Pediatric Vitiligo

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KEYWORDS

• Vitiligo • Depigmentation • Autoimmunity • Vitamin D • Corticosteroids • Tacrolimus

KEY POINTS

- Vitiligo is an autoimmune pigment loss.
- Children with nonsegmental vitiligo have a tendency toward other autoimmune diseases including thyroid disease, not seen with segmental disease. The presence of low 25-hydroxyvitamin D can herald the presence or tendency to secondary autoimmunity in children with vitiligo.
- Psychological sequelae including impaired quality of life are often noted in children, especially adolescents with vitiligo of large surface areas, genitalia, and noticeable locations.
- Therapy for vitiligo in children and adolescents is based on a cyclic model of topical therapies with ultraviolet light adjunctively.

INTRODUCTION

Vitiligo is a cutaneous illness caused by melanocyte destruction or damage, resulting in reduced or absent pigmentation of the skin, hair, and/or mucous membranes. Vitiligo affects 0.5% to 2% of the world's population.[1–4] Vitiligo is caused by a genetic propensity paired with environmental triggering that initiates the self-recognition of melanocytes. Autoimmune destruction of melanocytes is the leading theory supported by patient and family history of autoimmunity, absence or reduction of melanocytes on biopsy, presence of lymphocytes at the periphery of active vitiligo lesions, and the detection of antimelanocyte antibodies in the sera of patients with vitiligo. Other theories of the pathogenesis of vitiligo and include neuronal triggers, Koebner phenomenon,[5] and oxidative damage. Each of these is likely contributory to disease development.[6,7]

The Koebner phenomenon is a traumatic induction of lesions. In the setting of vitiligo, the Koebner phenomenon triggers melanocytorrhagy, a rounding of melanocytes and loss of adhesion to surrounding cells in the epidermis. This process results in functional loss of pigment production. Free radicals and tetrahydrobiopterin pathway–generated oxidative species seem to further induce loss of melanocyte activity and enhance damage to melanocytes. The combination of events results in apoptosis of the melanocyte and cell loss.[8–10]

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EPIDEMIOLOGY

One half to two percent of the population has vitiligo worldwide.[1–4] Historically in the American literature, about half of cases of vitiligo begin in childhood, with a slight female predominance.[11] A recently published Chinese population-based survey of more than 17,000 people confirms that this trend is still true, and seems to transcend cultures and countries. The investigators reported that 0.56% of subjects had vitiligo. A slight female predominance was noted in childhood, but lost in adulthood.[12,13]

There are sometimes deviations from this trend in prevalence, as population-based genetic differences and/or environmental factors may affect disease presentation. Prevalence of 0.18% of vitiligo was reported in a population-based study of 2194 Egyptian children living in the Sinai desert, suggesting that lifestyle and socioeconomic status can affect the prevalence.[14]

PATHOPHYSIOLOGY

It has been recently demonstrated that atopy seems to have a linkage to early-onset (ie, childhood) vitiligo in both European and American cohorts. The specific mechanism of interaction is unknown, but this has been demonstrated previously in another pediatric cutaneous autoimmune entity, alopecia areata.[15,16] The only association now noted with atopy is the presence of raised borders, with the notation of inflammatory vitiligo as a subtype.[17] At present, no therapeutic differences in response to treatment have been reported in the literature based on atopy in vitiligo, other than the possible greater severity of disease over time.[16]

Vitiligo is a polygenic or multifactorial disease, 23% of identical twins with vitiligo having an identical twin with vitiligo.[18,19] Genetically vitiligo has been linked to more than a dozen genes in genome-wide association studies in the United States, Europe, and China.[20,21] The genes thus far identified as participatory in vitiligo support a role for different aberrations of immunity in the process of moving from autoimmune antibodies to loss of pigment.

The genetic aberrances that contribute to the development of vitiligo include genetic alteration or polymorphism in pigmentation genes that allow these genes to trigger the recognition of self more easily. Genes involved include tyrosinase, an enzyme that promotes melanin production (TYR), OCA2, the pigment gene that is abnormal in oculocutaneous albinism type 2, the melanin transcription downregulator HERC2, and MC1R, the α–melanocyte-stimulating hormone receptor.[20,22]

These antigens may compete at altered major histocompatibility complex loci that allow for further promotion of self antigens. HLA-A*02:01 has been linked to enhanced development of vitiligo.[21]

Recent studies support the age-old theory that vitiligo is an antibody-dependent cellular immune destruction of pigment cells. First, there are data on production of antibodies to melanocytes by patients with vitiligo[23] and by melanoma patients who develop vitiligo while undergoing therapy.[24] Second, recent biopsy studies have demonstrated that early vitiliginous lesions have dendritic cells consistent with antigen-presenting cells, whereas older lesions contain mature T cells. This finding demonstrates that antigen presentation occurs early on in vitiligo, whereas the inflammatory process may be more cell mediated at a later time.[25] Furthermore, mature T cells have been identified at the border of vitiliginous lesions.[26]

A variety of altered immune processes must occur to generate vitiligo, including autoreactive T-cell augmentation[27] and B-cell activation resulting in autoantibody production, thereby creating a target for aberrant T cells.[28] B- and T-cell genes linked to vitiligo include CTLA4, BACH2, CD44, IKZF4, and LNK.[20] Abnormalities in the innate