Skin changes in the neck and selenium content in patients with thyroid diseases

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ABSTRACT

**Purpose:** Occurrence of skin changes, in the form of discolouration on neck and in form of a so-called "thyroid shadow", was observed in patients with: Hashimoto’s disease, Graves’ disease, struma nodosa euthyrotica or hyperthyreosis. Effects of selenium status and smoking on the risk of those skin changes were investigated.

**Materials and methods:** The study group consisted of 267 patients with different kinds of thyroid disease. The control group included 34 healthy people. Selenium concentrations in serum were determined by electrothermal absorption spectrometry method.

**Results:** Thyroid shadow was observed in 70 percent of the subject. Selenium levels in serum were lower in patients with thyroid disease (65.051±16.70 µg/L), especially in smokers (62.477±15.21 µg/L) than in the control group (75.162±19.92 µg/L).

**Conclusions:** Thyroid shadow syndrome would be the diagnostic signal of thyroid diseases, especially Hashimoto disease. Selenium status is important in the studied thyroid diseases. Cigarette smoking decreases the concentration of selenium in the serum of patients with thyroid diseases.

**Keywords:** Thyroid shadow, selenium, smoking

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INTRODUCTION

There are numerous classifications of chronic thyroiditis, some of them based on clinical symptoms and immunological status and other related to microscopic criteria [1-3]. Hashimoto’s thyroiditis and Graves’ disease are different expressions of a basically similar autoimmune process. People with classic Hashimoto’s thyroiditis have serum antibodies reacting with thyroglobulin and thyroid peroxidase [4]. Among various external and environmental factors, cigarette smoking seems to play a role in the pathogenesis of autoimmune thyroiditis, along with viral infections, excess of iodine and recently – also selenium deficiency. Some drugs, for instance Amiodaron, lithium salts, interferon-alpha, granulocyte growth factor or interleukin-2, may induce synthesis of thyroid antibodies in previously healthy subjects. Moreover, the aforementioned factors play a role in the manifestation of hypothyroidism and exacerbation of autoimmune process in patients with previously demonstrated thyroperoxidase (ATPO) and thyroglobulin (ATG) autoantibodies [5-9]. Currently more attention is being paid to the association between selenium supplementation and natural course of autoimmune thyroid disorders. The thyroid is the organ with the highest selenium content per gram of tissue. Selenium status appears to have an impact on the development of thyroid pathologies [10].

Recent studies revealed positive effects of several weeks of selenium administration. Results showed decreased titers of thyroperoxidase antibodies in patients with autoimmune thyroid diseases [11, 12]. Negro et al. [13] revealed that selenium supplementation during pregnancy and postpartum period inhibits progress of Hashimoto’s thyroiditis and results in decreased ATPO titers and improved ultrasound thyroid echogenicity. Recent studies indicate a link between autoimmune disorders such as Hashimoto thyroiditis and the incidence of skin changes, for instance chronic spontaneous urticaria or vitiligo [14,15]. Effects of selenium status and smoking on the risk of skin changes were investigated.

MATERIALS AND METHODS

Two hundred sixty seven patients (260 women and 7 men) aged 49±14 years were treated in three endocrinology outpatient clinics in various towns of Poland (Białystok, Zambrów, Kętrzyn). Patients eligible for the study were not earlier treated for thyroid disorders. In the examined patients, levels of TSH, fT3, fT4 and titers of thyroglobulin and thyroperoxidase antibodies were evaluated. Thyroid disorder was confirmed by means of a standard ultrason while histopathological examination of thin needle biopsy was performed whenever feasible. Patients qualified for the study were examined thoroughly with the visual inspection of the skin on the neck in daylight. Patients did not report any other skin problems. Moreover, they were asked about smoking. Control group was composed of 34 healthy volunteers – 33 women and 1 man (average age 43±13 years). Both subjects, patients and healthy individuals included in the study did not take dietary supplements of selenium. Protocol of the study was approved by the Local Ethical Committee. Patients and control group data are shown in Table 1.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients with thyroid diseases (n = 267)</th>
<th>Control group (n = 34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (F/M)</td>
<td>260/7</td>
<td>33/1</td>
</tr>
<tr>
<td>Age (years) – Mean (range)</td>
<td>49 ± 14 (17-75)</td>
<td>43 ± 13 (19-65)</td>
</tr>
<tr>
<td>Smoking/No-smoking*</td>
<td>150/117</td>
<td>14/20</td>
</tr>
</tbody>
</table>

F – female, M – male; *number of cigarettes: 5-20 daily

Samples of venous blood from patients and control group were drawn using the vacutainer system test tubes containing clot activator (Becton Dickinson, France). The samples were allowed to clot within 30 minutes then centrifuged within 10 minutes at approximately 1000 x g. Serum was removed and kept frozen at - 20°C. The concentration of selenium in the serum was analyzed by the electrothermal atomic absorption spectrometry technique with the Zeeman background correction on the Hitachi spectrometer of Z-5000 model. The accuracy of selenium determination methods was verified using the following certified standard materials MIO 181 (Seronorm Trace Elements, Serum Level 1, Sero AS, Norway). The samples were determined in the Department of Bromatology of the Medical University in Białystok, which is involved in a quality control program for trace elements analysis supervised by the Institute of Chemistry and Nuclear Techniques and the National Institute of Public Health National Institute of Hygiene in Poland.

Statistical analyses were performed using Statistica v.10.0 software. Differences between independent groups were tested by the Mann-Whitney U-test. P values less than 0.05 were considered statistically significant.
RESULTS

Skin lesions in the form of discolorations and disorder of pigmentation in the thyroidal region of neck (Fig.1) were observed in 70% of subjects with thyroid diseases (from 45% in struma nodosa euthyrotica to in ca 86% of Hashimoto’s disease patients (Table 2). Their frequency and intensity increased with the disease progress. The content of selenium in serum in the control group was 75.162±19.92µg/L. The average levels of selenium in serum of patients with thyroid diseases were decreased in: Hashimoto’s disease (63.026±17.31 µg/L), Graves’ disease (59.734±10.42 µg/L) and struma nodosa euthyrotica (67.593±15.88 µg/L); but not in struma nodosa hyperthyreosis (68.583±16.43 µg/L) (Table 2). The average content of selenium in serum of patients with Hashimoto disease with skin changes (64.998 ±16.93 µg/L; n=123) was significantly higher (p<0.0007) than in patients without skin lesion (50.776 ±14.72 µg/L; n=120). The concentrations of selenium in the smoking group of patients with Hashimoto’s disease (59.632±13.58 µg/L) and all of patients with thyroid diseases (62.477±15.21 µg/L) were significantly lower than in the non-smoking group (68.620±21.30 µg/L and 67.994±17.77 µg/L, respectively) (Table 3).

![Figure 1A and 1B: Photo documentation of skin changes in patients with Hashimoto’s disease.](image)

Table 2. The concentration of serum selenium in patients with thyroid diseases and skin changes.

<table>
<thead>
<tr>
<th>No.</th>
<th>Thyroid diseases</th>
<th>Concentration of selenium µg/L ± SD</th>
<th>Without skin changes (A) (n)</th>
<th>With skin changes (B)(n %)</th>
<th>Total (C) (n)</th>
<th>PAB</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Control</td>
<td>75.162±19.92 (34)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Hashimoto disease</td>
<td>50.776±14.72 (20)</td>
<td>64.998±16.93 (123 -86%)</td>
<td>63.026±17.31 (143)</td>
<td>0.0007*</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>P1/2A&lt;0.0003*</td>
<td>P1/2B&lt;0.004*</td>
<td>P1/2C&lt;0.0007*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Graves´ disease</td>
<td>63.467±13.80 (3)</td>
<td>57.686±9.21 (6 – 67%)</td>
<td>59.734±10.42 (9)</td>
<td>0.485</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(12)</td>
<td>(25 – 67%)</td>
<td>(37)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>Struma nodosa hyperthyreosis</td>
<td>68.280±19.94 (12)</td>
<td>68.735±14.85 (25 – 67%)</td>
<td>68.583±16.43 (37)</td>
<td>0.939</td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Struma nodosa euthyrotica</td>
<td>68.581±17.37 (43)</td>
<td>66.379±13.98 (35 – 45%)</td>
<td>67.593±15.88 (78)</td>
<td>0.546</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(43)</td>
<td>(35 – 45%)</td>
<td>(78)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>All studied diseases</td>
<td>63.941±18.42 (77)</td>
<td>65.519±15.96 (183 – 70%)</td>
<td>65.051±16.70 (267)</td>
<td>0.488</td>
<td></td>
</tr>
</tbody>
</table>

n - number of patients; p – significance level ; % - percent of total patients in studied group
SD - Standard deviation
### DISCUSSION

Skin of hypothyroid patients is usually dry, rough and cold. These changes result from the direct effects of thyroid hormones on the skin trophism and perfusion. Consequently, the measurements of skin perfusion by means of laser Doppler flowmetry [16, 17] revealed that such parameters as mean capillary flow velocity, capillary pulse wave amplitude, and capillary flow oscillation amplitude were decreased in non-treated hypothyroid patients compared to those with normal levels of thyroid hormones. The aforementioned changes were even more pronounced if compared to hyperthyroid subjects. In hypothyroidism, the reactive constriction of blood vessels, responsible for maintenance of proper body temperature under hypothermia, results in visible pallor and coolness of skin [17]. Lack of carotene metabolism in liver causes its accumulation in the stratum corneum of skin. Carotene is eliminated with sweat and reabsorbed through skin and its deposits are formed mostly in the regions rich in sebaceous glands. It is another factor responsible for the change in skin color to a characteristic, yellowish one, also known as carotenodermia. Hashimoto’s thyroiditis is oligosymptomatic and its signs are mostly related to the consequences of that disorder, i.e. the initial hyper- and subsequent hypothyroidism. There are no pathognomonic symptoms for the condition besides the biochemical parameters.

Skin lesions in the form of discoloration, like carotenodermia, on neck, may be characteristic of the studied disease. Because of their shape, they are sometimes described as “thyroid shadow”. This characteristic feature constitutes an important and easy to distinguish symptom and hence enables identification of the risk group among Hashimoto’s thyroid patients. The symptom described, if widely recognized and understood by family physicians and dermatologists will facilitate referral of patients to endocrinology outpatient clinics and the implementation of proper treatment of Hashimoto’s thyroiditis. Considering 70% incidence of the symptom, its clinical application is likely to reduce the redundant costs of diagnosis. These skin changes demonstrate direct positive correlation with smoking. Thyroid belongs to a group of organs with the highest concentration of selenium per mass unit. Selenoproteins participate in cellular antioxidative protection and redox control systems, such as glutathione peroxidase (GPX) and thioredoxin reductases (TxnRd). Consequently, they play a role in the protection of thyroid against the excess of hydrogen peroxide and reactive oxygen radicals synthesized by its follicles in course of hormonal biosynthesis [18]. In iodine deficiency, the excessive supplementation of selenium (selenium saturation) results in the increased activity of type 1 5’-deiodinase and subsequent enhanced metabolism of T4. That, in turn, exacerbates the existing hypothyroidism, since – deficient in iodine –thyroid is unable to compensate for the increased degradation of T4 [8,19-21]. Despite its role in thyroid metabolism, serum levels of selenium in patients with various thyroid disorders were decreased in all patients, without subjects with struma nodosa hyperthyreosis. Consequently, the study proved the importance of that element for the proper function of the thyroid. The reference level of selenium in the serum is 70 – 140 µg/L [22].

We observed decreased the mean selenium concentration in the serum of examined patients with thyroid diseases, whereas the average level of selenium was within the reference range in the control

### Table 3. Smoking and concentrations of selenium in serum in patients with thyroid diseases.

<table>
<thead>
<tr>
<th>No.</th>
<th>Thyroidis disease</th>
<th>Concentration of selenium µg/L ± SD</th>
<th>pA/B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Smokers (A)</td>
<td>Non smokers (B)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(n)</td>
<td>(n)</td>
</tr>
<tr>
<td>1.</td>
<td>Hashimoto disease</td>
<td>59.632±13.58 (95)</td>
<td>68.620±21.30 (48)</td>
</tr>
<tr>
<td>2.</td>
<td>Graves’ disease</td>
<td>59.568±11.06 (4)</td>
<td>59.868±11.19 (5)</td>
</tr>
<tr>
<td>3.</td>
<td>Struma nodosa hyperthyreosis</td>
<td>68.312±16.68 (21)</td>
<td>68.962±16.64 (16)</td>
</tr>
<tr>
<td>4.</td>
<td>Struma nodosa euthyrotica</td>
<td>67.385±17.43 (30)</td>
<td>67.950±15.01 (48)</td>
</tr>
<tr>
<td>5.</td>
<td>Total</td>
<td>62.477±15.21 (150)</td>
<td>67.994±17.77 (117)</td>
</tr>
</tbody>
</table>

n - number of patients; p – significance level; SD - Standard deviation
group. Studies showed that selenium levels in subjects from different regions of Poland are low [23].

Our results indicate the need for selenium supplementation in patients with thyroid diseases. On the other hand, studies from the Austrain region showed no significant decrease in the concentration of selenium in patients with Hashimoto's thyroiditis, selenium concentrations in both the examined and control group were within the reference range [24].

Review of research [25] has demonstrated that currently there is no confirmed evidence of the benefits of supplementation in patients with Hashimoto's thyroiditis. The review highlights the need for randomised placebo-controlled trials to evaluate the effects of selenium in people with Hashimoto disease. Studies also indicate that the effect of selenium depends on the genetic background and the baseline level of selenium in the serum. Genetic polymorphism has a functional significance and it is associated with different response of Gpx1 activity to selenium [26,27].

It was revealed, however, that the serum selenium concentration in patients with thyroid disorders was not correlated with the skin changes in our study. Other studies have demonstrated that antioxidant supplements improve parameters related to skin structure in humans [28]. Selenium plays a role in immunotolerization, a cell-mediated process involved in many aspects of immune function. The consumption of yeast low in selenium induced energy in skin responses and increased counts of natural killer cells and T lymphocytes, but did not change them in the high-selenium supplementation group [29].

In conclusion, skin lesions in the form of decolorations and discolorations on the neck were observed in 70% of patients with the studied thyroid diseases; mainly in 86% of cases with Hashimoto’s thyroiditis patients. Serum levels of selenium in patients with thyroid diseases, without struma nodosa hyperthyreosis, were decreased and should be raised by supplementation of this trace element, after the initial determination the concentration of selenium in the serum. Despite being below the normal limit, selenium concentration in serum in Hashimoto’s thyroiditis patients with skin lesions was higher, compared to those with the same disease, but unaffected skin. Cigarette smoking additionally decreases the concentration of selenium in the serum of patients with thyroid diseases; therefore, people diagnosed with thyroid disorders should stop smoking cigarettes.

Conflicts of interest
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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REFERENCES


