Association of Autoimmune Thyroiditis and Systemic Lupus Erythematosus

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Abstract
This study was designed to investigate the relationship between Systemic Lupus Erythematosus (SLE) and autoimmune thyroiditis disease. Forty one SLE patients diagnosed by latex agglutination test with twenty age and sex matched controls were included in this study. Results revealed that twenty one (51%) of SLE patients had antithyroglobuline antibody and ten of the SLE had elevated TSH. These results suggests that there was an association between SLE and autoimmune thyroiditis.

Keywords: Systemic lupus erythematosus, Thyroiditis, Hypothyroidism, Thyroglobulin antibodies.

Introduction
Hashimoto's thyroiditis is an organ specific autoimmune disease. In this disorder, there is a specific lesion in the thyroid associated with infiltration of mononuclear cells and damage to follicular cells. Antibody of thyroid constituents can be demonstrated in nearly all cases. It is an inflammatory disorder of unknown cause, which results in progressive destruction of the thyroid gland. Found mostly in the middle aged and elderly, it also occur in other groups, including children in whom it may cause goiter. A thyroid gland is made up of a series of saclike follicles lined with cuboidal epithelium. Within the follicles is found homogeneously stained colloid, the principal of constituent of which is a glycoprotein. This high molecular weight protein (about 650,000). Thyroid autoimmune diseases are associated with the occurrence of differentiated autoantibodies and are thought to be related to a genetic pre-disposition. These autoantibodies are directed against membrane-located and/or extracellular antigens of the thyroid cells: thyroglobuline, microsomal antigen, TSH receptors and colloid antigen. An association between thyroid and rheumatic disorders has been known for over a century and is of three types. Hypothyroidism or thyrotoxicosis may produce a variety of musculoskeletal symptoms, drug treatment of thyrotoxicosis is occasionally followed by rheumatological sequelae and lastly there may be an association between organ-specific autoimmune thyroid diseases and non-organ-specific rheumatological disorders. Recognized associations with thyroiditis include Sjogren's syndrome and giant cell arteritis. A clinical association of Hashimoto's thyroiditis with (SLE) has been suspected for some time and is supported by the finding of a positive antinuclear factor (ANF) in 13% of Hashimoto patients. One of the 40 patients in the last quoted study had clinically-apparent SLE. Moreover, 28% of patients with juvenile autoimmune thyroiditis also had a positive ANF. However, others have found only an equivocal association between autoimmune thyroiditis and SLE. This lack of association has also been suggested by others on theoretical grounds. Links between various autoimmune diseases have been regarded as an overlap of a general autoimmune diathesis, associations being increasingly likely when the conditions are close together in the organ-specific to non-organ specific disease spectrum. For diseases at the opposite ends of the spectrum, such as thyroiditis and SLE, overlap should be extremely unusual and it has been claimed that the cases reported in which the two conditions occur together are highly selected because of this rarity.

Materials and Methods

Patients
Blood samples were collected from 41 randomly selected patients with SLE 2 male, 39 female; mean age (±SD), 36 (±10) and compared with 20 age- and sex-matched controls aspirated from hospital staff. All patients with SLE diagnosed by criteria for the diagnosis of SLE.

Anti thyroglobulin Antibody (anti-TG)
Were assayed by ELISA method Biomeghrib (Tunisia) diagnostics that is based on double antibody sandwich technique, Table (1) show cut off values of anti-TG.
The patients were admitted to Monther Mustafa, Al-Fanar Clinical Laboratories and Rheumatology Department in Baghdad Teaching Hospital. Each blood sample obtained in plain tube at room temperature, centrifuged as soon as possible at 3000 rpm. for 45 min. and the sera were stored at -20 °C until used in the assay.

<table>
<thead>
<tr>
<th>Normal values of anti-TG.</th>
<th>Anti-TG (IU/ml)</th>
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<tr>
<td>Normal</td>
<td>&lt;100</td>
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<td>Border line</td>
<td>100-150</td>
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<td>Elevated</td>
<td>&gt;150</td>
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Results

Age Distribution: In our study, the mean age of clinically autoimmune thyroiditis in SLE patients was 50 years Fig.(1).

Anti-TG Antibody

The distribution of anti-TG amongst patients is shown in (Fig.(2)). Overall, 21 (51%) of the SLE patients had anti-TG whereas no healthy subject had a positive results for anti-TG antibody or ANF.

TSH levels

None of the patients or controls had TSH values in the hyperthyroid range. All control group have a normal value TSH level, while SLE patients had levels (6-25 mU/L), 10(24%) of the SLE patients had TSH levels above the upper limit of the normal reference range (0.5-5mU/L). All eight of SLE patients with elevated TSH levels had anti-TG antibody. Two SLE subjects with elevated TSH levels (6.0 and 6.8 mU/L) had neither antibody. Fig.(3).

Discussion

In this study we have examined the prevalence of thyroid antibodies in patients with SLE compared to age- and sex-matched controls. In our study, the mean age of the clinically autoimmune thyroiditis in SLE patients was 50 years, Fig.(1) others [14] the mean age was 53.6 yr. These results strengthen the hypothesis of slow universal progression of the autoimmune process[15]This model suggests a ‘disease pyramid’ in autoimmune thyroiditis, in which patients progress from mild thyroiditis to clinical disease over time. The half-time for progression from mild thyroiditis to clinical disease is estimated to be 80 years [15]. SLE may accelerate progression up this disease pyramid.

These antibodies were associated with unsuspected thyroid failure (as marked by elevation of TSH) in 24% of this randomly selected group of SLE patients, our results agree with Chan[14], Kausman[16] and Viggiano[17] their results were 23.2%, 21% and 23% respectively, while Appenzeller et.al[18] observed 6.1% symptomatic autoimmune thyroiditis of SLE patients and 17% positive
thyroid autoantibodies in the absence of thyroid disease. Pyne and Isenberg\textsuperscript{19} the presence of anti Tg antibody was 41% in patients of SLE. It is established that thyroid antibodies correlate strongly with lymphocytic thyroiditis and, in the absence of any clinical or biochemical change, the presence of these antibodies is nonetheless likely to reflect morphological changes within the thyroid\textsuperscript{20}. Two of the SLE patients had modestly elevated TSH levels without detectable Tg antibody. This could be the result of spontaneous fluctuations in TSH\textsuperscript{21}, thyroiditis in the absence of Tg.

Antibody\textsuperscript{20} reflecting another type of thyroid autoimmunity\textsuperscript{22}. 

Another uncontrolled prospective study found thyrotoxicosis or hypothyroidism in 12 (3.8%) of 319 SLE patients and nine of these patients had Tg or Mic antibodies\textsuperscript{23}. The reason for this association between SLE and thyroiditis is not clear. It may represent an overlap of some general tendency towards autoimmunity, although this would not fit into the concept of an organ-specific/non-organ-specific spectrum\textsuperscript{12}. A similar genetic predisposition may be implicated, since SLE and autoimmune atrophic (but not Hashimoto's) thyroiditis are associated with HLA-DR\textsuperscript{24,25}. Thyroid function and Thyroid antibodies tests should be performed as part of the biochemical and immunological profile in SLE patients. Those who are at high risk (female, raised TSH, positive thyroid Ab) should have thyroid function follow-up and should be given appropriate treatment in due course. As thyroid serology follows a fluctuating course, often dependent on disease activity, follow-up of larger numbers of SLE patients with age- and sex-matched controls would be of interest\textsuperscript{14}. 

In conclusion, these results from a controlled study support an association between SLE and autoimmune thyroiditis and indicate that many patients with SLE have minor hypothyroidism, which in some will progress to overt thyroid failure\textsuperscript{16}. Recognition of this may be of clinical importance.

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References