H&E X 100)
Fig.(2b): A close up of the previous (H&E X 200)
Fig.(2c): Another field of the same patient. The clusters of follicular cells show Hurthle cell changes. (H&E X 200)
Fig.(2d): A close up of Figure 2a (H&E X 400)

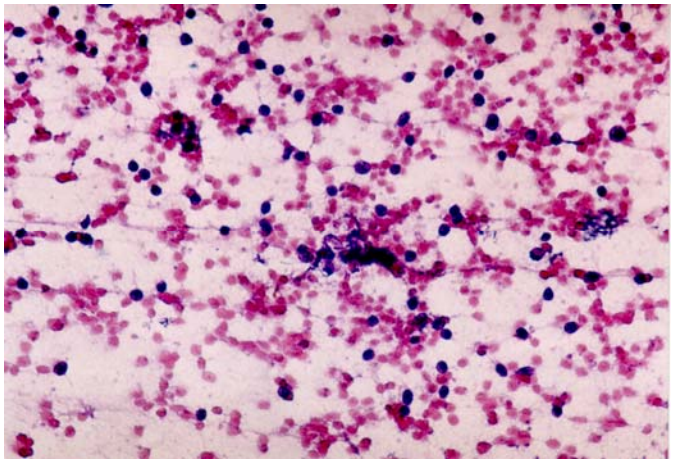

Figure 3: ***FNAC showing lymphocytic thyroiditis. Clusters of bland looking follicular epithelial cells. A background of lymphocytes is also noted.***

DISCUSSION

Thyroiditis syndromes comprise nearly all aspects of clinical thyroidology. It is, therefore, mandatory to have a high index of suspicion and to utilize all available clinical, laboratory and imaging facilities to reach a diagnosis. It deserves the effort since many thyroiditis patients could be saved unnecessary thyroid surgery.

It was noted in the current study that patients with subacute thyroiditis were significantly younger than those with chronic thyroiditis (t=5.62, p=0.002). Many authors reported similar finding. [1-,4,6-,8)]

In the present study, over two-thirds of patients with chronic thyroiditis (71.5%) had associated autoimmune disease. Moreover, 30 of them (61.2%) had a family history

of autoimmune disease. These observations, along with

similar findings by other authors[9] support the autoimmune origin theory for chronic thyroiditis. On the other hand, all studied patients with subacute granulomatous thyroiditis (SAGT) had a history of a recent attack of upper respiratory tract infection. This would support the hypothesis of viral etiology of SAGT. [10]

Patients with chronic thyroiditis showed subclinical hypothyroidism. The reduced gland function may be so subtle that special provocative tests are needed to elicit it. An accentuated increase in thyrotropin level in response to an intravenous injection of thyrotropin-releasing hormone is one of the sensitive indicators of early hypothyroidism.[11] On the other hand, a transient elevation in thyroid hormones and reduction in TSH level was noted in the early phase of SAGT, a finding which is well reported in the literature.[8,12,13]

In support to the clinical diagnosis, estimation of thyroid antibody level was considered a suitable tool. In the current study, AMA was detected in all patients with Hashimoto's thyroiditis. It was found in 70-90% of the patients in other studies.[14,15] ATGA could also be detected in all patients with chronic thyroiditis. This was not the case in other published reports.[15,16] They could detect the antibody in only 20-60% of their patients. This may be attributed to the difference in technique used for antibody detection. As would be expected, the sera of patients with SAGT did not contain antithyroid antibody. This observation is further supported by a similar report.[8]

Ultrasonography is not largely considered to be a conclusive diagnostic tool for thyroiditis. However, since it has been widely used lately for the imaging of goiters, researchers tried to identify sonographic patterns that would raise suspicion of the disease. In this study, ultrasonographic examination showed hypoechogenisity in 67.3% of patients with autoimmune thyroiditis and in 80% of those with SAGT with statistically significant association. Hypoechogenisity is generally agreed upon to raise suspicion of thyroiditis. It was reported to be found in 18–77% of patients with autoimmune thyroiditis[17,18] and in up to 100% of those with SAGT.[19]

Looking at the results of FNAC plotted against histopathology of the excised glands showed that this test is specific but not sensitive for the diagnosis of chronic thyroiditis. FNAC could not diagnose any of the ten patients with SAGT, and could diagnose only three cases of SAGT out of 31 in a similar study conducted by Ofner et al[20] who concluded that FNAC is not a reliable technique in the diagnosis of SAGT especially in its acute phase.

Based on the data presented it may be concluded that:

1. The mean age of patients with subacute thyroiditis is significantly lower than that of those with chronic thyroiditis,
2. Patients with chronic thyroiditis tend to have concomitant and/or family history of autoimmune disease, while those with subacute thyroiditis usually give a history of recent upper respiratory tract infection,
3. There is a tendency towards hypo-thyroidism associated with chronic thyroiditis and towards hyperthyroidism associated with subacute thyroiditis,
4. Both AMA and ATGA were significantly higher in patients with chronic thyroiditis compared to those with subacute thyroiditis,
5. Hypo-echoic ultrasonographic pattern is a significant predictive test for chronic thyroiditis,
6. FNAC is specific but not sensitive in diagnosing chronic thyroiditis.

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