

Research Article

Association between Vitiligo and Thyroid Autoimmunity

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Received 16 December 2010; Revised 18 February 2011; Accepted 4 March 2011

Academic Editor: Guillermo Juvenal

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Background. Vitiligo is a common skin disorder characterized by macular depigmentation of the skin. The etiopathogenesis of the disease is still unclear, but there is evidence that autoimmunity and endocrine dysfunction may be involved. *Objective.* The aim of this study was to determine whether vitiligo is statistically associated with thyroid autoimmunity. *Method.* In a prospective case-control study, we compared the frequency of thyroid autoantibodies (thyroglobulin antibody, anti-Tg and thyroid peroxidase antibody, and anti-TPO) in 33 patients with vitiligo and in 33 healthy volunteers. Thyroid autoantibodies and thyroid hormones (thyroxine (T4), triiodothyronine (T3), and thyroid stimulating hormone (TSH)) were measured in all subjects. *Results.* Thyroid functional abnormalities were found in 6 (18.18%) patients. Anti-Tg and anti-TPO were positive in 9 (27.27%) and 8 (24.24%) patients, respectively. In control group, only one subject (3.03%) had abnormalities in thyroid hormonal status, and two subjects had positive thyroid autoantibodies. Compared with the control group, the frequency of both anti-Tg and anti-TPO was significantly higher in those with vitiligo ($P < .05$). *Conclusion.* This study shows a significant association between vitiligo and thyroid autoimmunity, and that tests to detect thyroid autoantibodies are relevant in patients with vitiligo.

1. Introduction

Vitiligo is one of disorders of melanin pigmentation that affects approximately 0.5–2% of the population [1]. It is characterized by macular depigmentation of varying sizes or shapes with a tendency to progress. Depending on the extent of the lesions, vitiligo can be classified into two main categories: generalized and localized. Although the pathogenesis of vitiligo is not yet fully understood, the autoimmune hypothesis is the most commonly accepted. This theory is supported by the clinical association of vitiligo with autoimmune disorders, the frequent detection of circulating autoantibodies to surface and cytoplasmic antigens of melanocytes [2, 3]. Furthermore, there are findings of activated T cells in the periphery of actively progressing lesions in some vitiligo patients [4]. Thyroid functional disorders and autoimmune thyroid diseases have been reported in association with vitiligo, and it seems that the incidence of clinical and subclinical thyroid involvement is more common in vitiligo patients than healthy subjects [5, 6].

The aim of this study was to determine whether vitiligo is statistically significantly associated with thyroid autoimmunity.

2. Patients and Methods

The study included 33 patients with vitiligo, 19 female and 14 male, median age 42.39 (± 13.66) years. Of them, there were 14 (42.4%) patients with generalized vitiligo and 19 (57.6%) patients with localized form of disease. A detailed history and examination were taken in all study subjects, including patients age, age at onset, duration of disease, associated diseases, history of thyroid disorders, and the extent and severity of disease. The diagnosis of vitiligo was made on clinical grounds. Skin biopsy was performed in selected cases. The control group consisted of 33 volunteers, 19 female, and 14 male, median age 40.33 (± 14.78) years. Blood samples were taken and a physical examination and thyroid sonography was performed. All subjects gave their informed consent in accordance with the requirements of the institutional Ethics Committee.

TABLE 1: Demographic data of patients (Vitiligo group) and volunteers (Control group).

	Vitiligo group <i>n</i> (%)	Control group <i>n</i> (%)	<i>P</i>
Men, <i>n</i> (%)	19 (58)	19 (58)	
Women, <i>n</i> (%)	14 (42)	14 (42)	
Age range, years	16–64	17–69	
Age, mean years (SD)	42.39 (13.66)	40.33 (14.78)	.558

TABLE 2: Clinical characteristics of patients with vitiligo.

Mean age of onset (SD) (year)	37.74 (12.45)
Age of onset range (year)	14–58
Mean duration (SD) (month)	55.85 (66.24)
Duration Range (month)	2–252
Type of vitiligo <i>n</i> , (%)	
Generalized 14 (42)	
Localized 19 (58)	

Thyroid autoantibodies (thyroglobulin antibody, anti-Tg and thyroid peroxidase antibody, anti-TPO) and thyroid hormones (thyroxine (T4), triiodthyronine (T3), and thyroid stimulating hormone (TSH) were measured in all subjects. Total T4 (normal range: 70–180 nmol/L) and total T3 (normal range 1.3–3.3 nmol/L) were measured by use of radioimmunoassay (RIA); TSH (normal range: 0.3–4.2 mIU/L) was determined by use of immunoradiometric assay (IRMA) (BRAHMS Aktiengesellschaft, Hennigsdorf, Germany). Serum levels of anti-Tg (threshold value: 115 IU/mL) and anti-TPO (borderline value: 34 IU/mL) were measured by use of electrochemiluminescence immunoassay (ECLIA) according to standard protocols (COBAS, Roche Diagnostics GmbH, Germany). The upper limit of autoantibody was determined by the laboratory.

Statistical comparisons were performed using χ^2 test. Data were considered statistically significant at $P < .05$.

3. Results

We performed a cross-sectional study in 33 consecutive patients with vitiligo and 33 age- and sex-matched controls. Demographic data of patients and controls are shown in Table 1. The mean (SD) age of the patient and control groups was 42.39 (± 13.66) and 40.33 (± 14.78), respectively ($P = .558$). The duration of vitiligo ranged from 2 to 252 months. Fourteen patients had generalized, and nineteen patients had localized vitiligo (Table 2). A family history of thyroid diseases was recorded in 2 (6.06%) patients. Thyroid functional abnormalities were found in 6 (18.18%) patients. In the control group only one (3.03%) subject had abnormalities in hormonal status. Hypoechoic thyroid tissue was seen in 2 (6.06%) patients. Goitre was diagnosed in 4 (12.12%) patients with generalized vitiligo, from which 3 (9.09%) of them had elevated levels of thyroid autoantibodies and 2 (6.06%) had hormonal abnormalities.

The ultrasound examination of the thyroid gland in control group was interpreted as normal in 32 (96.96%), and 1 (3.03%) volunteers had small simple goiter.

In patients with vitiligo anti-Tg titers were ranging from 11 to 1012 IU/mL and anti-TPO antibody titers from 6 to 457 IU/mL. In control group anti-Tg titers were ranging from 10 to 153 IU/mL, and anti-TPO antibody titers from 5.1 to 129 IU/mL. Anti-Tg antibody in 9 (27.27%) patients, anti-TPO antibody in 8 (24.24%) and both anti-Tg and anti-TPO antibodies in 6 (18.18%) were higher than the normal antibody titres. In the control group, one subject (3.03%) had positive anti-Tg and one volunteer (3.03%) had positive anti-TPO. The frequency of thyroid autoantibodies was significantly higher in vitiligo patients than in control group (Table 3). Statistically significant difference was also found in values of anti-Tg and anti-TPO between patients with generalized and patients with localized vitiligo ($P < .05$).

A Chi-square test for independence (with Yates Continuity Correction) indicated significant association between higher values of anti-Tg (values more than 115 IU/ml) and vitiligo, $\chi^2 (1, n = 66) = 5.775, P = .0163$.

A Chi-square test for independence (with Yates Continuity Correction) indicated significant association between higher values of anti-TPO (values more than 34 IU/ml) and vitiligo, $\chi^2 (1, n = 66) = 4.632, P = .0314$.

4. Discussion

Vitiligo is an ancient disease that was known to Egyptians even in the pre-Christian time [7]. Despite its long history, our knowledge is actually limited. A number of genetic and environmental factors have been implicated in the etiology of vitiligo, but the mechanism of initiation of melanocyte destruction and progression of disease is not yet clear [8].

Vitiligo has been reported in association with numerous endocrine disorders. One of the main associations is with thyroid abnormalities. It was already in 1941, when Robert suggested that vitiligo might be connected with an increased activity of the thyroid gland [9]. He noted a distinct rise of the basal metabolism in 10 out of 20 vitiligo patients tested. Several authors reported a significantly increased prevalence of autoimmune thyroid disease in vitiligo patients; the rate of positivity of thyroid autoantibodies varied from 2.2% [10] to 50% [11]. In addition, there is also a study reporting a significantly increased prevalence of vitiligo in patients with autoimmune thyroid disease compared to patients with nonautoimmune thyroid disease [5, 6].

In accordance to previous studies, we also demonstrated that antithyroid autoantibodies were significantly increased in vitiligo patients in comparison to healthy subjects. We detected elevated anti-Tg in 9 (27.27%) and elevated anti-TPO in 8 (24.24%) of patients with vitiligo. Usually about 10% of general population has positive antithyroid antibodies; in this study the prevalence of autoantibodies in control group is much lower than expected. The difference it may partly be attributed to genetic factors. Compared with the control group, the frequency of both anti-Tg and anti-TPO antibodies was significantly higher

TABLE 3: Frequency of thyroid autoantibodies in the study group.

Group	Anti-Tg (threshold value 115 IU/mL)		Anti-TPO (threshold value 34 IU/mL)	
	Negative <i>n</i> (%)	Positive <i>n</i> (%)	Negative <i>n</i> (%)	Positive <i>n</i> (%)
Vitiligo	24 (73)	9 (27)	25 (76)	8 (24)
Control	32 (97)	1 (3)	32 (97)	1 (3)
Total	56 (85)	10 (15)	57 (86)	9 (14)
Difference <i>n</i> (%)	8 (24)		7 (21)	
χ^2, P	$\chi^2 = 5.775, P = .0163$		$\chi^2 = 4.632, P = .0314$	

in those with vitiligo. Our results are consistent with a clinical study performed by Sedighe and Gholamhossein [12]. They analyzed antithyroid antibodies in 109 Iranian patients with vitiligo and found that anti-TPO and anti-Tg antibody were positive in 40 (36.7%) and 35 (32.1%) cases, respectively. Daneshpazhooh and colleagues measured only the serum level of anti-TPO antibody and reported significantly high levels in vitiligo patients compared to healthy controls [13]. In study that was carried out in India, the anti-TPO antibody was positive in 31.4% cases [14]. Our findings showed that the frequency of anti-TPO was more significant than anti-Tg. This antibody, historically referred to as the antimicrosomal antibody, is established as a sensitive tool for the detection of early subclinical autoimmune thyroid diseases and identification of at-risk cases for autoimmune thyroid diseases [15]. Nordyke et al. reported that anti-TPO antibody tends to have more correlation with thyroid dysfunction than does the anti-Tg antibody [16].

Vitiligo frequently precedes the thyroid involvement, thus screening vitiligo patients for thyroid antibody seems plausible [17].

5. Conclusion

The study revealed a significant association between vitiligo and thyroid autoimmunity and showed the tests used to detect thyroid autoantibodies to be relevant in patients with vitiligo. Vitiligo offers many benefits as a model for the study of autoimmunity, in that it can be used to identify the contributing roles of immunogenetics and endocrine factors in the initiation and propagation of autoimmune disease.

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