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Ultrasonography related to clinical and laboratory findings in lymphocytic thyroiditis

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Abstract. The value of ultrasonography compared with established diagnostic procedures was investigated by reviewing medical records of 92 patients (88 women and 4 men, age 11–81 years, mean age 47) with lymphocytic thyroiditis. Clinical manifestations of the disease and serum antimicrosomal antibodies and TSH were determined in all patients. The thyroid was examined by ultrasound. 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. Antimicrosomal antibodies were undetectable in 12 (13%) patients, 16 (17.4%) had low titres 1:32–1:100, and 64 (69.6%) ≥ 1:320. TSH (reference values 0.3–3.9 mU/l) 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%) patients. Ultrasound 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 alone was diagnostic in 84 (91.3%) patients. In conclusion, ultrasound can suggest lymphocytic thyroiditis. If antimicrosomal antibodies are undetectable or titres are not significant and/or clinical symptoms are uncertain, fine-needle aspiration can confirm the sonographic finding. Epidemiological studies including ultrasonography are necessary to obtain reliable data on the prevalence of lymphocytic thyroiditis.

In Germany, lymphocytic thyroiditis (LT) is believed to be a rare disease that is not well recognized (1). LT often causes uncertainty for both patient and physician, because little is known about its importance and impact upon the patient's health status throughout life. Reports from countries where iodine ingestion is high or where iodine prophylaxis has been introduced suggest an increasing incidence of LT (2–5). These data have caused alarming controversies concerning iodine supplementation in endemic goitre areas. The aim of this study was to evaluate different diagnostic procedures for the study of LT.

Subjects and Methods

We reviewed the charts of all ambulatory and hospitalized patients (N = 106) from the department of internal medicine, where LT was suspected by fine needle aspiration cytology (FNA) between January 1984 and December 1987. The study included only patients (N = 92, 88 women, 4 men, age 11–81 years, mean age 47) where the following four diagnostic procedures were available: 1. measurement of antimicrosomal antibodies (Mi-ab); 2. TSH; 3. ultrasonography and 4. FNA of the thyroid. Frequently patients were discovered prior to diagnostic (iodine-containing contrast media) or therapeutic (amiodarone) procedures where thyroid disorders had to be excluded, or by inadvertently testing the thyroid.

Clinical manifestations were recorded; Mi-ab was determined by immunofluorescence (6); TSH was run in duplicate by a supersensitive luminescence immunoassay from Henning, Berlin, FRG (7); T_4 and T_3 were measured using commercial kits (Henning). Thyroid morphology was investigated by ultrasound (SRT, linear MHz 5, General Electric, Rancho Cordova, CA). The echopatterns, focal or scattered, were classified according to their echogenity in normal, solid, no echo, sonolucent and echocomplex, the sonolucent muscles serving as

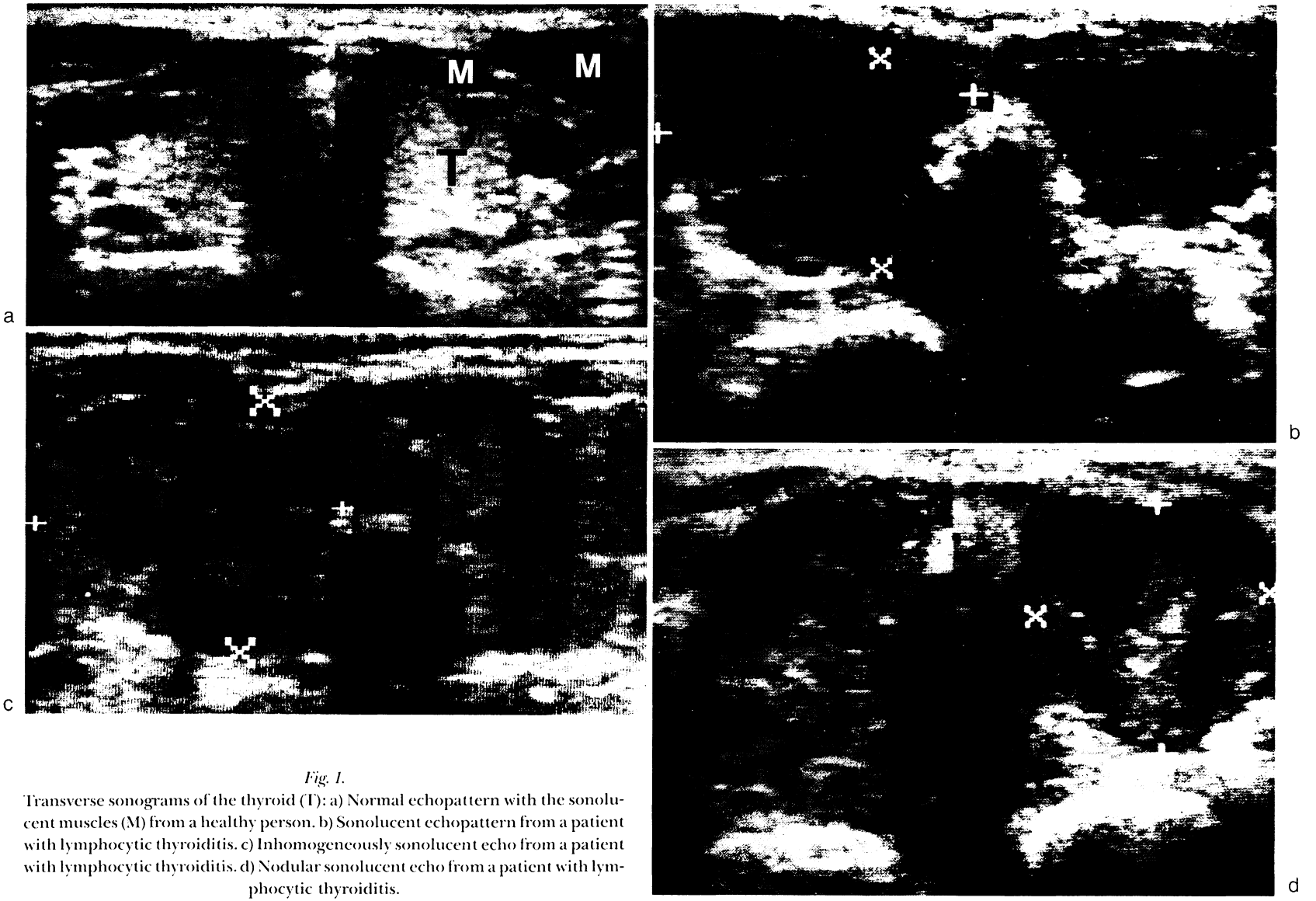

Fig. 1.
Transverse sonograms of the thyroid (T): a) Normal echopattern with the sonolucent muscles (M) from a healthy person. b) Sonolucent echopattern from a patient with lymphocytic thyroiditis. c) Inhomogeneously sonolucent echo from a patient with lymphocytic thyroiditis. d) Nodular sonolucent echo from a patient with lymphocytic thyroiditis.

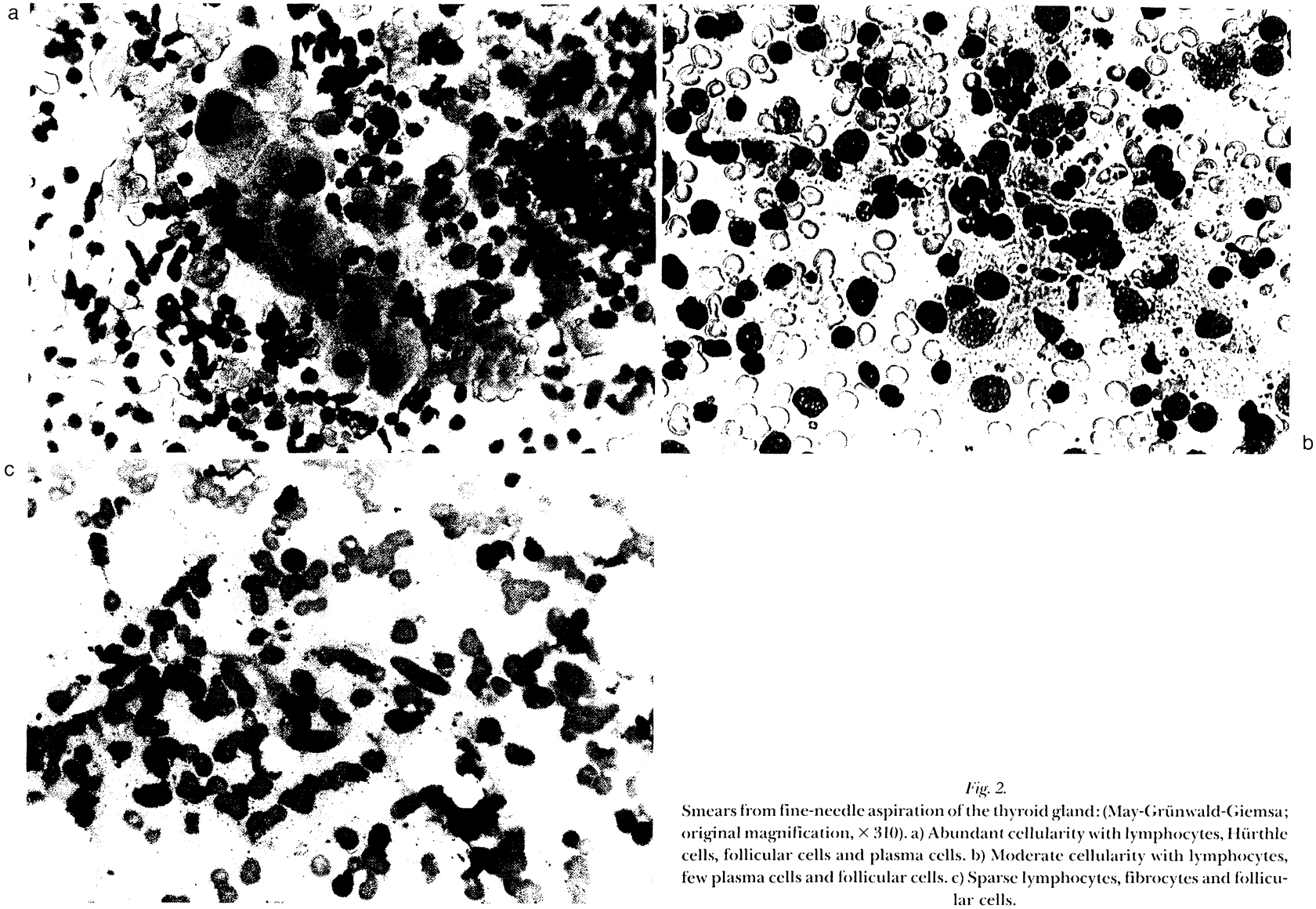

Fig. 2.
Smears from fine-needle aspiration of the thyroid gland: (May-Grünwald-Giemsa; original magnification, × 310). a) Abundant cellularity with lymphocytes, Hürthle cells, follicular cells and plasma cells. b) Moderate cellularity with lymphocytes, few plasma cells and follicular cells. c) Sparse lymphocytes, fibrocytes and follicular cells.

the reference echo (8), Fig. 1a. Thyroid volume was calculated as the sum of the products of maximal thickness, width, length and a corrective factor, 0.479, for each lobe (8). Sonograms from population studies were used as controls (9). In addition, both thyroid lobes were biopsied under sonographic control with a fine needle (outer diameter 0.6–0.7 mm). The smears were air-dried and stained by the May-Grünwald-Giemsa technique for morphological evaluation.

Results

Clinical manifestations

The clinical presentation varied widely. Twenty-seven (29.3%) patients had no typical symptoms for thyroid disease; 41 (44.6%) patients observed an increase in weight; 34 (37%) had palpable goitres; 32 (34.8%) reported unspecific mental complaints, and 22 patients had (23.9%) myxedema.

TM-ab

In 12 (13%) patients Mi-ab were undetectable. Mi-ab titres 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 shifted towards higher titres.

TSH

In 4 patients (4.3%), TSH serum levels were < 0.3 mU/l (reference values 0.3–3.9). Three of those patients had elevated T_3, but only one of those 3 had an elevated serum T_4 level. Forty-one (44.6%) patients had TSH levels between 0.3–3.9, 26 (28.3%) between 4–20, 14 (15.2%) > 20–50, and 7 (7.6%) > 50 mU/l.

Ultrasonography

Thyroid volume. Forty-three (48.9%) women had normal thyroid volume (< 18 ml, range 3–17.8, mean 12), and 45 (51.1%) had enlarged glands (range 18.2–> 140, mean 35.3). The 4 men had a thyroid volume (normal < 25 ml) of 8, 23, 27 and 64 ml. Two of them were considered enlarged.

Echopatterns. All except 5 (5.4%) patients had scattered sonolucent echopatterns. In 13 (14%) patients solid nodules were detected (Fig. 1a-d).

Cytology

The smears were graded according to the amount of lymphocytes: abundant, moderate, sparse (Fig. 2a-c).

Abundant. The smears of 30 (32.6%) patients were hypercellular showing a vast number of mature lymphocytes in small clusters or dispersed with scattered clusters of Hürthle cells, normal or hypertrophic follicular cells, some plasma cells, and sometimes a few multinucleated giant cells.

Moderate. Fifty-four (58.7%) smears presented a scanty to moderate overall cellularity with scattered lymphocytes, some plasma cells, few follicular cells, hardly any or no Hürthle cells.

Sparse. Eight (8.7%) smears were not diagnostic for LT alone. However, sparse lymphocytes, sometimes fibrocytes scattered between rare follicular cells suggested LT. Laboratory and sonographic findings could confirm the diagnostic.

Correlations

Cytology-TSH. There was no correlation between the cellularity of the smear and thyroid function.

Cytology-Mi-ab. The Mi-ab titres show no correlation to the cellularity in cytology.

Mi-ab-TSH. There was no correlation between Mi-ab titres and thyroid function.

Negative sonography versus Mi-ab, TSH, and cytology. Five (5.4%) patients, all females, had normal sonographic echopatterns. In 2 of them thyroid volume was enlarged. Mi-ab were detectable in all 5 patients, 1:320 in 2 and 1:1000 in the other 3. TSH was normal in 2 patients, 3 had elevated serum levels. Cytology was diagnostic in all cases, 2 revealing abundant cellularity and 3 showing moderate cellularity.

Discussion

In our understanding there are at least five hazards in detecting LT and in establishing reliable epidemiological data.

1. Definition of LT. It is unclear whether silent thyroiditis, painless thyroiditis, post partum thyroiditis, Hahimoto's disease, and lymphocytic infiltrates either focal or those occurring within and about papillary carcinoma belong to one consistent entity of autoimmune origin.

2. Clinical manifestation. As shown in previous

studies (10–13) 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.

3. Determination of serum Mi-ab is not always conclusive for the diagnosis of LT. In this study, Mi-ab were absent in 13% and low in 17.4% (<320, generally considered as negative, 14). More than 13% of all cases would have been missed without ultrasound and/or FNA. On the other hand, in 2–20% of the healthy population TM-ab can be found without apparent thyroid disease (14–19). Our data clearly sustain the assumption that serum findings only incompletely reflect thyroid status.

4. Thyroid function is poorly related to LT (10–13,19). The prevalence of hypothyroidism in elderly people based on elevated TSH serum levels varies between 0.5–6% (20,21). Little is known about the cause and the severity of their clinical symptoms. Since subtotal thyroidectomies are frequently performed in endemic goitre areas, some cases of myxedema must be due to insufficient hormone replacement therapy. On the other hand, half the patients in this study were euthyroid. Thus, the prevalence of hypothyroidism probably underestimates the prevalence of LT. Since TSH and Mi-ab titres are poorly correlated, the sensitivity of the combination of elevated TSH and detectable Mi-ab for detection of LT in population studies must be even lower.

5. Imaging techniques. a. Scintiscanning has been used as a diagnostic tool for LT. However, the uptake of radionuclides depends on thyroid function as well as the iodine content of the gland (1,22). Furthermore, scintigraphy is impractical for screening end epidemiological studies. b. Though a diffusely sonolucent echo pattern of the thyroid is associated with LT and Graves' disease (2–25), clinical evaluation will in most cases provide the final diagnosis. The specificity of ultrasound is difficult to calculate from the scarce data available. Furthermore, the specificity depends on the population in which the test is being evaluated. In a population of unselected factory workers, we found a scattered sonolucent echo pattern in 2.5% (9). These 2.5% include an unknown number of subjects with LT. Owing to the high sensitivity (94.6%) of ultrasound demonstrated in the present study, the 97.5% of the population without sonolucent pattern can only include a very marginal fraction of LT patients. Thus we can conclude in this kind of population that the specificity of ultrasound alone exceeds 95%. Although the test does not differentiate between LT and Graves' disease, it surely is a useful tool for screening in unselected groups. If we consider a selected population of patients with thyroid diseases, the specificity of ultrasound alone for detecting LT must be low, since this group will contain many patients with Graves' disease. Again, clinical manifestations will allow further differentiation. Thus, combination of ultrasound and clinical evaluation will result in high specificity even in a selected group.

FNA has a high diagnostic value and accuracy (26). Only in exceptional cases does the cytological distinction between LT and the rare lymphoma of the thyroid cause problems (27). Interpretation of the varying amounts of lymphocytes is, however, difficult. These findings could either indicate different LT diseases or merely reflect various inflammatory stages. If only one lobe is aspirated LT can be confused with focal lymphocytic reactions, which are common in endemic goitres (5). Only in rare instances can lymphocytes be found in focal sonolucent or solid alterations. To confirm the diagnosis of LT, FNA from one site suffices, if the scan is homogeneously sonolucent. Otherwise both lobes have to be aspirated, preferably under sonographic control.

The present study cannot provide epidemiological data on the prevalence of LT. Whether its increased recognition is related to improved recognition rather than a true rise in incidence remains unclear. However, the number of missed LT cases owing to undectable Mi-ab, normal TSH, and sonography where FNA was not justified, suggests that LT must be far more common than generally assumed (1).

In conclusion, this study confirms that sonography combined with clinical evaluation is rather specific for LT. When compared with Mi-ab determination, ultrasound additionally provides information about the size, topography and the nodularity of the thyroid, which is crucial in goitre endemic areas. Sonography is safe, repeatable, inexpensive, time-saving and moreover practical for epidemiological studies. In patients where ultrasound is performed primarily, it can proceed to further examinations. Otherwise, it can support the laboratory and/or clinical findings that suggest

LT. Sonography should be used as a rapid preliminary screen in patients where LT is suspected as well as in epidemiological studies. When clinical features are inconclusive, LT can only be confirmed by appropriate combination of serological and morphological test. Finally, LT must be more common in iodine-deficient areas than generally assumed.

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