Case Report

Two Cases of Systemic Lupus Erythematosus Associated with Hyperthyroidism

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We have experienced two cases (Case 1: 21-year-old female, Case 2: 26-year-old female) of systemic lupus erythematosus (SLE) associated with hyperthyroidism. Case 1 had been treated with methimazole (MMI) and betamethasone for approximately two years. Although thyroid function improved with the treatment, laboratory data of SLE deteriorated. She was successfully treated with betamethasone alone. Case 2, who had severe side effect (severe hemorrhage due to gastric ulcer) during prednisolone treatment for SLE, was found to have an additional hyperthyroidism. She was treated with intermittent prednisolone administration alone. Physical findings as well as laboratory data of both SLE and hyperthyroidism improved by the therapy.

Key Words: SLE, Hyperthyroidism, Anti-thyroid drugs, Steroid hormone treatment.

In general, it is not uncommon that more than one autoimmune disease can be seen in an individual. Hyperthyroidism is a relatively common condition in the adult female population. It is therefore interesting that only several reports so far have described coexistence of hyperthyroidism and SLE. We have experienced two cases of hyperthyroidism whose coexisting clinical features satisfied the American Rheumatoid Association (ARA) criteria for the diagnosis of SLE. The significance of the association as well as the treatment of the two diseases is discussed.

Case 1: A 21-year-old woman who had been diagnosed as SLE and Graves’ disease and had been treated with betamethasone (0.5–2.0 mg/day) and methimazole (MMI, 5–20 mg/day) for approximately two years (Fig. 1) in Ogaki Municipal Hospital was referred to Gifu University Hospital for further treatment of the two diseases on Nov. 20, 1975.

On physical examination, she was 160 cm tall and weighed 53 kg. Heart rate was 90/min and was regular. Blood pressure was 122/84 mmHg. Upper and lower eyelids were puffy and butterfly rash was noted on her face. Her thyroid gland was soft and diffusely enlarged. Graefe’s and Möbius’ signs were both negative. Neither finger tremor nor excessive sweating was noted.

Although laboratory data of thyroid function tests in Sept. 1975 had been improved (T4, 7.5 μg/dl (Eiken T4 RIA kit, normal range, 4.5–13.0 μg/dl), Triosorb, 22%), titer of anti-DNA antibodies (DNA PHA Test; Fuji Zoki, Tokyo, normal range, less than 1:80) had been gradually increased to the level of 1:2560, in Oct. 1975. Treatment with MMI was discontinued on Oct. 22, 1975, and then she was treated with 0.5–3.0 mg per day of betamethasone alone. In Dec. 1975, DNA PHA test had been decreased to the level of 1:160. In Feb. 1976, the values of serum T3 (110 ng/dl, Eiken T3 RIA kit; Eiken, Tokyo, normal range, 90–210 ng/dl), T4 (8.2 μg/dl), TSH (3.0 μU/ml, Daiichi TSH kit; Tokyo, normal range, less than 8 μU/ml), Triosorb (23.5%, Triosorb S; Dainabot Lab., Tokyo, normal range, 23–35%), and Res-O-Mat T4 (12.8 μg/dl, Stac T4 RIA; Daiichi, Tokyo, normal range,
5–13.7 μg/dl) were all within normal range. Plasma TSH response after intravenous infusion of 500 μg of thyrotropin releasing hormone (TRH; Tanabe Co., Osaka) was normal, namely basal and maximal response (30 min after infusion) of TSH were 3.0 and 15.1 μU/ml, respectively. Since increase in titer of DNA PHA test and acceleration of ESR were observed at the end of Jan. 1976, daily dose of dexamethasone had been increased to 3 mg/day. Titer of DNA PHA test again decreased to 1:160 (Fig. 1). In March 1976, she was discharged. Treatment with betamethasone was discontinued until Jan. 1979, when she was again started to treat with 2 mg per day of betamethasone followed by stopping the medication in July. At present (Sept. 1986) she continues to do quite well. She married when she was 25 years old and has two normal children (a boy when she was 27 years old and a girl when she was 29 years old).

Case 2: A 26-year-old female who had been diagnosed as SLE and had been treated with prednisolone was referred to Gifu University Hospital for further treatment of SLE on July 7, 1977, since she had severe hematoemesis and bloody stool due to gastric ulcer which required a gastrectomy. On physical examination, she was 144 cm tall and weighed 42.5 kg. Her pulse rate was 96/min and was regular. She had moon face but no rash was noticed. She had neither tremor nor struma. She had muscle weakness of extremities and atrophy in distal muscles of arms was noticed. Her grasping power was decreased remarkably (r; 6 kg, l; 7.5 kg). Achilles and patellar jerks were normal. Laboratory data and results of endocrine function tests at the time of her admission to Gifu University Hospital are as the followings. On immunological data in July 1977, she had negative CRP, RA, LE cell, DNA PHA test, and Coombs test. Anti-nuclear antibodies was 1:160 with shaggy and speckled type. Serum concentration of IgG, IgA, and IgM were 1480, 160, and 58 mg/dl, respectively. On endocrine data in Sept. 1977, BMR, 131I-uptake, Triosorb, Res-O-Mat T4, serum T3, and T4 were +21%, 73.7%, 29.1%, 4.0 μg/dl, 415 ng/dl, 14.6 μg/dl, respectively. Basal TSH concentration was 3.2 μU/ml and did not increase after TRH administration (500 μg, i.v.). From these results a diagnosis of primary hyperthyroid-
is was made. Her clinical course is shown in Fig. 2. She was treated with prednisolone alone inter-
mittently according to the schedule in our labora-
tory9. Improvement of symptoms of both hyper-
thyroidism and SLE was observed. Laboratory 
data of both diseases, including plasma T3 and T4 
levels, 131I-uptake, ESR, and titer of anti-nuclear 
antibodies improved. On Aug. 21, 1978 she dis-
charged. The weekly dose of intermittent pred-
nisolone was gradually reduced since Oct. 1978. 
Side effects such as moon face, which had been 
caused due to preceding daily steroid therapy, dis-
appeared during the intermittent prednisolone treat-
ment. The intermittent prednisolone treatment 
had been continued for about six years until April 
1983, when she stopped medication by herself. Al-
though serum anti-TSH receptor antibody activity 
(TRAb) measured by commercially available RIA 
kit (R.S.R. Limited, U.K., normal range, below 
10%) was still positive (16.0%) on July 11, 1985, 
on signs of exacerbation of SLE and hyperthyroid-
ism have been observed up to now (Sept. 1986).

DISCUSSION

In patients with SLE, high prevalence with the 
association of other autoimmune diseases has been 
reported10. As to the association with thyroid au-
toimmunity, higher incidence of anti-thyroid 
antibodies has been reported11-12, though thyroid-
itis is not common in SLE10. It is well recognized 
that Graves’ disease is also associated with other 
autoimmune disease, usually organ specific dis-

erases such as Hashimoto’s thyroiditis and Addi-

son’s disease. It is not, however, regularly found in 
association with non-organ specific autoimmune 
diseases such as rheumatoid arthritis, SLE, and 
scleroderma. Thus, concerning the association of 
hyperthyroidism and SLE, only several cases have 
hitherto been reported2-7. Without thyroid biopsy, 
it is not clear whether primary hyperthyroidism 
in our cases was caused by either Graves’ dis-

ease or Hashitoxicosis. The primary cause of the 
two diseases, however, is attributed to the produc-
tion of anti-TSH receptor antibodies which react 
with TSH receptors in an identical manner to TSH 
leading to thyroid hormone overproduction13,14.

Despite the high prevalence of membrane-binding 
antibodies15,16 including TSH displaceable anti-
bodies16 in sera from patients with SLE, the rea-
son why association of the two diseases has hither-
to been described by only several authors is so far 
not clear.

Treatment of hyperthyroidism associated with 
SLE is complex because of the possibility that anti-
thyroid drugs themselves can induce drug-induced 
lupus and can cause exacerbation of symptoms of 
SLE. This might be true in Case 1 who had been 
treated with MMI and glucocorticoid and titers of 
anti-nuclear and anti-DNA antibodies increased, 
possibly because of either the use of MMI or a too 
small dose of betamethasone for the treatment of 
SLE. In Case 2, levels of plasma thyroid hormone
and thyroidal $^{131}$I-uptake became normal with the use of intermittent prednisolone alone, and concomitant decrease of the ESR and titer of antinuclear antibodies as well as improvement of clinical pictures of both diseases was also observed. Thus, in Case 2 it is clear that steroid treatment alone improved clinical and laboratory data of both hyperthyroidism and SLE.

The underlying mechanisms of improvement of their hyperthyroidism could be speculated upon as follows: (1) Since it has been well known that glucocorticoid suppresses the biosynthesis of immunoglobulins, the production of anti-TSH receptor antibodies which belong to immunoglobulin G class was also suppressed. (2) Glucocorticoids acted directly on thyroid gland and suppressed the overproduction of thyroid hormone. (3) Glucocorticoid is known to suppress 5'-deiodination of T4$^{17}$, and thus, the production of T3 which is more potent than T4 was suppressed. However, the latter 2 possibilities are highly unlikely. Although short term (3–4 months) remission of thyrotoxicosis by large daily dose of prednisone (80–169 mg per day) treatment alone has been reported$,^{18}$ treatment of Graves’ disease with glucocorticoid alone usually does not bring healing or long-term remission. Although it is very difficult to generalize the treatment of the patients with primary hyperthyroidism associated with SLE from our two cases, two other cases similar to ours who had been successfully treated with glucocorticoid alone have been reported. (4) We have to be careful using anti-thyroid drugs in such patients, because, as could have been happened in Case 1, symptoms and laboratory data of SLE may deteriorate with he medication.

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REFERENCES


