There is a high prevalence of papillary thyroid cancer in patients with systemic lupus erythematosus

Antonelli A, Mosca M, Fallahi P, Neri R, Ferrari SM, D'Ascanio A, Ghiri E, Carli L, Miccoli P, Bombardieri S.Thyroid cancer in systemic lupus erythematosus: a case-control study. J Clin Endocrinol Metab 2010;95:314-8. jc.2009-0677 [pii];10.1210/jc.2009-0677 [doi]

SUMMARY

BACKGROUND

A previous large retrospective cohort study of patients with systemic lupus erythematosus (SLE) found a high incidence of several cancers, including thyroid cancer. This is a prospective study aimed at further investigating the prevalence and features of thyroid cancer in a large series of unselected patients with SLE.

METHODS

The study subjects were 153 consecutive patients with SLE who were seen in the Department of Internal Medicine at the University of Pisa from January 1995 through December 2007. The diagnosis of SLE was established according to the 1997 revised classification of SLE by the American College of Rheumatology. The duration of SLE, which was 12±8.1 yr (range 1 to 29, median 9), was established according to the European Consensus Lupus Activity Measurement (ECLAM) scale score of five. Although iodine intake differs between areas of Tuscany, reliable data on local levels of intake were available from urinary iodine excretion data. Patients who had resided in an iodine-deficient area for at least 20 yr were included in the iodine-iodine-deficient group.

CONTROLS

The study population was classified into two groups: iodine-deficient and iodine sufficient.

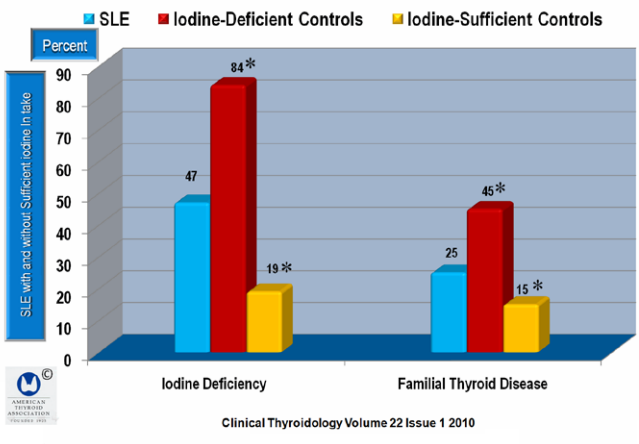

Figure 1. This figure shows the difference between iodine-deficient the Iodine-sufficient control subjects and patients with SLE. *P< 0.05 comparing patients with SLE and familial thyroid disease. This figure is derived from data in Table 1 by Antonelli et al.

Iodine-deficient controls:

Three controls matched for gender and similar age (±5 yr) were randomly selected from 2011 subjects from the general registry of North-West Tuscany who had been systematically screened from 1994 through 2004 for thyroid disorders. The majority (84%) of this control group had resided in an iodine defiant area for 20 years or more, which was considered the minimum criterion for historical iodine deficiency.

Iodine-sufficient controls:

The iodine-sufficient control group was obtained by selecting three individuals of the same gender and similar age (±5 yr) for each SLE patient from the population of an iodine-sufficient area (central Tuscany) that had been previously screened for thyroid disorders. Only 19% of this group of controls had resided in an iodine-deficient area for 20 yr or more (Figure1).

Thyroid function was evaluated in all SLE patients and controls by clinical examination including measurement of serum TSH, free T_3, free T_4 (FT_4) anti-thyroglobulin antibodies (AbTg) and anti-thyroperoxidase antibodies (TPOAb).

RESULTS *(Figure 1)*

The SLE group comprised 153 patients with a mean age of 38±13 years, and 9 men (6%) and 144 women (94%). Of this group, 47% were in the iodine-deficiency group and 25% had familial thyroid disease. (Figure 1)

A family history of thyroid disease was significantly more frequent in the iodine-deficient controls. The serum TSH, TgAb, and TPOAb levels were significantly higher in SLE patients, but FT_3 and FT_4 levels were significantly lower than those in the two control groups. Hypothyroidism (TSH >4 μ/ ml) was significantly more common in the patients with SLE as compared with the two control groups. Subclinical and clinical hyperthyroidism (TSH <0.3 μIU/ml, with or without high serum FT_3 or FT_4 levels) was significantly higher in patients with SLE as compared with those in the two control groups. Nonthyroidal illness syndrome (low serum T_3, normal FT_4, high reverse (rT_3) and normal TSH) was found in 4% of patients with SLE.

Thyroid nodules were significantly more common in patients with SLE (25%) and in control subjects in iodine –deficient areas (27%); P<0.001, comparing both control groups. (Figure 1) Fine-needle aspiration biopsy (FNAB) was performed in 24 patients with SLE (16%), and on 31 nodules (mean 1.2, nodules per patient, range 1 to 2). The median nodule size was 19 mm. The cytologic samples were classified as follows: class 1, (macrophages and colloid with no or rare follicular cells); class 2, (benign nodule); class 3, (indeterminate follicular lesion), and class 4, (suspect of or frankly malignant). The cytology was class 1 in 8%, class 6 in 6%, class 4 in 13%, class 9 in 12%.

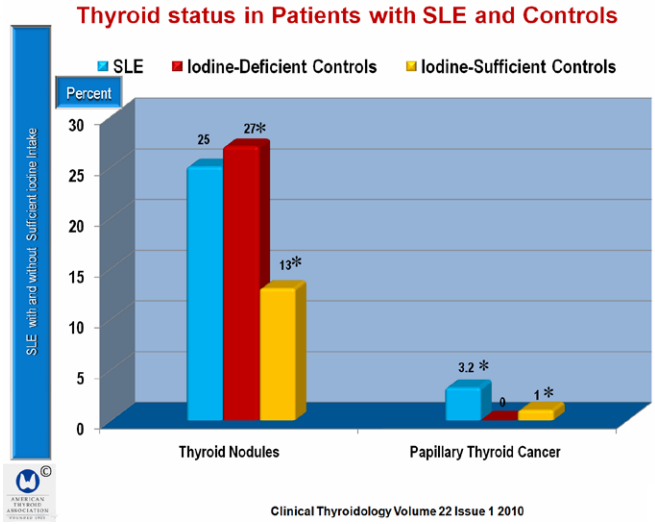

Figure 2. This figure shows the incidence of thyroid nodules and papillary thyroid cancer in patients with SLE, iodine deficiency or sufficiency. *P = 0.001 comparing findings in SLE and iodine deficiency and iodine sufficiency.

There were no significant differences in the distribution of class 1,2, and 3 among the three study groups (P = 0.9). A total of five papillary thyroid cancers were detected in the SLE group, and none were identified in the controls (P< 0.001) comparing the SLE group with the control groups.

The SLE patients with papillary thyroid cancer did not differ significantly from the other SLE patients in terms of sex (9 men and 5 women), mean age (38± 12 vs. 37±13 yr), serum TSH FT_3 FT_4 and TPOAb levels and serum TgAb. Four patients with SLE who had papillary thyroid cancer had circulating TgAb and TPOAb. Of the patients with SLE and papillary thyroid cancer, 80% had evidence of thyroid autoimmunity, as compared with thyroid autoimmunity in 31% of SLE patients without thyroid cancer. (P = 0.02)

CONCLUSION

This study suggests that the prevalence of papillary thyroid cancer in patients with SLE is higher than that in age-matched controls, particularly in patients with thyroid autoimmunity. As a result, careful thyroid surveillance is recommended during the follow-up of patients with SLE.

COMMENTARY

The impetus for the study by Antonelli et al came from a retrospective cohort study of patients in California by Parikh-Patel(1) et al. that examined the risk for cancer in a large cohort of patients with SLE (1). In that study, statewide patient discharge data were provided from 1991 through 2002, and patients with SLE had follow-up using a cancer registry to examine the patterns of cancer development. The study cohort comprised 30,478 patients with SLE that was observed for 157,969 person-years during which a total of 1,273 cancers occurred. The standard incidence ratios (SIRs) were significantly elevated (SIR = 1.14, 95% CI = 1.07-1.20), showing that SLE patients had higher risks of vagina/vulva (SIR = 3.27, 95% CI = 2.41-4.31) and liver cancers (SIR = 2.70, 95% CI = 1.54-4.24). In addition, there were elevated risks of lung, kidney, and thyroid cancers and several hematopoietic malignancies. These data thus suggested that risks of several cancer types are elevated among patients with SLE. The authors concluded that detailed studies of endogenous and exogenous factors that drive these associations are needed.

Antonelli et al found that 5 of 153 patients with SLE (3.2%) had papillary thyroid cancer, only one of which was observed in the iodine-sufficient control group. To eliminate bias, the observed prevalence of thyroid cancer due to differences in iodine uptake, control groups from both high and low iodine intake regions were used. Still, the results illustrate a significantly higher prevalence of papillary thyroid cancer in patients with SLE as compared with the incidence of papillary thyroid cancer (0%) in both control groups. These results corroborate the studies by Parikh-Patel, et al. and extend their observations. Antonelli et al. suggest that their study has a number of advantages over that in the California study. First, the Antonelli study used a prospective follow-up design over a 12-year period as compared with a retrospective follow-up in the California study. Secondly, the Pisa investigators were able to establish a definitive diagnosis of SLE, whereas the California group was unable to verify the diagnosis of SLE from the hospital discharge data. Thirdly, the results of the Pisa study were able to confirm the high incidence of thyroid cancer, 3.2%, which is in the range of papillary thyroid cancers found in patients undergoing FNAB for thyroid nodules.

Why patients with SLE might develop thyroid cancer is uncertain, but Antonelli et al. suggest that the increased risk for thyroid cancer in patients with SLE might be caused by autoimmunity, the presence of which was verified by the Pisa investigators.

Antonelli et al. advise neck ultrasonography on the basis of the current findings, which seems reasonable, considering the increased incidence of thyroid cancer in this group.

— Ernest L. Mazzaferri, MD, MACP

References

1. Parikh-Patel A, White RH, Allen M et al. Cancer risk in a cohort of patients with systemic lupus erythematosus (SLE) in California. Cancer Causes Control 2008;19:887-94.