CONCISE REPORT

Autoimmune thyroid disease in systemic lupus erythematosus

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Ann Rheum Dis 2002;61:70–72

Background: The reported prevalence of autoimmune thyroid disease (3.9–24%) and antithyroid antibodies (11–51%) in SLE varies considerably. Early reports were mainly based on short term studies of small cohorts.

Objective: To report the prevalence of autoimmune thyroid disease and thyroid antibodies in 300 patients with SLE, followed up at our centre between 1978 and 2000, by a retrospective analysis of case notes.

Results: The prevalence (5.7%) of hypothyroidism in our cohort was higher than in the normal population (1%), while that of hyperthyroidism (1.7%) was not significantly different. Overall 42/300 (14%) of our cohort had thyroid antibodies, rising to 15/22 (68%) in the subgroup who also had thyroid disease ($p < 0.001$). Both antimicrosomal and antithyroglobulin antibodies were detected. The antibodies were found in equally high frequency in the hyperthyroid subgroup (80% patients), whereas in the hypothyroid subgroup antimicrosomal antibodies were more frequent than antithyroglobulin antibodies (64% v 41%). There was no significant difference in the frequency with which antimicrosomal or antithyroglobulin antibodies were detected between the hyperthyroid and hypothyroid subgroups ($p > 0.2$).

Conclusion: Our patients with SLE had a prevalence of hypothyroidism, but not hyperthyroidism, greater than that of the normal population. The presence of either condition was associated with a higher frequency of both antimicrosomal and antithyroglobulin antibodies.

Autoimmune thyroid disease, marked by the presence of antibodies directed against thyroid antigens, has been associated with a number of non-organ-specific rheumatological disorders. These associations include systemic lupus erythematosus (SLE),^{1–5} Sjögren's syndrome,^{6,7} and giant cell arteritis.⁸ A number of studies have suggested that thyroid disease is more common in SLE than in the general population, but there is disagreement as to whether both hypothyroidism and hyperthyroidism are more common^{1,2,4} or whether this finding is restricted to hypothyroidism alone.⁹ Both antithyroglobulin and antimicrosomal antibodies have been found with greater frequency in SLE than in the general population, even in lupus patients who do not have clinical thyroid disease.^{9,10} It is still a subject of discussion as to whether SLE is an independent risk factor for these thyroid abnormalities or whether this is a coincidental finding because the group most at risk for SLE, young to middle aged women, is precisely the same group most at risk for autoimmune thyroid disease.¹¹

In the main, earlier studies reporting the prevalence of thyroid antibodies and clinical thyroid disease in patients with SLE were based on relatively small cohorts of patients. As a result the reported prevalence (3.9–24%)¹² of both clinical thyroid disease in SLE and the frequency (11–51%)^{11,12} of antithy-

roid antibodies in SLE have varied widely depending on the study cited. Here we report the prevalence of both hyperthyroid and hypothyroid disease in a group of 300 patients with SLE with follow up periods of up to 22 years at a single centre. We also report the prevalence of antithyroid microsomal and antithyroglobulin antibodies in this cohort.

PATIENTS AND METHODS

Clinical records and laboratory data on patients with SLE have been maintained at the Middlesex Hospital since January 1978. All these patients satisfy the American Rheumatism Association's revised criteria for SLE published in 1982.¹³ The overwhelming majority (>85%) of patients seen between January 1978 and July 2000 had thyroid serology performed at or shortly after the diagnosis of SLE and then intermittently every two to four years thereafter. A small number of patients with SLE had been looked after elsewhere before referral to our unit; in these cases thyroid serology was initially performed at the time of referral. Thyroid serology was performed by haemagglutination (Wellcome) before 1984, and by particle agglutination (Fujirebio) from 1984 onwards. Thyroid stimulating hormone (TSH) levels were measured by radioimmunoassay (NETRIA, normal range 0.5–5.0 mU/l) before 1985, by immunoradiometric assay (NETRIA, normal range 0.5–5.0 mU/l) from 1985 until June 1993, and by micro-peptide enhanced enzyme immunoassay (Abbot IMX, normal range 0.3–5.0 mU/l) from June 1993 onwards.

Clinical records of these patients were studied retrospectively. χ^2 Tests were used to analyse the association between the presence of thyroid antibodies and clinical thyroid disease. The χ^2 test was also used to compare the frequency of thyroid antibodies between the hyperthyroid and hypothyroid subgroups.

RESULTS

Thyroid disease

Of our 300 lupus patients, 22 (7%) had thyroid disease. There were 17 (5.7%) cases of hypothyroidism; eight were diagnosed before the onset of SLE, six after, and three simultaneously. There were five cases (1.7%) of hyperthyroidism, two diagnosed before the onset of SLE and three afterwards.

Serology

Of the 300 lupus patients, 42 (14%) had thyroid autoantibodies. Of the 22 patients with both SLE and thyroid disease, 15 (68%) had thyroid antibodies (table 1). In those who had thyroid disease diagnosed after the diagnosis of SLE, thyroid antibodies were present before the diagnosis of thyroid disease was made. Both antimicrosomal and antithyroglobulin antibodies were detected in the cohort, 11 patients (3.7%) with

Abbreviations: ELISA, enzyme linked immunosorbent assay; SLE, systemic lupus erythematosus; TSH, thyroid stimulating hormone

Table 1 The number of lupus patients in our cohort with or without thyroid disease according to the presence or absence of thyroid antibodies (total n=300): $p<0.001$, χ^2

	Thyroid autoantibodies	No thyroid autoantibodies
SLE and thyroid disease	15	7
SLE and no thyroid disease	27	251

Table 2 Studies of the prevalence of antimicrosomal antibody (anti-MIC Ab) and antithyroglobulin antibody (anti-TGB Ab) in patients with SLE

Reference number	Number of lupus patients	Number with anti-MIC Ab	Number with anti-TGB Ab	Number with both antibodies
This study	300	36	28	25
3	41	16	15	10
4	45	21	13	—
5	129	43	21	18
16	100	19	11	9
10	35	7	10	—
14	42	7	3	—
19	4	4	5	2

antimicrosomal antibodies only, three (1.0%) with antithyroglobulin antibodies only, and 25 (8.3%) with both (table 2). Antithyroid antibodies were not expressed differently in those whose thyroid disease was diagnosed before SLE onset.

Both the antibodies were found in equally high frequency in the hyperthyroid subgroup with four out of the five cases (80%) having both antibodies and one having neither. In the hypothyroid subgroup there was a trend towards a higher frequency of antimicrosomal antibodies than antithyroglobulin antibodies; seven patients had both antibodies, six had neither, and four had only antimicrosomal antibodies. There was no significant difference in the frequency with which the autoantibodies were detected between the hyperthyroid and hypothyroid subgroups ($p>0.2$, χ^2).

DISCUSSION

In our series of 300 patients with SLE the prevalence (5.7%) of hypothyroidism was much higher than that quoted for the normal background population (1%),¹⁴ while the prevalence (1.7%) of hyperthyroidism was not significantly different.¹⁴

A number of studies have looked at the prevalence of thyroid disease in SLE (table 3). The largest of these studies looked at the prevalence of thyroid disease in 332 patients with SLE admitted to hospital in the United States during a

five year period.¹⁵ The overall prevalence of thyroid disease was 7.5%–6.6% with hypothyroidism and 0.9% with hyperthyroidism—results similar to our study.

Of the three UK studies cited in the table, one reported the prevalence of hypothyroidism in SLE as 24%.³ However, these patients were clinically euthyroid, although biochemically hypothyroid as defined by a raised TSH. This high figure is discordant with most other studies and may be a result of the small patient numbers and very sensitive enzyme linked immunosorbent assay (ELISA) assay used to measure TSH. When an immunometric technique was used to detect TSH, as in the study by Vianna *et al*,¹⁶ a much lower prevalence (6%) of hypothyroidism was found.

Although most studies have shown that the prevalence of hypothyroidism in SLE is greater than the 1% quoted for the general population, the issue of whether hyperthyroidism is more prevalent in lupus than in the background population is still debatable. The frequency of hyperthyroidism in the normal population is approximately 1.9%,¹⁴ and some studies (table 3) have quoted higher rates in their lupus cohorts. However, the larger studies,^{3, 14, 16} including our own, suggest there is no increase in the prevalence of hyperthyroidism in patients with SLE.

The prevalence of thyroid autoantibodies in our study was 14%. This is lower than figures from most previous studies. Weetman and Walport,³ Magaro *et al*,¹⁷ and Kausman and Isenberg¹⁸ reported prevalences of thyroid antibodies of 51%, 45%, and 21% respectively in their lupus patients. In agreement with other studies,^{3, 16} we found a higher prevalence of thyroid antibodies in lupus patients with thyroid disease (68%).

Both antithyroid and antimicrosomal antibodies were detected in our study. Overall, there was a trend towards antimicrosomal antibodies being found more frequently, owing to their greater prevalence in the hypothyroid subgroup. This trend has been observed in earlier studies (table 2). We did not however find a statistically significant difference in the frequency with which either antimicrosomal or antithyroglobulin antibodies were detected between the hyperthyroid and hypothyroid subgroups.

Of our 300 patients, 42 had thyroid antibodies but only 22 had thyroid disease. It is recognised that the number of patients with SLE who test positive for thyroid antibodies on a single occasion is greater than the number who have clinical thyroid disease. Isenberg *et al* showed that the serological status of a significant minority of patients fluctuates and patients may become thyroid antibody negative with time.¹⁸ This subgroup is unlikely to develop clinical thyroid disease.

The main shortcoming of our study is the lack of an age and sex matched population for comparison. Because the group affected with lupus—predominantly young to middle aged women—is largely identical to the group who develop autoimmune thyroid disease, it may be argued that any association seen is purely coincidental. Two studies have suggested that there is no statistically significant difference in the

Table 3 Studies of the prevalence of hyperthyroid and hypothyroid disease in SLE

Reference number	Number of patients with SLE	Number hypothyroid	% Hypothyroid	Number hyperthyroid	% Hyperthyroid
2	64	3	4.7	7	10.9
3	41	10	24	0	0
4	45	2	4.4	1	2.2
5	129	5	3.9	1	0.8
16	100	6	6	2	2
10	35	4	11.4	0	0
15	332	22	6.6	3	0.9
19	175	9	5	0	0
20	93	—	—	6	6.5

prevalence of thyroid disease in SLE compared with age and sex matched controls,^{4,16} despite a higher prevalence of antithyroglobulin antibodies being found in the SLE group.¹⁶ Because only a few studies have examined this issue, and numbers were small, the question as to whether lupus patients have an excess of thyroid disease over and above that of age and sex matched controls remains debatable.

Despite this, our study indicates that a percentage (7%) of patients with SLE will develop thyroid disease and that the prevalence of hypothyroidism, but not hyperthyroidism, is greater than the overall prevalence in the background population. Furthermore, the presence of either condition in SLE is associated with a high prevalence of both antithyroglobulin and antimicrosomal antibodies. We would thus recommend the intermittent biochemical screening of thyroid function in patients with SLE, particularly if they are known to have thyroid antibodies, to identify clinical/subclinical thyroid disease.

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Accepted 30 May 2001

REFERENCES

- Goh KL, Wang F. Thyroid disorders in systemic lupus erythematosus. *Ann Rheum Dis* 1986;45:579–83.
- Byron MA, Mowat AG. Thyroid disorders in systemic lupus erythematosus. *Ann Rheum Dis* 1987;46:174–5.
- Weetman AP, Walport MJ. The association of autoimmune thyroiditis with systemic lupus erythematosus. *Br J Rheumatol* 1987;26:359–61.
- Tsai RT, Chang TC, Wang CR, Chuang CY, Chen CY. Thyroid disorders in Chinese patients with systemic lupus erythematosus. *Rheumatol Int* 1993;13:9–13.
- Boey ML, Fong PH, Lee JSC, Ng WY, Thai AC. Autoimmune thyroid disease in SLE in Singapore. *Lupus* 1993;2:51–4.
- Karsh J, Pavlidis N, Weintraub BD, Moutsopoulos HM. Thyroid disease in Sjögren's syndrome. *Arthritis Rheum* 1980;23:1326–9.
- Perez EB, Kraus A, Lopez G, Cifuentes M, Alarcon-Segovia D. Autoimmune thyroid disease in primary Sjögren's syndrome. *Am J Med* 1995;99:480–4.
- Dent GR, Edward OM. Autoimmune thyroid disease and the polymyalgia rheumatica-giant cell arteritis syndrome. *Clin Endocrinol* 1978;9:215–19.
- Miller FW, Moore GF, Weintraub BD, Steinberg AD, Burman KD. Thyroid stimulating and thyrotropin binding-inhibitory immunoglobulin activity in patients with systemic lupus erythematosus having thyroid function abnormalities. *Thyroid* 1993;1:229–34.
- Eberhad BA, Laxer RM, Eddy AA, Silverman ED. Presence of thyroid abnormalities in children with systemic lupus erythematosus. *J Pediatr* 1991;119:277–9.
- Scofield RH. Autoimmune thyroid disease in systemic lupus erythematosus and Sjögren's syndrome. *Clin Exp Rheumatol* 1996;14:321–30.
- Hijmans W, Doniach D, Roitt IM. Serological overlap between lupus erythematosus, rheumatoid arthritis and thyroid autoimmune disease. *BMJ* 1961;iii:508–12.
- Tan EM, Cohen AJ, Fries JF. The 1982 revised criteria for the classification of systemic erythematosus. *Arthritis Rheum* 1982;25:1271–7.
- Tunbridge WMG, Evered DC, Hall R. The spectrum of thyroid disease in a community: the Whickham survey. *Clin Endocrinol (Oxf)* 1977;7:481–93.
- Miller FW, Moore GF, Weintraub BD, Steinberg AD. Prevalence of thyroid disease and abnormal thyroid function test results in patients with systemic lupus erythematosus. *Arthritis Rheum* 1987;30:1124–31.
- Vianna JL, Haga HJ, Asherson RA, Swana G, Hughes GRV. A prospective evaluation of antithyroid antibody prevalence in 100 patients with systemic lupus erythematosus. *J Rheumatol* 1991;18:1193–5.
- Magaro M, Zoli A, Altomonte L, Mirone L, La Sala L, Barini A, et al. The association of silent thyroiditis with active systemic lupus erythematosus. *Clin Exp Rheumatol* 1992;10:67–70.
- Kausman D, Isenberg DA. Thyroid autoimmunity in systemic lupus erythematosus: the clinical significance of a fluctuating course. *Br J Rheumatol* 1995;34:361–4.
- Kohno Y, Naito N, Saito K, Hoshioka A, Niima H, Nakajima H, et al. Anti-thyroid peroxidase antibody in sera of patients with systemic lupus erythematosus. *Clin Exp Immunol* 1989;75:217–21.
- Rodrique S, Laborde H, Catoggio PM. Systemic lupus erythematosus and thyrotoxicosis: a hitherto little recognised association. *Ann Rheum Dis* 1989;48:424–7.