Anatomical Colocalization of Vitiligo and Alopecia Areata

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Abstract: Alopecia areata (AA) and vitiligo are two common disorders in general population and coincidence of these two diseases is thus to be expected. However, anatomical coexistence of both conditions had rarely been reported. Many different etiological hypotheses have been suggested for both diseases. While alopecia areata is considered a T-cell mediated autoimmune disease, in the pathogenesis of vitiligo, both T cells and autoantibodies may play a role. Here we report a case which supports the hypothesis that vitiligo-induced autoimmunity could trigger AA and bulb melanocytes could act as a possible target in AA.

We report the case of a 53-year-old woman which was referred to Dermatology Department for treatment of AA. Twenty years previously, she had developed areas of vitiligo on the face and arms which remained stable for years. She presented with a 1-year history of alopecia on the scalp, with a loss of skin and hair color in the same location during this period. In our case, the chronological appearance, association and co-localization of vitiligo and AA could emphasize the hypothesis that melanocytes-derived antigens released during vitiligo pathogenesis could act as auto-antigens, inducing hair loss.

Keywords: Vitiligo, alopecia areata, autoimmunity.

TEXT ORGANIZATION

Alopecia areata and vitiligo are two common conditions with prevalence between 0.1 and 3% in general population [1-4]. Both diseases have been frequently described in association with other autoimmune and endocrinologic diseases (Tables **1** and **2**). Furthermore, concurrence of both diseases in the same patient is not uncommon and it has often been reported in the literature [1-6] (Table **3**). Nevertheless, anatomical coincidence of both diseases has rarely been reported. To our knowledge, only two previous reports have described the coincidence of these two dermatoses within the same lesions, both cases in paediatric patients [2, 3]. This case highlights the possibility that melanocytic antigens are likely an immune target in both vitiligo and AA.

Several autoimmune disorders such as thyroid disease, *diabetes mellitus*, bullous pemphigoid, p*emphigus vulgaris*, *lichen planus* or pernicious anaemia, have been reported to occur more frequently in patients with both disorders [1-9]. The immune-pathologic basis in these conditions relies on singular and interactive functions of antibodies, T cells, self antigens and organ specificity [10]. We report a 53-year-old woman which was referred to Dermatology Department for treatment of AA. Twenty years previously, she had developed areas of vitiligo on the face and arms which remained stable for years. She presented with a 1-year history of alopecia on the scalp, with a loss of skin and hair color in the same location during this period. No topical or systemic agents for these cutaneous conditions were applied during this period. She also denied any previous injury in the affected area. Familial stressful life events were reported to happen before AA development.

Table 1. Diseases Associated with Vitiligo and Alopecia Areata [17-34]

Anemia perniciosa	Ataxia telangiectasia
Eye abnormalities	Inflammatory bowel disease
Asthma	Dermatitis herpetiforme
Candidiasis	Castleman disease
Diabetes mellitus	Liquen ruber plano
Atopic eczema	MELAS
Esclerodermia	Giant cells Myocarditis
Multiple sclerosis	Plexopathies
Autoinmune hepatitis	Sarcoidosis
Suprarrenal insuficiency	Alezzandrini syndrome
LES	Bazex syndrome
Linfoma/leuKemia	Down syndrome
Melanoma	Parry-Romberg syndrome
Miastenia gravis	Schmidt syndrome
Psoriasis	Sjöegren syndrome
Deafness	Chronic Urticaria
Tyroidopathy	Uveitis
	Vogt-Koyanagi-Harada

Her medical history was relevant for hyperthyroidism and anxiety disorder. Complete blood test, including serum concentrations of cortisol, TSH, FT_3 and FT_4 were within

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Table 2. General Autoimmune Comorbidity and Endocrinopathies Observed in Vitiligo Patients

Authors	Frequency	Refs.
Hegedüs *et al.*	33 %	[17]
Spritz *et al.*	30 %	[18]
Dogra *et al.*	21,4 %	[19]
Bystryn *et al.*	18,18 %	[20]
Farrokhi *et al.*	18 %	[21]
Iacovelli *et al.*	12,1 %	[22]
Mandry *et al.*	10 %	[23]
Jacobson *et al.*	10 %	[24]
Hann *et al.*	6,7 %	[25]
Handa *et al.*	1,3 % (pediatric population)	[26]

normal limits. No other endocrine or autoimmune condition was elucidated by the anamnesis. No relevant family history of autoimmune diseases or endocrine conditions was found.

Physical examination revealed a fairly well defined depigmented, non-scaling, alopecic patches limited to the scalp. Eyebrows and eyelashes were present. Within the depigmented alopecic patches, sparse "exclamation point hairs" and round millimetric hyper-pigmented areas (peri-follicular repigmentation pattern) were observed. Other well-defined achromic macules on face and arms were found. On the scalp, all areas of hair loss were depigmented. Clinical diagnosis of generalized vitiligo and coincident vitiligo and *AA totalis* was made.

Skin biopsy specimen of the scalp revealed numerous hair follicles surrounded by a lymphocytic infiltrate and mild fibrosis in dermis. An absence of melanocytes in the basal layer of the epidermis was observed with Masson-Fontana stain. These histological findings confirmed the coexistence of vitiligo and AA.

Both AA and vitiligo are common skin and hair disorders in general population and coincidence of these two diseases is thus to be expected [2-6]. Nevertheless, anatomical coexistence of both conditions had rarely been reported [2, 3]. Various mechanisms have been proposed to explain why these two conditions coexist [2, 3, 7]. Pathogenesis of vitiligo and AA is complex and not well understood. T-cell-mediated immunologic changes, neuropeptides, autoimmunity, heredity or the effect of environmental stressors have all been proposed to be factors in the induction of both conditions [1-9]. The development of autoimmune diseases generally involves three components: 1) immune system, 2) environmental triggers and other exogenous precipitating factors and 3) target tissue [11]. There is strong evidence supporting the theory that both vitiligo and AA are tissue-specific, autoimmune-based disorders. There have been excellent studies using human hair bearing skin explants onto immunodeficient mice that have provided strong evidence for this [12] and a very similar study shows that this is likely true for vitiligo as well [13]. It has been hypothesized that tissue damage in both AA and vitiligo is melanocyte associated. Melanocytes are a significant component of the anagen hair bulb, which is the site of immunological attack in AA [7, 14]. However, the underlying biological phenomena of both conditions are not completely understood. In the setting of vitiligo, antibodies to autologous melanocytes may develop and cause different forms of tissue damage. In addition, antibodies can directly catalyse water oxidation resulting in reactive oxygen species that can mediate tissue dam-

Table 3. Frequency of Association Between Alopecia Areata and Vitiligo Observed in the Literature

Authors	Frequency	Country	Refs.
Demis and Weiner	16 %	United States	[27]
Koga and Tango	1,2 %	China	[28]
Schallreuter	3,4 %	Hamburg	[29]
Asem Alkhateeb *et al.*	1,1 %	India	[30]
	16 % adults		
Fermín Jurado	32,3 % pediatric population	Brasil	[31]
Liu JB	0,32 %	China	[32]
Gopal KV *et al.*	7,4 %	India	[33]
	1,58 % adults		
Hann *et al.*	0,0 % pediatric population	Korea	[34]
Handa *et al.*	0,4 %	India	[35]
Kemp *et al.*	0,8 % pediatric population	United Kingdom	[17]
Farrokhi *et al.*	10,90 %	Iran	[36]
Barisic-Drusko et al	3,1% pediatric population	Croatia	[31]

age in inflammatory diseases, like AA or pemphigus [10, 11, 15].

Murine models have shown that melanocyte-associated peptides are capable of functioning as auto-antigens, activating lesional T cells to induce hair loss [15].

Melanocyte peptide epitopes could function as auto-antigens for both AA and vitiligo, activating a TH1 autoimmune condition mediated by both CD4+ and CD8+ T cells [15,16] and evident pathogenic roles of T-cells and autoantibodies have been found in vitiligo [1-4, 11, 13]. Furthermore, many facts support this hypothesis [10, 11, 15, 16]: 1) the frequency of association between these autoimmune diseases, AA and vitiligo, 2) Histological and ultra-structural abnormalities in hair bulb melanocytes in patients with AA [7, 15], 3) Antibodies against hair follicle melanocytes found in patients with AA and vitiligo [10, 11, 15, 16] and 4) the possibility to induce lymphocyte-mediated alopecia in mice immunized against melanocyte-associated antigens [15], 5) the frequent clinical observation that pigmented hairs are lost preferentially to non-pigmented [15] and that with hair regrowth there is a tendency for the initial growing hairs to be white [7].

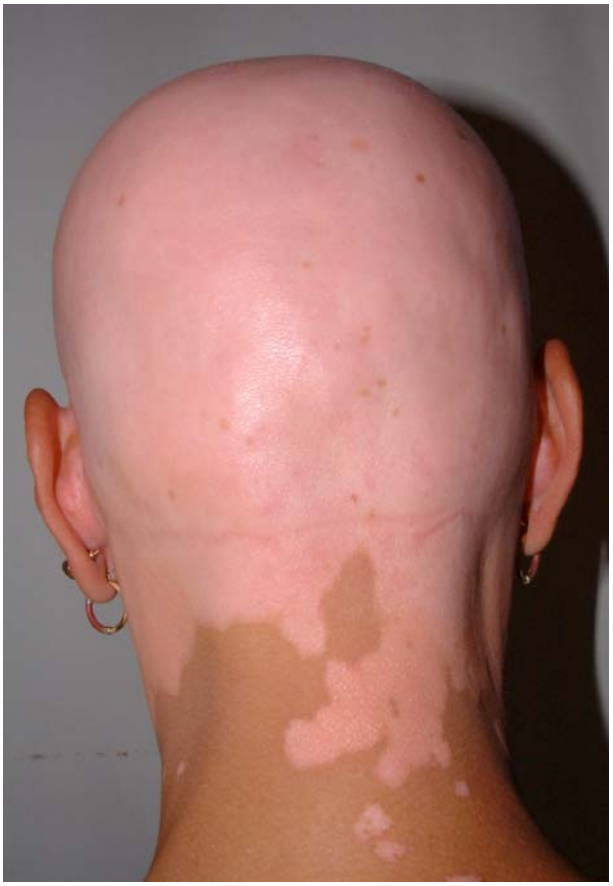

Fig. (1). Fairly well defined depigmented, non-scaling, alopecic patch limited to the scalp. The patient presented with other well-defined achromic macules on facial area and arms.

CONCLUSION

In our case, the chronological appearance, association and co-localization of vitiligo and AA could emphasize the hypothesis that melanocyte-derived antigens released during vitiligo pathogenesis (melanocyte epitopes) could act as auto-antigens, inducing hair loss. We suggest that melanocyte damage induced by vitiligo during several years, could induce a consequent presentation of *tolerogens* and the loss of immune tolerance could result in autoimmunity directed against hair bulb melanocytes. As AA and vitiligo are very frequent and chronic conditions with a severe psychological and quality of life impact in our patients, it is important to clarify their pathogenesis in order to obtain more effective treatments.

ABREVIATIONS

AA = alopecia areata

TSH = thyroid stimulant hormone

FT_3 = Free T3

FT_4 = Free T4

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