Thyroperoxidase and Thyroid Autoimmunity

Thyroperoxydase et auto-immunité thyroïdienne

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Contents

Sommaire

INVESTIGATION OF THYROID AUTOIMMUNITY
EXPLORATION DE L'AUTO-IMMUNITÉ THYROÏDIENNE

Thyroperoxidase and Thyroid Autoimmunity. Ed. P. Carayon, J. Ruf. Colloque INSERM/John Libbey Eurotext Ltd. © 1990. Vol. 207, pp. 321-327

The value of ultrasonography in the detection of lymphocytic thyroiditis

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INTRODUCTION

Lymphocytic thyroiditis (LT) is believed to be a rare disease in Germany that is not well appreciated (13). The aim of this study was to evaluate different diagnostic procedures for the study of LT (10).

SUBJECTS and METHODS

The charts of 106 hospitalized and ambulatory patients with LT treated between January 1984 and December 1987 were reviewed. The diagnosis of LT was based on physical examination and confirmatory findings in at least two of the following four procedures: measurement of antimicrosomal antibodies [TPO(mic)]; TSH; ultrasonography (US) and fine needle aspiration cytology (FNA) of the thyroid. Only patients (n=92, 88 women, 4 men, age 11-81, mean age 47 yr) where all four diagnostic procedures were available, were included in the study.

Clinical manifestations were recorded; TPO(mic) was determined by immunofluorescence (20), TSH run in duplicate by a supersensitive luminescence immunoassay (24), T4 and T3 were measured using commercial kits (Henning Berlin, FRG). Thyroid size and morphology were investigated by ultrasound using SRT, linear Mhz 5, General Electric, Rancho Cordova, CA (9). Sonograms from population studies were used as controls (8). In addition both thyroid lobes were biopsied under sonographic control with a fine needle (od, 0.6-0.7mm). The smears were air dried and stained by the May-Grünwald-Giemsa technique for morphological evaluation.

RESULTS

Clinical manifestations

	PERCENT	n=92
NO SYMPTOMS	29.3	27
INCREASE IN WEIGHT	44.6	41
GOITRE	37.0	34
MENTAL COMPLAINTS	34.8	32
MYXEDEMA	23.9	22
PARAESTHESIA	19.6	18
FATIGUE	18.5	17
ARTHRALGIA	18.5	17
GLOBUS HYSTERICUS	17.4	16
EPIGASTRIC DISCOMFORT	15.2	14
ANAEMIA	11.9	11
DYSPHAGIA	8.7	8
HYPERCHOLESTEROLEMIA	6.5	6
THYROTOXICOSIS	6.5	6

TPO(mic)
In 12 (13%) patients TPO(mic) were undetectable. TPO(mic) titers of 1:32 were found in 5 (5.4%), 1:100 in 11 (12%), 1:320 in 19 (20.7%), 1:1000 in 31 (33.7%) and >1:1000 in 14 (15.2%) patients respectively. The frequency distribution is shifted towards higher titers.

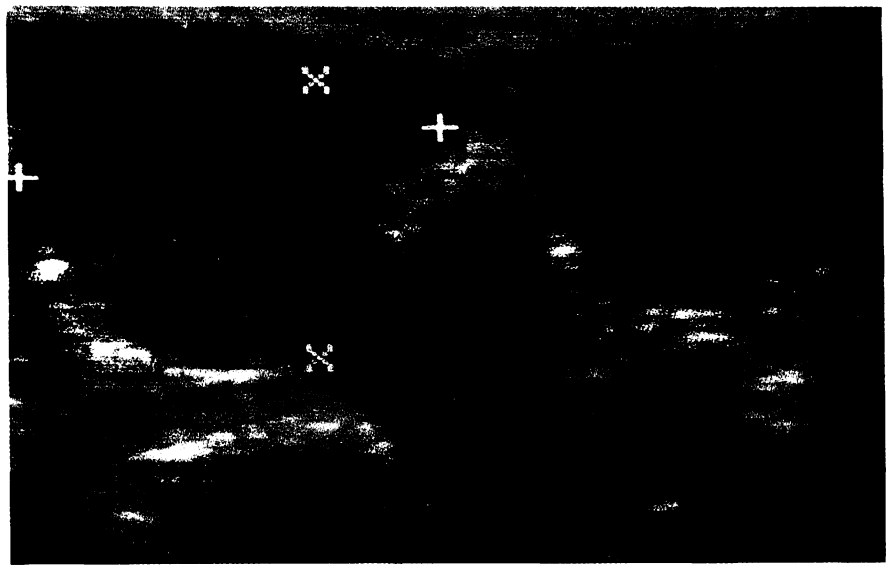
TSH
In 4 patients (4.3%) TSH serum levels were <0.3 µU/ml (normal range 0.3-3.9). Three of those patients had elevated T3, but only one of those three had an elevated serum T4 level. Forty-one (44.6%) patients had TSH levels 0.3-3.9, 26 (28.3%) 4-20, 14 (15.2%) >20 - 50, and 7 (7.6%) >50 µU/ml.

Ultrasonography
Thyroid volume: 43 (48.9%) women had normal thyroid volume (<18ml, range 3-17.8, mean 12), and 45 (51.1.%) had enlarged glands (range 18.2- >140, mean 35.3). The four men had thyroid volume (normal >25ml) of 8, 23, 27 and 64 ml.
Echopatterns: all except 5 (5.4%) patients had scattered sonolucent echopatterns. In 13 (14%) patients solid nodules were detected. (Fig. 1 A and B).

Figure 1. Transverse sonograms of the thyroid (T):

A. normal echopattern compared to the sonolucent muscles (M) from a healthy person.

B. sonolucent echopattern from a patient with LT.



Cytology
Thirty (32.6%) patients had hypercellular smears; 54 (58.7%) smears presented a scanty to moderate overall cellularity; and 8 (8.7%) smears showed sparse lymphocytes and were not diagnostic for LT alone.

Correlations
There were no correlations between the cellularity of the smear, thyroid function and/or the TPO(mic) titer.

DISCUSSION

As in previous studies (2, 12, 17, 18) we also found great clinical variation. A quarter of the patients had no complaints or physical findings. Many symptoms were nonspecific and subject to the individual bias of the physician.
Determination of serum TPO(mic) is not always conclusive for the diagnosis of LT. In this study TPO(mic) were absent in 13% and low in 17.4% (<1:320), generally considered as negative (1). More than thirteen percent of all cases would have been missed without ultrasound and/or FNA. On the other hand, in 2 - 20% of the healthy population TPO(mic) can be found without apparent thyroid disease (1, 3 - 5, 7, 11, 21, 22); in our area 3% (20). Our data clearly support the assumption, that serum findings only incompletely reflect thyroid status.
Thyroid function is poorly related to LT (2, 3, 12, 17, 18). The prevalence of hypothyroidism underestimates the prevalence of LT. Since TSH and TPO(mic) titers are poorly correlated, the sensitivity of the combination of elevated TSH and detectable TPO(mic) for detection of LT in population studies must be even lower.
Scintiscanning is impractical and rather unreliable as a diagnostic tool for LT, since the uptake of radionuclides depends on thyroid function as well as the iodine content of the gland (13).
Although ultrasound does not differentiate between LT and Graves' disease (6, 15, 19, 23), it surely is a useful tool for screening in unselected groups. If a selected population of patients with thyroid diseases is considered, the specificity of ultrasound alone for detecting LT must be low, since this group will contain many patients with Graves' disease. However the combination of ultrasound and clinical evaluation will result in a high specificity even in a selected group.
FNA has a high diagnostic accuracy. Interpretation of the varying amounts of lymphocytes is however difficult (14). These findings could either indicate different LT diseases or merely reflect various inflammatory stages. If only one lobe is aspirated LT may be confused with focal lymphocytic reactions, which are common in endemic goitres (16). Only in rare instances can lymphocytes be found in focal sonolucent or solid alterations. To confirm the diagnosis of LT, FNA from one site probably suffices, if the scan is homogeneously sonolucent. Otherwise both lobes have to be aspirated.
In conclusion, this study confirms that sonography combined with clinical evaluation is rather specific for LT. Ultrasound additionally provides information about the size, topography and the nodularity of the thyroid. In cases where ultrasound is performed primarily, one can proceed to further examinations. Otherwise, it can support the laboratory and/or clinical findings that suggest

LT. When clinical features are inconclusive LT can only be confirmed by appropriate combination of serological and morphological tests. These conclusions have to be confirmed in a prospective study.

SUMMARY

The value of ultrasound (US) compared to established diagnostic procedures was investigated by retrospectively reviewing medical records of 92 patients (88 women and 4 men, age 11-81 yr, mean age 47 yr) with lymphocytic thyroiditis (LT). Clinical manifestations of the disease, serum antimicrosomal antibodies and TSH were determined in all patients. The thyroid was examined by US. Both lobes were aspirated by a fine needle under sonographic control and smears examined cytologically. A total of 27 (29.3%) patients had no clinical symptoms. TPO(mic) were undetectable in 12 (13%) patients, 16 (17.4%) had low titers 1:32-1:100, and 64 (69.6%) ≥1:320. TSH (normal range 0.3-3.9 μU/ml) was <0.3 in 4 (4,3%), 0.3-3.9 in 41 (44.6%), 4-20 in 26 (28.3%), and >20 in 21 (22.8%) cases. US revealed a scattered sonolucent echo in 87 (94.6%) patients, and in 45 (48.9%) a normal thyroid volume (women <18, men <25 ml). Cytology was diagnostic in 84 (91.3%) patients.
In conclusion, US can suggest LT. If TPO(mic) are undetectable or TPO(mic) titers are not significant and/or clinical symptoms are uncertain, fine needle aspiration (FNA) can confirm the sonographic finding. LT can only be confirmed by appropriate combination of serological and morphological tests. Finally, LT si obviously be more common in iodine deficient areas than generally assumed.

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Résumé

Une étude rétrospective des dossiers médicaux de 92 patients (88 femmes et 4 hommes, âgés de 11 à 81 ans, moyenne d'âge: 47 ans), présentant une thyroïdite lymphocytaire (LT) a permis une comparaison entre le diagnostic établi par ultrasons (US) et un diagnostic établi par des méthodes habituelles. Les manifestations cliniques de la maladie, les anticorps anti-microsomiaux sériques et la TSH ont été évaluées chez tous les patients. Des prélèvements par aiguille fine sous contrôle échographique ont été effectués sur les lobes, et un examen cytologique a été effectué sur les prélèvements. Un total de 27 patients (29.3%) ne présentaient aucun aucun symptome clinique. La TPO n'était pas décelable chez 12 patients (13%), 16, (17.4%) présentaient une concentration basse de TPO 1:32 - 1:100, et 64 (69.6%) un taux > 1/320. La TSH (zone normale 0.3 - 3.9 uU/ml) était < 0.3 dans 4 cas (4.3%), 0.3 - 3.9 dans 41 cas (44.6%), 4 - 20 dans 26 cas (28.3%), et > 20 dans 21 cas (22.8%. Les US ont révélé une réponse positive diffuse chez 88 patients (94.6%) et un volume thyroïdien normal chez 45 sujets (48.9%) (femmes <18, hommes <25ml). Chez 84 patients (91.3%), le diagnostic a pu être confirmé par un examen cytologique. En conclusion, les US laissent supposer une thyroïdite lymphocytaire. Si les anticorps anti-TPO sont indétectables ou présentent des titres non significatifs et/ou si les symptômes cliniques sont incertains, une aspiration par aiguille fine peut confirmer les résultats échographiques. Les thyroïdites lymphocytaires peuvent seulement être confirmées par une combinaison appropriée de tests sérologiques et morphologiques. En conclusion, les thyroïdites lymphocytaires sont plus répandues dans les zones déficientes en iode qu'on ne l'a généralement supposé.