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FAMILIAL ALOPECIA ARETA, ATOPY AND THYROIDITIS HASHIMOTO

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ABSTRACT:

We present a case of morbid association of two organ-specific autoimmune diseases (Alopecia areata-AA and Thyreoiditis Hashimoto-TH) in two white sisters - 23 and 26 years old. There is no family history of AA or any autoimmune disorders.

The onset of AA, in the both sisters was in early childhood (3 and 7 years of age). The clinical and laboratory examinations showed engagement of the scalp with round or oval large patches of alopecia, without involvement of the body hairs and nails. There were also alterations of thyroid gland function, positive TMA (Thyroid Microsomal Antibodies) and Rц-data of Pituitary adenoma as well as episodes of allergic rhinitis (in one of the sisters), and bronchial asthma (in the other). According to Ikeda's classification, they have an "Atopic type" AA. We suppose that the observed case is not an occasional coincidence of AA and TH. HLA Aw32B18 determination could be support our suggesting about the familial pattern of these autoimmune diseases.

Key Words: familial alopecia areata, thyreoiditis Hashimoto, "Atopic type" of alopecia areata, Ikeda's classification, morbid associations of alopecia areata.

Alopecia areata (AA) is a disease, which has been known for more than 2000 years. In USA around 1.7 % of all the population [4] and 2-3 % of those requested for specialised dermatological help are patients with different severity of alopecia areata.

We present a case of morbid association of two organ-specific autoimmune diseases (AA and TH), accompanied with atopy and family history.

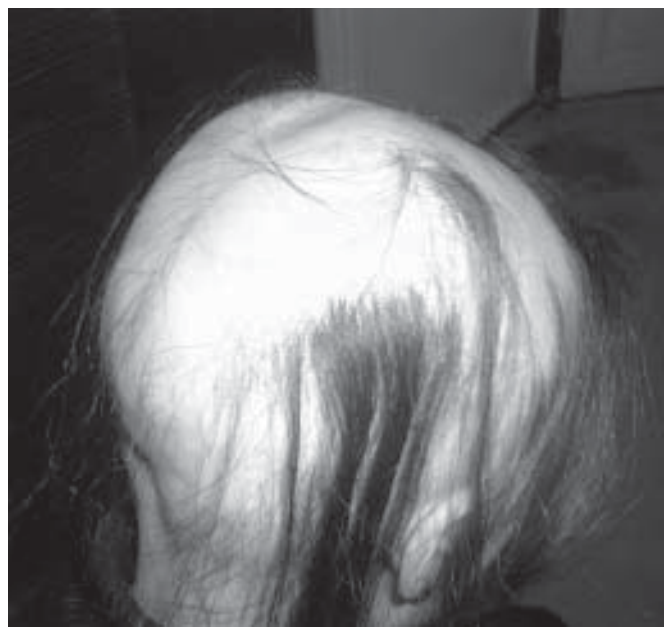
PATIENT I

History:

GK - 25 year old woman. The disease has started at the age of 3 with the appearance of several alopetic patches with diameter from 2 to 4 cm, localised mostly in the vertex and occipital area. Along with the recovery of the patches, during the next 5-6 months other alopetic areas appeared.

The disease has relapsing course without full remissions.

At the age of 14 because of thyroid hypofunction, a substituting therapy with L-Thyroxin (50 mkg/d) was administered. The histopathology investigation of the thyroid gland established lymphocitary type thyreoiditis, corresponding to the diagnosis Thyreoiditis Hashimoto.



The ddiscontinuation of the therapy with L-Thyroxin at the age of 20 coincided with the appearance of new alopetic patches enlarged in size, coalesced and formed ophiasis Celsii.

The patient complaints of recurring seasonal rhinitis.

Since the beginning of the disease till now, the patient was treated with local irritants, corticosteroids, acupuncture. During the last two years, 10 ampoules of ssystemic corticosteroids with depot-effect (Diprophos) were administered, with transient effect.

The sister has alopecia areata. Mother - data for thyroid disease.

Physical Examination:

On the scalp - extensive in size, irregular shaped with well distinct border alopetic areas, enveloping the vertex, parietal and occipital regions - S_4 B_0 N_1 - table 1. In most of the alopetic areas (except the vertex-occipital regions) the skin's follicular structure is preserved. No erythema, infiltrate

or desquamation is observed. The hairs have normal hair pluckability around the patches. Presence of a great number of broken hairs type "exclamation marks**"**, scattered over all alopetic areas is observed. Almost everywhere regrowth of single terminal and mostly velus hairs recovery is observed.

The disease tends to form ophiasis Celsii.

Nails - singular pittings and discrete longitudinal rows on the nails of the hands.

Neck lymphadenomegalia established.

Laboratory Data:

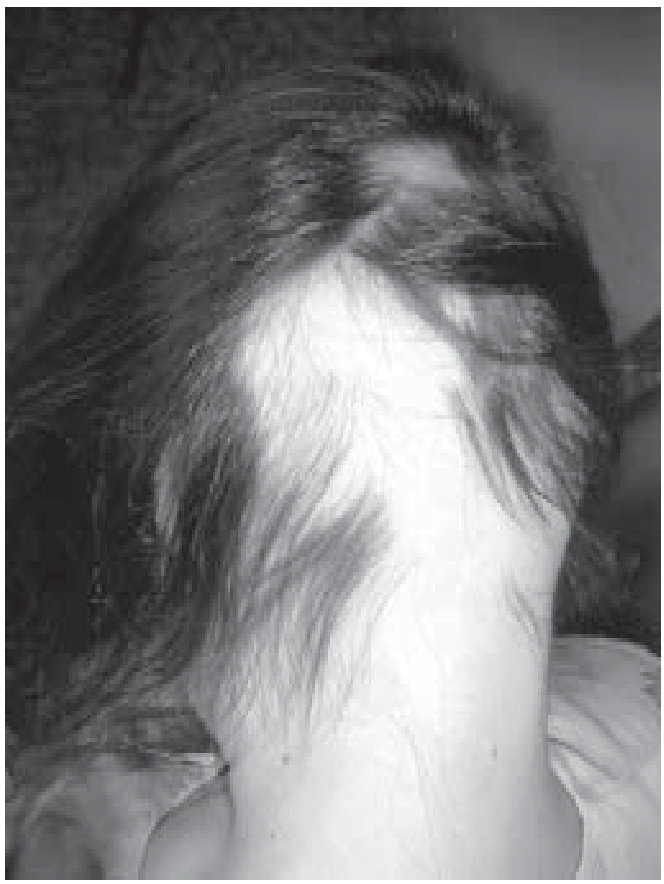
The routine laboratory test results are within normal boundaries.

Immunology - MAT titre - repetitively increased values - 5,7; 5,8 (ref. <0,6 Units).

X-ray of pituitary gland - Cela Brьcke and Adenoma Gl. Hypophisae established.

HLA Typing: HLA- A* **02**
B* **15**, **27**
DRB1* 07 (**B4***), 16 (**B5***)

PATIENT II



History:

NK - 26 year old woman. The alopecia has started at the age of 8, with the appearance of discrete small sized alopetic patches on the scalp. The disease has relapsing course, without full remissions.

In early childhood an allergy to house dust, cigarette smoke and pollens was established.

At the age of 15 - hypothyreoidism established, compensated with L-Thyroxin (100mkg/d - >50 mkg/d). The puncture biopsy of the thyroid gland revealed Thyreoiditis Hashimoto.

Asthma bronchiale was diagnosed at the age of 18, which is currently in clinical remission.

At the age of 20 - besides the scalp, the alopetic process involved the hairs of both eyebrows, which later recovered spontaneously and totally within one year. The trunk hairs are never engaged by the alopetic process.

Therapy with systemic corticosteroids, local irritants and acupuncture was conducted.

Physical Examination:

The pathological process affects the hairs of scalp and is represented by several irregularly shaped and distinct in size alopetic areas, located at the parietal and vertex-occipital regions. The skin of the alopetic areas has conserved its follicular structure, with no signs of inflammation and cicatrisation. The hairs have normal pluckabilty.

No "exclamation marks" hairs are present. Extent of involvement- $S_1B_0N_0$ – table 1. No nail alteration was observed.

Laboratory Data:

The routine laboratory test results are within normal boundaries.

The hormonal tests currently show normal state of the thyroid gland.

Immunology: MAT and TAT titre – negative.

HLA Typing: HLA- A* 01**, 02**
B* **27**, 57
DRB1* 04 (**B4***), 16 (**B5***)

DISCUSSION:

As an autoimmune disease, AA is frequently associated with other such diseases (ref. – table 4). In the case with our two patients – an autoimmune disease has been diagnosed – Thyreoiditis Hasimoto. According to the literature this is a very common association with AA in childhood. In approximately 24 % of the children with AA, a thyroid dysfunction is observed [11]. At the same time in 10 % of the patients with thyroid gland diseases AA is observed [18].

According to Ikeda [8], our two patients belong to the so calld "Atopic" type AA. They have a differnet signs of atopy- bronchial asthma and allergic rhinitis. On the grounds of the history and physical examination we assing the patients to this type. The pessimistic prognosis of the "Atopyc" type of AA (AT in 33-75%) coincides with our observations for the bad course of AA (developing of ophiasis and extending of the hairloss) in one of the sisters. In addition, in the two cases were observed 8 bad prognostic factors, correlating with

our impressions for the course of the disease.

AA is an organ-specific autoimmune disease and is caused by the complex influence of multiple genes [2, 3, 4] and environmental factors.

Similarly to other autoimmune diseases, AA is associated with various alleles of the MHC class I and II. According to the presumption that inheriting several HLA alleles might predispose certain individuals to AA initiation, we used molecular methods for HLA I and II investigation in our two patients.

The results from our tests for HLA-typing showed high correlation with those referred in the literature in respect of HLA-B27 and HLA-A2. It was established that AA DQB1*03 and DRB1*1104 [6], DR4, DR5 are markers for general susceptibility to AA [1, 5, 15, 16].

The rare allele DRB1*1104, subtype of DR11 is significantly increased in all groups of patients with AA.

The early beginning of AA is associated with HLA-DR5 [7, 9] and DQB1*0301 (DQ7), while AA with prolonged clinic and early initiation – with DR5 (DR11) [14].

Markers for more severe forms of AA are HLA-RDB1*0401 (DR4) and HLA-DQB1*0301 (DQ7) [10, 17, 20].

Most often HLA-A9; -B7; -B8; -B18; - B13 and –B27 are associated with AA. There exist no significant association between HLA- class I and AA.

In conclusion, our two cases are with confirming character regarding the correlation between the "bad prognostic factors" and prolonged course of AA.

Tabl. 1 - Criteria for measuring extent of involvement [13]

S: Scalp hair loss
S_0= No hair loss
S_1= ≤25% hair loss
S_2= 26-50% hair loss
S_3= 51-75% hair loss
S_4**= 76-99% hair loss**
a**= 76-95% hair loss**
b**= 96-99% hair loss**
S_5**=100% hair loss**
B: Body hair loss
B_0 =No body hair loss
B_1 =Some body hair loss
B_2 = 100% body (excluding scalp) hair loss
N: Nail involvement
N_0 = No nail involvement
N_1 = Some nail involvement
a= Twenty-nail dystrophy/trachyonychia (must be all 20 nails)

Table 2. - AA classification – according to Ikeda [8]:

AA	Type
I	**"Common" type** The onset is in older children or adults between 20-40 years of age. The isolated alopecic patches dating for less than 3 years. The separate lesions show aptitude for spontaneous recovery within 6 months. Alopecia totalis (AT)- in only 6 % from the patients.
II	**"Atopic" type** Frequent early onset- in childhood, prolonged cours- more than 10 years. The patches last for about 1 year. AT- in 33-75 % of the patients. The presence of atopia decreases the frequency of remissions.
III	**"Prehypertensive" type** Young adults, with personal or family history of hypertension, manifests rapid often fluctuating cours. AT- in 20-39 % of the patients
IV	**"Combined" type** Adult onset- around 40 years. Frequently associated with autoimmune and endocrine diseases. AT- in 3 %

Table 3. – Bad prognostic significance factors in alopecia areata [12].

Onset – before the puberty *
Male sex
Family history*
Atopic diathesis *
Impaired immune state*
Involvement of more than 30 % of the scalp*
Predominant occipital involvement *
Presence of pseudocommedones.
Nail involvement *
Duration of the disease more than 1 year. *

*- criteria which we observed in our patients

Table 4. – Diseases, describe in association with alopecia areata

Endocrine	Dermatological	Others
Hashimoto's thyroiditis	Atopy (10-20%)	Pernicious anemia
Juvenile diabetes	Vitiligo (4%)	Autoimmine hemolitic anemia
Hypo-/hyperthyroiditis	Psoriasis	Ulcerative colitis
Addison's disease	Sclerodermia	Coeliac disease
	Lupus erythematosus	Myasthenia
	Lichen planus	Thymom
		Rheumatoid arthritis
		Polymyositis
		Polyneuropathia

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