A Study on the Frequency of the Autoimmune Disorders in Vitiligo Patients

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Background **: The increase of the incidence of autoimmune diseases and the autoimmune pathogenesis of vitiligo were reported.**

Objective **: We studied the frequency of autoimmune disorders and positivity of antinuclear antibody in Korean vitiligo patients.**

Methods **: Vitiligo patients (439 patients) and control subjects (197 patients) were interviewed about their history of autoimmune diseases. Laboratory studies including complete blood cell count, urine analysis, blood chemistry, fasting blood sugar, thyroid function test (T3, free T4, TSH), and antinuclear antibody were performed for the screening of autoimmune disorders.**

Results **: The diseases associated with vitiligo were microcytic hypochromic anemia (3.64%), non-insulin dependent diabetes mellitus (2.96%), thyroid disease (3.96%), atrophic gastritis, and alopecia areata. In the control subjects, the associated diseases were microcytic hypochromic anemia (1.62%), non-insulin dependent diabetes mellitus (4.65%), and thyroid disease (3.49%). These results show that the frequency of autoimmune disorders in vitiligo patients is not significantly higher than that in control subjects. Six (54.5%) out of 11 vitiligo patients with thyroid disease were diagnosed as having thyroid disease for the first time. Four (0.91%) out of 438 vitiligo patients showed positive to antinuclear antibody. Positivity of antinuclear antibody was not higher in vitiligo patients than that in control subjects (1.16%).**

Conclusion **: Frequency of autoimmune diseases and positive reaction to antinuclear antibody in vitiligo patients were not significantly higher than those in control subjects.**

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Key Words : Vitiligo, Autoimmune disorders

Though the pathogenesis of vitiligo is not clear yet, the immune hypothesis takes the high priority because of the frequent associations of vitiligo with autoimmune disorders such as pernicious anemia, diabetes mellitus, thyroid diseases or Addison's disease, and the frequent development of serum organ-specific autoantibody[1-3].

The reports on the frequency of the associated autoimmune diseases and the positive reaction to the autoantibody show variety, and there was no comprehensive report on those observations in Korean vitiligo patients. Thus, we have investigated the frequency of association of autoimmune disorders and the positive reaction of the antinuclear antibody (ANA) test in Korean vitiligo patients.

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Table 1. Age at visiting

Age	Vitiligo			Control		
	Male(%)	Female(%)	Total (%)	Male(%)	Female(%)	Total (%)
0-9	19(8.8)	14(6.3)	33(7.5)	4(4)	0	4(2.0)
10-19	62(28.8)	37(16.5)	99(22.6)	14(14)	9(9.3)	23(11.7)
20-29	40(18.6)	37(16.5)	77(17.5)	24(24)	19(19.6)	43(21.8)
30-39	29(13.5)	31(13.8)	60(13.7)	19(19)	21(21.6)	40(20.3)
40-49	35(16.3)	31(13.8)	66(15)	20(20)	25(25.8)	45(22.8)
50-59	14(6.5)	44(19.6)	58(13.2)	9(9)	9(9.3)	18(9.1)
60-69	11(5.1)	25(11.2)	36(8.2)	7(7)	9(9.3)	16(8.1)
>70	5(2.3)	5(2.2)	10(2.3)	3(3)	5(5.2)	8(4.1)
Total	215	224	439	100	97	197

Table 2. Associated disease and abnormal laboratory findings

	vitiligo	control
	No.(%)	No.(%)
Anemia (hemoglobin<12.0 g/dl)	16(3.64)	3(1.62)
Non-insulin dependent diabetes	14(3.18)	8(4.65)
Thyroid disease	10(3.59)	3(3.49)
hyperthyroidism	8	2
simple goiter	1	0
thyroid cancer	1	1
ANA (+) subjects	4(0.91)	2(1.16)
Alopecia areata	3(0.48)	0
Atrophic gastritis	1	0

MATERIALS AND METHODS

1. Study subjects

Subjects were 439 vitiligo patients and 197 control subjects who visited our department of dermatology for the first time from January 5, 1995 to November 30, 1999. The age distribution of the vitiligo patients was from 5 to 75 years old. There were 215 male (average age: 29.6) and 224 female patients (average age: 37.2). We selected 197 patients as control subjects who have psoriasis[4], mycosis, and folliculitis. The control subjects were known as not showing the increase of the frequency of the autoimmune diseases and the positive reaction of ANA. Among the control patients, there were 100 male (average age: 34.7) and 97 female patients (average age: 38.2) (Table 1).

2. Methods

For the vitiligo and the control patients, we did the physical examination and interviewed about their history of pernicious anemia, diabetes, thyroid disorders, Addison's disease, alopecia areata, lupus erythematosus, halo nevus, and other autoimmune diseases. In the laboratory studies, we tested complete blood cell count (CBC), urine analysis, blood chemistry, thyroid function (T3, free T4, TSH)[7], serum ANA, while the patients were in the fasting.

For the diagnosis of the pernicious anemia, the peripheral blood smear and the level of blood vitamin B12 were examined[8], when the number of megalocyte increased (mean corpuscular volume>100fL) in CBC. For the diagnosis of diabetes, we examined insulin, C-peptide, and hemoglobin A1c of the blood, when urine sugar was detected and/or high blood sugar was shown. When patient showed thyroid dysfunction, thyroid autoantibody and the radioactive iodine uptake rate were measured. When the patient showing positive result in serum ANA test, anti-ds-DNA antibody, anti-Ro antibody, anti-La antibody, anti-sm antibody, and anti-RNP antibody tests were carried out for the diagnosis of connective tissue disease.

3. Statistical analysis

With the use of the SPSS (Statistical Package for Social Science) Ver. 8.0 program, the frequency of associated diseases and positive reactions of ANA in the vitiligo patients and the control subjects were compared and, through χ^2 test method, the result significance was judged.

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RESULTS

Anemia patients (hemoglobin <12.0 g/dl) were 16 (3.64%) out of 423 vitiligo patients and 3 (1.62%) out of 185 control subjects. Anemia patients had all microcytic hypochromic anemia. No one had pernicious anemia.

Fourteen (3.18%) out of 439 vitiligo patients and 8 (4.65%) out of 172 control subjects were diagnosed as diabetes patients. All the diabetes patients had non-insulin dependent diabetes mellitus (NIDDM).

Ten (3.59%) out of 278 vitiligo and 3 (3.49%) out of 86 control patients were diagnosed as thyroid disease patients.

The association frequency between those two subjects showed no statistically significant difference in anemia, diabetes, and thyroid diseases.

Three out of 14 vitiligo patients were diagnosed as diabetes, and 6 out of 11 vitiligo patients as thyroid disease for the first time.

In the serum ANA test, 4 (0.91%) out of 438 vitiligo and 2 (1.16%) out of 172 control patients showed positive result and the association frequency between those two subjects showed no statistically significant difference. In those patients with positive serum ANA, none showed abnormalities in the other autoantibody test and none were diagnosed as connective tissue disease.

Among other associated autoimmune disorders, there were 3 alopecia areata, 1 atrophic gastritis, and 1 halo nevus patient.

Associated diseases and abnormal laboratory findings are summarized in table 2.

DISCUSSION

It is generally known that vitiligo patients show the frequent association with autoimmune diseases, such as pernicious anemia, insulin dependent diabetes mellitus, thyroid disease, alopecia areata, atrophic gastritis, halo nevus, and the frequent development of organ-specific autoantibody[1-3].

We examined the frequency of the autoimmune diseases and the positive reaction of ANA for the Korean vitiligo patients. Because autoimmune diseases show the different prevalence with races and regions, it is impossible to compare the prevalence of a nation with other ones. There were no reports concerning the incidence of autoimmune diseases and the positive reaction ratio of ANA in normal Korean population except diabetes mellitus (prevalence 5-8%)[9]. So we selected psoriasis[4], mycosis and folliculitis patients as control subjects who were not reported to show the increase or decrease in the incidence of autoimmune diseases and positive reaction of ANA.

It is reported that the frequency of the rare disease, pernicious anemia, increases in the case of vitiligo patients, and the prevalence rate is 1.6- 10.6%[1,8]. Our results showed that no vitiligo patient was associated with pernicious anemia.

Among vitiligo patients, 1-7.1% were reported to be associated with diabetes[1]. The insulin dependent diabetes mellitus (IDDM) were reported to have a autoimmune pathogenesis, and high prevalence in the vitiligo patients[1,10]. In our study, there was no IDDM patient in both vitiligo and control subjects.

The frequency of thyroid disease in vitiligo patients varied from 0.6 to 30%[1,4-7]. Autoimmune thyroid diseases such as hypothyroidism, Graves' disease, or Hashimoto's thyroiditis showed a high rate of association. Cunliffe et al[4] reported 30%, and Betterle et al[5] 7.5%, of the association frequency of thyroid disease in vitiligo patients. That rate was much higher than that of control subjects. Schallreuter et al[6] also reported that 25 (7.8%) out of 321 vitiligo patients were associated with thyroid disease and suggested to carry out the thyroid function test once a year as the possibility of thyroid disease for vitiligo patients was so high. Differently from those reports, our results showed that 11 (3.96%) vitiligo patients were associated with thyroid disease and the association frequency showed no statistically significant difference from that of control subjects(3.49%). Six (2.1%) vitiligo patients were diagnosed to have thyroid disease for the first time and they took the 54.5% of total thyroid patients in the vitiligo patients.

In the ANA test for the screening of connective tissue disease, a kind of autoimmune disorders, 0.91% of the vitiligo patients showed ANA positive reaction rate and did not show any significant difference from that of control subjects (1.16%). It was reported that 1.6% of ANA positive reaction in the Korean vitiligo patients[11]. That rate is higher than that of our result of vitiligo patients, but that is not statistically significant.

Our results showed that the association frequency of the autoimmune diseases and the positive reaction of ANA in the vitiligo patients did not show a statistically significant difference from that of control subjects.

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