SHORT REPORT

Differences between familial and sporadic cases of vitiligo

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Abstract

Background Most cases of vitiligo are sporadic, but about 10–36% of the patients have positive family history.
Objective The aim of our study was to describe differences between familial and sporadic cases of vitiligo.
Methods A total of 186 adult vitiligo patients were examined, in 173 of whom the level of thyroid peroxidase antibodies, gastric parietal cell antibodies (PCA), antinuclear antibodies (ANA), anti-adrenal cortex antibodies and rheumatoid factor in blood was measured. All patients were divided in two groups: the cases with positive family history of vitiligo (51) and the sporadic cases (135).
Results The risk of onset of the disease up to 20 years of age was higher in the familial group \(P = 0.008\). Patients in familial group showed more widespread depigmentation compared with sporadic cases [body surface area (BSA) over 10%: \(P = 0.004\); BSA over 50%: \(P = 0.001\)]. In familial group, patients had darker skin phototype \(P = 0.045\) and the disease had started more often as a vulgar vitiligo \(P = 0.008\). In sporadic vitiligo group, female gender was a risk factor for more widespread depigmentation (BSA over 10%, \(P = 0.001\)). Extensive depigmentation was associated with reported triggering factors and mucosal involvement in both groups and with leukotrichia only in familial group. Widespread depigmentation related to the risk of presence of autoantibodies \(P = 0.03\) in sporadic cases of vitiligo (especially of PCA: \(P = 0.04\) and ANA: \(P = 0.0002\)).
Conclusions In this study, we demonstrated first time that patients with familial vitiligo have a higher risk for vulgar type at the beginning of the disease and female gender increases the risk for more extensive depigmentation in sporadic cases.

Conflict of interest
None declared.

Introduction
Vitiligo is a common pigmentary disorder characterized by pigment loss of the skin, hair and mucous membranes, because of selective destruction of melanocytes. The prevalence of vitiligo in different geographical regions varies from 0.1% to 8.8%\(^1\).\(^2\) Vitiligo affects both genders equally and in half of the cases the disease appears before the age of 20\(^3\). Vitiligo has a complex pathogenesis, comprising autoimmunity, involvement of genetic and external factors and not all mechanisms are still understood. Most cases of vitiligo are sporadic, about 10–36% of the patients have familial vitiligo\(^4\). Recently, very high family involvements were shown in India and Saudi Arabia, 57% and 74% respectively\(^5\).\(^6\) Up to today, there are little information about clinical features and serological differences between familial and sporadic cases of vitiligo. Studies have pointed out that positive family history is associated with an early onset of the disease and increased risk of other autoimmune diseases\(^5\)–\(^8\). The aim of our study was to find differences between familial and sporadic cases of vitiligo.

Patients and Methods
The study was approved by the Ethical Review Committee on Human Research of the University of Tartu and all participants signed a written informed consent. The data of adult’s vitiligo patients were collected from June 2005 to December 2009. Patients were examined at the Dermatology Department of Tartu University and the questionnaire, including age, gender, nationality, skin...
phototype, location and pattern at the onset of vitiligo, distribution of lesions during the first 1–2 years, duration of vitiligo, triggering factors, concomitant diseases, spontaneous repigmentation of patches, previous treatment, familial history of vitiligo was filled by the dermatologist. The diagnosis of vitiligo was based on characteristic loss of skin pigmentation and the examination under Wood’s lamp. The clinical types of vitiligo were classified as focal (one or few macules in a non-dermatomal distribution), segmental (unilateral segmental distribution), acrofacial (distal extremities and face), vulgaris (scattered over the body) and universal (over 90% depigmentation). The presence of leukotrichia, Koebner phenomenon, halo nevi was noted and body surface area (BSA) was assessed. Vitiligo was stable when depigmentation did not increase during the last 3 months and active when new lesions appeared and existing lesions increased in size over the past 3 months. Anti-nuclear antibodies (ANA), gastric parietal cell antibodies (PCA) and anti-adrenal cortex antibodies (AAA) were determined by indirect immunofluorescence method using rat liver as antigenic substrate for ANA and mouse stomach for detection of PCA. AAA was detected on normal human adrenal tissue. Chemiluminescence immunosassay was used for the determination of thyroid peroxidase antibodies (TPO-Ab) and immunoturbidimetric assay for rheumatoid factor (RF).

All patients with vitiligo were divided in two groups: the first group consisted of the cases with positive family history of vitiligo and the second group was formed from the sporadic cases. In total, 186 patients, 51 familial cases (15M⁄36F, average age 41.7 year) and 135 sporadic cases (42M⁄93F, average age 45.5 year) were enrolled in the study. Autoantibodies were measured in 173 cases.

Statistical analysis was performed by using chi-square test and strength of associations was estimated by odds ratio and 95% confidence interval of chi-square determination. A level of $P<0.05$ was considered statistically significant.

**Results**

In 67% of the familial cases, the subject had one relative with vitiligo, in 33% of the familial cases two or more. The average age of onset of vitiligo was 24.8 years (age range 3–76 years) in the familial group and 30.0 years (age range 2–69 years) in the sporadic cases. (Fig. 1). The risk of onset of the disease up to 20 years was higher in the familial group ($P=0.008$, OR 2.407, 95% CI 1.246–4.543). In addition, we established positive PCA antibodies in 21 cases, ANA in six cases, AAA in five cases and RF in 14 cases in the whole group of vitiligo patients. The numbers of concomitant autoimmune diseases besides thyroid disease were halo nevi in 28 cases, psoriasis in 10 cases, rheumatoid arthritis and diabetes both in seven cases, alopecia areata and pernicious anaemia both in four cases.

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**Table 1** Clinical type of vitiligo at the onset of disease compared with type at the examination in groups of familial and sporadic vitiligo

<table>
<thead>
<tr>
<th>Clinical type</th>
<th>Familial vitiligo: number of the subjects (%)</th>
<th>Sporadic vitiligo: number of the subjects (%)</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>At the onset</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitiligo vulgaris</td>
<td>43 (84%)</td>
<td>87 (65%)</td>
<td>0.008*</td>
</tr>
<tr>
<td>Focal vitiligo</td>
<td>5 (10%)</td>
<td>26 (19%)</td>
<td>0.123</td>
</tr>
<tr>
<td>Segmental vitiligo</td>
<td>1 (2%)</td>
<td>4 (3%)</td>
<td>0.706</td>
</tr>
<tr>
<td>Acrofacial vitiligo</td>
<td>2 (4%)</td>
<td>18 (13%)</td>
<td>0.065</td>
</tr>
<tr>
<td>At the examination</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitiligo vulgaris</td>
<td>46 (90%)</td>
<td>107 (79%)</td>
<td>0.082</td>
</tr>
<tr>
<td>Focal vitiligo</td>
<td>0 (0%)</td>
<td>9 (7%)</td>
<td>0</td>
</tr>
<tr>
<td>Segmental vitiligo</td>
<td>1 (2%)</td>
<td>5 (4%)</td>
<td>0.548</td>
</tr>
<tr>
<td>Acrofacial vitiligo</td>
<td>1 (2%)</td>
<td>11 (8%)</td>
<td>0.125</td>
</tr>
<tr>
<td>Universal vitiligo</td>
<td>3 (6%)</td>
<td>3 (2%)</td>
<td>0.207</td>
</tr>
</tbody>
</table>

$*P<0.05$. 

Family history of vitiligo was not associated with concomitant autoimmune diseases, but we saw several autoimmune diseases in the whole group of vitiligo patients. Thyroid disease was the most common autoimmune disease, specifically 61 TPO positive subjects in whole vitiligo group were found. Moreover, thyroid disease among relatives was reported higher in familial group comparing with sporadic cases ($P=0.03$, OR 2.200, 95% CI 1.064–4.548). In addition, we established positive PCA antibodies in 21 cases, ANA in six cases, AAA in five cases and RF in 14 cases in the whole group of vitiligo patients. The numbers of concomitant autoimmune diseases besides thyroid disease were halo nevi in 28 cases, psoriasis in 10 cases, rheumatoid arthritis and diabetes both in seven cases, alopecia areata and pernicious anaemia both in four cases.
cases, scleroderma in two cases, sclerosis multiplex, ankylosing spondylitis and autoimmune thrombocytopenia all in one cases. Nevertheless, when the frequency of concomitant diseases, autoimmune diseases and positive autoantibody findings between familial and sporadic vitiligo patients were compared, statistically significant differences between the groups were not found.

In sporadic cases, female gender and disease duration of 10 years and longer were a risk factors for more extensive depigmentation (BSA over 10%; \( P = 0.001 \), OR 3.984, 95% CI 1.668–9.520 and \( P = 0.001 \), OR 3.560, 95% CI 1.681–7.539; respectively).

Very extensive depigmentation, BSA over 50%, was associated with reported triggering factors (mechanical injury, psychological stress, hormonal changes, sunburn, radiation, skin irritation, drug intake and other disease) both in familial (\( P = 0.0005 \), OR 10.560, 95% CI 2.451–45.497) and sporadic (\( P = 0.004 \), OR 7.630, 95% CI 1.580–36.858) cases. BSA over 50% was also a risk factor for mucosal involvement both in familial (\( P = 0.01 \), OR 8.000, 95% CI 1.261–50.772) and sporadic (\( P = 0.004 \), OR 7.375, CI 1.550–35.096) groups. Association between widespread depigmentation (BSA over 50%) and leukotrichia was seen in both groups, but statistical difference was significant in familial group (\( P = 0.0001 \); OR 26.923, 95% CI 3.178–228.060). Patients with sporadic vitiligo with BSA over 50% had higher risk for serological autoantibody findings (\( P = 0.03 \), OR 4.941, 95%CI 1.005–24.300), especially the presence of PCA and ANA antibodies (\( P = 0.04 \); OR 4.457; 95%CI 0.994–19.978 and \( P = 0.0002 \); OR 28.250; 95%CI 2.307–345.989 respectively) (Table 2).

**Discussion**

In this study, the average age of onset of vitiligo was earlier (24.8 years) and the risk of having vitiligo up to the age of 20 was statistically higher in familial group comparing with sporadic cases. Our data are in agreement with most previous findings that female gender and female gender increases the risk for more widespread vitiligo have a higher risk for vulgar type at the beginning of the disease and female gender increases the risk for vulvar type at the onset of the disease.

An opposite to Ando et al. and Misri et al., who did not find correlation between the extension of depigmentation and positive family history of vitiligo, our study confirms that patients with familial vitiligo have higher risk for more widespread depigmentation and the association gets stronger in cases with BSA over 50%.\(^5,^7\) We found that positive family history is high among Caucasian patients with III–IV skin phototype, cited also by Alzolibani in Saudi-Arabic population.\(^6\)

Similarly to other investigators, we could not find statistical correlation between positive family history of vitiligo and disease activity, areas involved, leukotrichia, mucosal involvement, Koebner sign and triggering factors.\(^5,^6,^8,^11\) Family history of vitiligo was not associated with reported concomitant diseases, including autoimmune diseases and positive autoantibody finding. Despite this, thyroid disease among relatives was reported higher in familial group comparing with sporadic cases, demonstrated also by Laberge et al.\(^8\)

Our results stress the importance of female gender in vitiligo, as in sporadic cases female gender raises the risk for more widespread depigmentation. No-one has pointed it out yet. Widespread depigmentation, BSA over 10%, was also correlated with prolonged duration of vitiligo. We could not reveal any correlation between female gender and attendance of other autoimmune diseases, including thyroid disease and antibodies positivity, as previous studies have shown.\(^12–14\)

In addition, patients with sporadic vitiligo and very extensive depigmentation have higher risk for mucosal depigmentation, the presence of triggering factors, PCA and ANA antibodies. In the same time, patients with very widespread depigmentation and positive family history of vitiligo have higher risk for leukotrichia, mucosal depigmentation and the presence of triggering factors. This finding supports overall agreement that external factors as well as concurrent autoimmune conditions predict the widespread eruption.

**Conclusion**

In this study, we demonstrated first time that patients with familial vitiligo have a higher risk for vulgar type at the beginning of the disease and female gender increases the risk for more extensive depigmentation in sporadic cases.

**Acknowledgements**

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