CUTANEOUS MANIFESTATIONS ASSOCIATED WITH THYROID DISEASE

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CUTANEOUS MANIFESTATIONS ASSOCIATED WITH THYROID DISEASE (Abstract): Aim: To present the clinical and laboratory features of patients with dermatologic disorders associated with thyroid diseases, diagnostic criteria, type of administered treatment and its effectiveness. Material and methods: This study is a retrospective study based on the medical records of patients with thyroid diseases admitted to the Dermatovenerology Clinic of the Iași “Sf. Spiridon” University Emergency Hospital between January 1, 2012-December 31, 2013. Data on clinical manifestations, methods of investigation, therapeutic approach, and associated dermatologic and systemic diseases were reviewed. Results: A total of 38 patients were enrolled in this study of which 36 females and two males. An high incidence of cases with autoimmune thyroiditis (63%), followed by polynodular goiter (26.3%) and hypothyroidism (10.7%) was found during the study. The identified dermatologic disorders associated with thyroid diseases were in order of frequency alopecia areata (22%), followed by lichen planus (18%). Conclusions: This study demonstrates that there is a significant association between certain dermatologic disorders and thyroid diseases, requiring periodic thyroid function tests. Keywords: THYROID DISORDERS, CUTANEOUS MANIFESTATIONS, AUTOIMMUNE THYROIDITIS

Thyroid disorders are recognized for their involvement in all systems of the human body, and the skin is no exception. Some skin changes and dermatologic disorders may be the first symptoms of thyroid disease.

Some studies have suggested that thyroid hormones play a pivotal role in the embryonic development of the skin, as well as in maintaining normal skin function in adult skin (1).

Skin changes occur both in hyperthyroidism and in hypothyroidism. In hyperthyroidism the skin is soft, moist, and
warm associating hyperpigmentation (diffuse, localized or Addison disease) or palmar erythema. Heat is due to increased skin blood flow and peripheral vasodilatation, which can also lead to flushing and palmar erythema. Hyperhidrosis more marked on the palms and soles may be present. In hyperthyroidism hair is described as soft, fine with or without non-scarring alopecia. The presence of thyroid hormone receptors in dermal papilla and external epithelial sheath has been demonstrated (2).

In hypothyroidism, the skin tends to be pale, both because of dermal mucopolysaccharides and dermal water content. The increased dermal carotenoid levels cause a yellow discoloration of the palms, soles and nasolabial sulcus. The most characteristic clinical sign of hypothyroidism is generalized myxedema resulting from the deposition of hydrophilic mucopolysaccharides in the dermis, especially hyaluronic acid and chondroitin sulfate. The skin may appear edematous, dry, pale as wax and firm to touch. Hair in hypothyroidism is coarse, dry, brittle, with reduced diameter, showing an increased tendency to fall, often resulting in partial alopecia (2, 3).

The term of thyroid ophthalmopathy is currently used but the disease process involves the orbital and periocular soft tissues with secondary effects on the eye. Thus, Thyroid-associated orbitopathy (TAO) is a more appropriate definition. The ocular manifestations of TAO can coincide or even precede other systemic complications and include superior eyelid retraction, periorbital edema with secondary proptosis, conjunctival injection and chemosis and impaired ocular motility. While ocular involvement is usually not threatening vision excepting the very severe cases of exposure keratopathy, compressive optic neuropathy and ocular hypertension almost 20% of the patients consider the ocular morbidity in TAO more troublesome than the systemic complications of dysthyroidism (4).

Some skin conditions and diseases with predominantly cutaneous manifestations were associated with thyroid dysfunction or presence of thyroid antibodies. These conditions can be grouped into connective tissue disease (systemic lupus erythematosus, scleroderma, Sjogren's syndrome, dermatomyositis), bullous dermatoses (bullous pemphigoid, pemphigus vulgaris, pemphigus foliaceus, herpetiform dermatitis), pigmentation disorders (melasma, vitiligo) and other diseases (alopecia, lichen planus, granuloma annulare) (5).

The aim of this study was to present the clinical and laboratory features of patients with dermatologic disorders associated with thyroid diseases, diagnostic criteria, types of administered treatment and their effectiveness based on the study of the patients admitted to the Iasi Dermatology Clinic in the interval January 1, 2012-December 31, 2013.

MATERIAL AND METHODS
This is a retrospective study of the patients with thyroid diseases admitted to the Dermatology Clinic of the Iasi "Sf. Spiridon" University Emergency Hospital in the interval January 1, 2012-December 31, 2013. Data on clinical manifestations, methods of investigation, therapeutic approach, and associated dermatologic and systemic diseases were reviewed.

A total of 38 patients, 36 females and 2 males, were included in the study.

The study was based on patient medical records and photos. Based on the obtained data the patients were grouped according to distribution by age, sex, area of residence, socioeconomic status, clinical features,
association with other diseases, type of administered treatment and its effectiveness.

RESULTS
Between January 1, 2012-December 31, 2013 at the Dermatology Clinic of the Iasi "Sf. Spiridon" University Emergency Hospital of the total of 7672 admissions, 38 patients were admitted for dermatologic disorders associated with thyroid diseases. Thus, the prevalence of thyroid diseases was 0.5%. Based on the obtained data we found that the prevalence of thyroid diseases had increased each year as follows: from 28 in 2012 to 34 in 2013. In the study group thyroid diseases were more common in the rural population (58% vs. 42%), corresponding to a ratio of 1:1.36. A higher frequency of thyroid disorders was found among female patients (95%).

The age of the study patients ranged between 14 and 79 years, most patients belonging to age groups 50-60 years (31.8%) and 60-70 years (21%) (fig. 1).

During the study an increased incidence of the cases with autoimmune thyroiditis (63%), followed by polynodular goiter (26.3%) and hypothyroidism (10.7%) was noted. Of the 24 cases with autoimmune thyroiditis, 11 cases presented hypothyroid status and 13 cases euthyroid status, no cases of autoimmune thyroidopathy with hyperthyroid status being recorded.

Thyroid diseases are accompanied by various skin manifestations. In this study these manifestations were: xerosis, xanthelasma, keratoderma, onycho-dystrophy and oral candidiasis. Given the predominance of thyroid dysfunction with hypothyroid status, xerosis was the most common manifestation (45.8%) (fig. 2).

In the study certain dermatologic disorders associated with thyroid pathology were identified. There was an increased incidence of alopecia areata (7 cases, accounting for 22% of all skin disorders associated with thyroid diseases) followed by 6 cases (18%) diagnosed with lichen planus and 4 cases each (12%) with chronic urticaria and psoriasis (12%). There were 3 cases (9%) of lupus erythematosus. Also, vitiligo and scleroderma were found in a similar percentage as lupus erythematosus, 9% respectively. The lowest incidence of skin diseases associated with thyroid disease was recorded for pemphigus vulgaris (1 case), pemphigus foliaceus (1 case) and granuloma annulare (1 case), accounting for 3% of the cases.
The youngest age at onset of *alopecia areata* in our patients was 19 years and the oldest age at onset 68 years, the age group over 40 years being most commonly affected (71%). There was a higher frequency of alopecia in women (86%) (fig. 3).

The association of *lichen planus* with autoimmune diseases is well-known; in this study 6 cases with different clinical forms and anatomical locations being found. The most common anatomical sites were the oral and anogenital regions. The role of autoimmune pathogenesis is supported by the association with numerous autoimmune diseases; in our study of the 6 cases of *lichen planus* associated with thyroid diseases 3 cases were associated with *vitiligo*. The youngest age of patients with *lichen planus* was 39 years and the oldest age 65 years, most cases in age group 40-60 years and with a female predominance (86%). Of the 6 cases of *lichen planus*, 3 cases were associated with autoimmune thyroid disease with euthyroid status, 3 cases with polynodular goiter and 2 cases with autoimmune thyroid disease with operated nodules.

Of the 38 study patients only 3 were diagnosed with *vitiligo* associated with autoimmune thyroiditis. The age ranges were 39-65 years, with a female predominance. In the 3 cases diagnosed with *vitiligo* the associated thyroid diseases were: euthyroid autoimmune thyroiditis (2 cases) and autoimmune thyroiditis with hypothyroid status (1 case).

Age of patients with scleroderma ranged from 53 to 73 years. All three patients were females. Thyroid diseases associated with scleroderma were autoimmune thyroiditis with hypothyroid status (2 cases) and polynodular goiter (1 case).
Of the 38 cases with thyroid disease anti-thyroid antibodies were positive only in 5 of the 7 patients with alopecia areata, 2 of the 3 cases with vitiligo, 1 of the 4 cases with psoriasis, 1 of the 3 cases with scleroderma, 2 of the 6 cases with lichen planus and one case diagnosed with granuloma annulare. Antithyroid antibodies were positive in all patients diagnosed with systemic lupus erythematosus and chronic urticaria, and in patients with pemphigus antithyroid antibodies were not measured.

All patients were systematically evaluated by an ophthalmologist and none of the signs mentioned above were noticed. A degree of mild conjunctival injection and dry eye symptoms could be noticed and were treated with topical medication.

The treatment was individualized for each patient depending on associated diseases. As there are no cases of hyperthyroidism, only hypothyroid patients were treated. Levothyroxine replacement therapy was initiated depending on thyroid hormone levels, no treatment being administered to euthyroid patients. Of the 38 patients, 18 were received levothyroxine. To the treatment of thyroid disease was associated the treatment of skin disease.

**DISCUSSION**

The prevalence of thyroid diseases at the Iasi Dermatology Clinic is 0.5%, much lower compared with literature data according to which the prevalence is estimated to be 2-5% (6, 7). Our data are in agreement with the data in the literature according to which all ages are affected by thyroid disease, with a peak incidence between 35 and 65 years.

The prevalence of lichen planus (16%) is similar with that reported in the literature. Kreuter et al. (8) conducted a retrospective study and found that 15.4% of patients with atrophic lichen sclerosus presented an associated autoimmune disease. 16.3% of patients with atrophic lichen sclerosus had a thyroid disease of Hashimoto thyroiditis and Graves’s disease type and positive anti-thyroid antibodies in 9.4%.

It has been reported that patients with chronic spontaneous urticaria also have associated autoimmune diseases, particularly autoimmune thyroid disorders such as Hashimoto thyroiditis. Several studies have shown that a significant number of patients (33%) had elevated anti-thyroid antibody levels (9, 10), whereas in our study group this percentage was of only 12%. Compared to the literature, the incidence of cases with of psoriasis vulgaris at the Iasi Dermatology Clinic was higher than that reported in a study on 1236 patients, 12% vs. 1.77%, respectively (11).

**CONCLUSIONS**

This study demonstrates that there is a significant association between certain dermatologic and thyroid disorders, requiring periodic thyroid function tests.

**REFERENCES**


**NEWS**

**INCREASED THICKNESS OF ABDOMINAL SUBCUTANEOUS ADIPOSE TISSUE OCCURS MORE FREQUENTLY IN STEATOHEPATITIS THAN IN SIMPLE STEATOSIS**

The incidence of obesity is increasing and contributes to the rising incidence of fatty liver. Body mass index (BMI) is used to assess the degree of obesity but does not take into account the pattern of body fat distribution. The incidence of fatty liver disease, both nonalcoholic steatohepatitis (NASH) and simple steatosis, is increasing in the Western world. In a large autopsy study of obese patients and controls, a 6.2% incidence of NASH was found. The need to distinguish between NASH and simple steatosis is essential; as patients with NASH can go on to develop portal hypertension and cirrhosis. Body mass index (BMI) is commonly used to define overweight and obesity but does not predict the presence of NASH or simple steatosis. Despite a normal BMI, patients may still develop nonalcoholic fatty liver disease (NAFLD), especially if they have a more prominent abdominal distribution of their adipose tissue. Thicker abdominal subcutaneous adipose tissue is associated with steatohepatitis, but not simple steatosis, also for patients with BMI below 25 kg/m2. There is good correlation between abdominal subcutaneous adipose tissue thickness and BMI. A trend noted in this study is that patients with NASH died at a younger age. Fibrocongestive splenomegaly, despite the absence of cirrhosis, may occur in some patients with steatohepatitis (Fiel MI, Sima HR, Desman G, et al. Increased Thickness of Abdominal Subcutaneous Adipose Tissue Occurs More Frequently in Steatohepatitis than in Simple Steatosis. Arch Pathol Lab Med. 2013; 137: 642–646).

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