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Case Report

Association of Alopecia Universalis, Generalized Vitiligo, and Graves' Disease

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ABSTRACT

We present a 21-years old woman with alopecia universalis, generalized vitiligo, and Graves' disease. She had had thyroidectomy in early childhood and was receiving replacement therapy with levothyroxine. The patient was treated with systemic PUVA and glucocorticoid in combination with topical treatment for alopecia. After 6 months of treatment, alopecia was reversed but vitiligo was unchanged.

Key words: alopecia areata, vitiligo, Graves' disease, glucocorticoid , systemic PUVA therapy

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Alopecia universalis, generalized vitiligo, and Graves' disease are three autoimmune diseases that affect hair follicle, melanocyte, and thyroid gland, respectively. Even though association of each two of these disorders is common, but according to literature review by MEDLINE, this was the first case report of Graves' disease, alopecia universalis, and generalized vitiligo all together in one patient. Pathogenic mechanisms of multiple autoimmune responses and treatments of her skin problems are discussed.

Case Report

In November 2002, a 21-years old white housewife married woman came to our clinic with alopecia universalis from 2.5 years before (figure 1). She had a history of bilateral exophthalmus since she was 7-years old. Her thyroid function tests had revealed hyperthyroidism and her diagnosis had been Graves' disease. Thyroidectomy had been performed at age of seven. After that, she had been treated with 0.1-0.2mg of levothyroxine per day. One year later, she had some depigmented patch on her fingers and toes and around her vermilion and areola (lip-tip syndrome). After six months, depigmentation had become generalized and her hair had grown white. She, clinically, had been diagnosed as generalized vitiligo. Since 2.5 years ago, she developed some small patchs of alopecia on her scalp and after one year, her disease turned to full alopecia universalis. She denied any stressful accidents that were relevant to exacerbation of her diseases. Her family history for autoimmune disease was negative. Laboratory tests, including complete blood count (CBC), platelet, ESR, CRP, FBS, thyroid function tests, and other hormonal studies were normal. ANA (antinuclear antibody) and anti-dsDNA (double stranded DNA antibody) were negative. Anti-TPO wan not measured. She was treated with systemic PUVA, oral prednisolone, topical minoxidil 5%, and topical anthralin 0.5-2% (short contact) for six months. Systemic PUVA therapy was done in 2-3 sessions per week. Prednisolone started at 50 mg per day, two days per week for two months. After that, it was tapered to 50 mg per day, once per week for another two

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months and then 5 mg per day, once per week, for 2 months. After 4 months of treatment, her hairs started to regrew completely (but white) and there was no response of generalized vitiligo (figure 2). In a follow up period of 18 months there was no alopecia, but after that, small patches of alopecia returned.

Discussion

Thyroid disease is evident in 8% of patients with alopecia areata. Thyroid antibodies are present in 30% of females and 10% of males with alopecia areata. Associations of vitiligo with thyroid disease or alopecia areata is well known.

Approximately 5% of the US population suffers from a disease in which autoimmunity play a role. In autoimmune disorders self tolerance (avoiding a harmful immune response to self antigens) becomes impaired. In all autoimmune diseases induction of self-reactive CD4 T-helper cells play a significant role. Five inductive mechanisms are proposed. They are: molecular mimicry, cryptic epitopes, superantigens, adjuvant effect of infections, and defective deletion (defect in negative selection and consequent colonal deletion of self-reactive T-cells in the thymus). The last mechanism plays some role in multiple autoimmune responses and diseases [1].

After induction, two pathogenic mechanisms become activated. The first and more important is cell-mediated immune responses and the second is antibody-mediated immune responses. In all of these three diseases, both mechanisms play some role but like many more autoimmune diseases the primary changes are due to T-cell-mediated immunity.

In addition to topical treatment, our patient was treated with systemic PUVA and glucocorticoid. Both of these treatments have been reported to be effective in management of both vitiligo and alopecia areata. Complete response (>90% hair regrowth) of alopecia universalis to systemic PUVA has been variably reported between 13.3 and 55% [2].Systemic steroid, specially if given early and in pulse mode, is an effective modality in management of this disorder [3, 4].

PUVA is a standard treatment with persistent effect in the management of widespread vitiligo and its pattern of repigmentation is perifollicular. Systemic steroids induce a diffuse pattern of repigmentation that is rapid but not persistent. It seems prudent that combination therapy with both modalities results in more rapid and persistent effects [5].

In spite of complete hair regrowth, depigmentation of our patient did not respond to treatment. We did not have narrow-band UVB or 308-nm excimer laser available in our clinic to try them for her.

Finally, it must be said that if T-cell mediated autoimmune pathogenesis would be accepted for Graves' disease and vitiligo, other therapeutic approaches such as oral cyclosporine, topical calcineurin-inhibitors, topical imiquimod, and calcipotriol must be tried. Future treatments include application of immunosuppressive cytokines like TGF-beta and IL-10, inhibition of apoptosis mediated by the Fas-FasL system, inhibition of the lymphocyte homing receptor CD44v10, induction of tolerance, and gene therapy [6].

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