A Case Study: Vitiligo Regression Secondary to the Onset of Puberty

Nicole Skalka BS[1], Mary Tidwell BS[1], Elizabeth Tchernogorova BA[1], Olnita Martini MS[2], Ryan Cox BS[1], Parker Miller BS[1], Benjamin Brooks PhD[1]

1. Rocky Vista University, College of Osteopathic Medicine, Ivins, UT
2. Rocky Vista University, College of Osteopathic Medicine, Englewood, CO

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Abstract

Vitiligo is a chronic skin disorder characterized by hypopigmented patches on various parts of the body. This study explores the spontaneous re-pigmentation of vitiligo in a white female from the age of 10 to 22. At age 10, the patient developed a hypopigmented patch on her right hip that rapidly spread to other areas of her body. By age 11, she was diagnosed with nonsegmental vitiligo and began a treatment regimen that included UVB light therapy, topical clobetasol propionate 0.05% ointment, tacrolimus 0.1% ointment, and compounded oral droplets of 1 mg B12 and 5mg folate. Despite these interventions, the response was limited, and treatment was discontinued at age 13. Following the onset of menarche at age 14, the patient experienced progressive re-pigmentation, which became noticeable at age 15 and led to 90% re-pigmentation by ages 18 to 22. This study investigates the potential influence of hormonal changes on vitiligo remission, aiming to address a knowledge gap. Exploring the impact of hormonal factors on melanogenesis and immune response mechanisms offers an avenue for developing innovative therapeutic strategies and improving treatment outcomes.

Introduction

Vitiligo is the most prevalent pigmentation disorder, impacting about 1-2% of the global population.[1] Nearly half of all vitiligo cases begin during childhood, with an average age of onset of 6.9 years.[2,3] Vitiligo is an autoimmune disorder where the immune system attacks and destroys melanocytes, the cells responsible for producing melanin, leading to depigmented patches on the skin.[4] This process involves genetic predisposition, oxidative stress, and immune-mediated inflammation.[4]

Hormonal changes, particularly during puberty, are also believed to influence melanocyte regeneration and vitiligo progression.[5] Estrogen, a key hormone during puberty, has been shown to regulate melanogenesis and influence melanocyte activity.[6] However, the specific role of menarche remains underexplored. Few case studies have examined how menarche influences vitiligo, highlighting a gap in the current literature.

This case study chronicles the journey of a white female with nonsegmental vitiligo from age 10 to 22, focusing on her treatment challenges and remarkable spontaneous re-pigmentation that occurred after menarche. By exploring the potential role of hormonal changes in vitiligo remission, this study aims to bridge a critical gap in understanding and offers insight into potential therapeutic approaches for managing the condition.

Case Presentation

A 10-year-old white female reported noticing a large hypopigmented patch on her right hip, which rapidly progressed with notable white patches on hips, abdomen, back, inner thighs, knees, shins, ankles, elbows, wrists, neck, and face. The patient reported significant concern for the rapidly progressing condition, noting an increase in stress, which was identified as a possible trigger of the hypopigmented patches.

At age 11, the patient was diagnosed with nonsegmental vitiligo. Upon diagnosis the patient began a strict treatment regimen of handheld UVB light therapy lamp once per week for 15 minutes, topical clobetasol propionate 0.05% ointment, tacrolimus 0.1% ointment daily, and compounded oral droplets of 1 mg B12 and 5mg folate daily. The patient's vitiligo showed signs of being treatable, with minor pigmentation restored from treatment regimen in 2 years.

After 2 years of treatment, the patient did not feel motivated to continue, as she felt the results were minor. She stopped treating her vitiligo at the age of 13. No treatment has been used since age 13, but the patient noted that menarche began when she was 14 years old, just before she started to see large patches of re-pigmentation. No baseline or premenarche hormonal lab evaluations were obtained. At 11-years-old, the patient started using MicroSkin to camouflage her vitiligo patches and later transitioned to spray tanning at age 14. These cosmetic procedures were used solely for camouflage, and although MicroSkin is not recognized in current literature, spray tanning has been proven to have no direct effect on melanocyte function. Therefore, these cosmetic procedures would not confound the observation of spontaneous re-pigmentation.

At the age 15, spontaneous re-pigmentation began, progressing gradually. By age 18, significant remission was evident, with remaining patches limited to the knees, ankles, elbows, and wrists. By 22 years-old, vitiligo on the knees, elbows, abdomen, and back had resolved. Currently, only small patches remain on the wrists and ankles, with the patient continuing to see slow spontaneous pigmentation. A complete timeline of the patient’s vitiligo onset, pigmentation, and coverage used for treatment is shown in Table 1 with distribution of vitiligo depicted in Figure 1.

This case report was approved by the Institutional Review Board at Rocky Vista University College of Osteopathic Medicine (IRB #2023-269). Written consent as obtained from the patient for the publication of clinical details and images.

Year	**Age**	**Estimated BSA Affected (%)**	**Key Events**
2010	10	~5%	Initial presentation. Begins B12, folate, tacrolimus, and clobetasol. 3 mm punch biopsy performed; re-pigmentation noted around halo nevus.

2011	11	~10%	Treatment augmented with UVB therapy. New lesions appear; existing lesions remain. Starts using MicroSkin for camouflage.
2012-2013	12-13	~10%	Perifollicular re-pigmentation on arms/legs. Minor visible improvement.
March 2013	13	~10%	Slight follicular re-pigmentation on legs.
2014	14	~10%	Menarche begins. Transition from MicroSkin to spray tanning.
2015	15	Decreasing	First signs of spontaneous re-pigmentation in previously affected areas.
2015-2024	15-22	Decreasing to < 1%	Re-pigmentation persists. By 18, most areas resolve except wrists and ankles.
2024	22	< 1%	Patches on wrists/ankles continue to re-pigment. Patient reports improved quality of life.

Table 1. A table displaying the timeline of the patient's vitiligo onset, pigmentation, and coverage used.

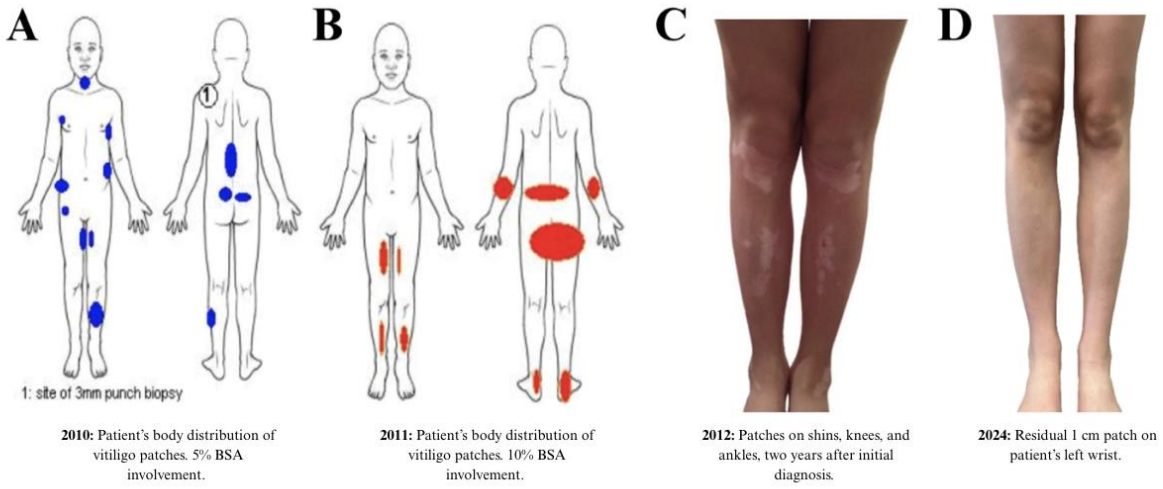

Figure 1. A) Patient's distribution of vitiligo in 2010 prior to starting treatment. See the encircled 1 for the site of 3mm mole punch biopsy, which was performed to evaluate a clinically suspicious, unspecified pigmented lesion concerning for atypia. After the punch biopsy, the patient had full re-pigmentation of the vitiligo patch that surrounded the mole. The body surface area affected at this time was 5%. B) Patient's distribution of vitiligo in 2011 after about a year of treatment. The body surface area affected at this time was 10%. C) Patient's vitiligo on shins, knees, and ankles in 2012 two years after initial diagnosis. D) Patient's vitiligo on shins, knees, and ankles in 2024 after experiencing spontaneous re-pigmentation. The apparent difference in pigmentation between images C and D is attributable to differences in lighting conditions. No self-tanner was applied.

Discussion

The correlation observed in this case between menarche and spontaneous vitiligo remission suggests a potential hormonal influence, possibly through increased estrogen levels.[6] However, the specific mechanisms remain unclear, warranting longitudinal studies to elucidate the role of hormonal fluctuations in vitiligo progression and remission.

Estrogen's immunomodulatory effects may influence melanocyte function and the immune responses in vitiligo pathogenesis.[7] Elevated levels of tumor necrosis factor-alpha (TNF-α) and Tumor necrosis factor beta (TNFB) are observed in vitiligo patients compared to controls, with female patients showing significantly higher levels of TNFB and intracellular adhesion molecule 1 (ICAM-1) than male patients.[8,9] This gender difference in cytokine levels could be linked to hormonal variations or provide an alternative explanation for the female predisposition to autoimmune diseases like vitiligo. However, no laboratory testing was performed to assess the patient's ICAM-1 and TNF-α levels, limiting comparison with the cited studies. Similarly, estrogen and progesterone levels were not obtained, limiting the ability to correlate hormone levels with vitiligo re-pigmentation. Monitoring prepubertal hormone levels in pediatric vitiligo patients may serve as a clinical indicator of potential for spontaneous re-pigmentation.

One cross-sectional study conducted in 2019 that included 167 patients with vitiligo reported an approximate 20% rate of spontaneous re-pigmentation, with no significant correlation to age, sex, age of onset, mode of onset, sun exposure, thyroid disease, or type of vitiligo.[10] This study demonstrated that spontaneous remission can occur independently of identifiable clinical factors. While our case may have reflected this phenomenon in part, the timing of re-pigmentation, which occurred several years after treatment cessation and closely followed the onset of menarche, underscores the possibility of a hormonally influenced mechanism.

Studies indicate local synthesis of estrogen in epidermal keratinocytes, playing a crucial role in protecting human epidermal melanocytes from oxidative stress-induced damage.[11] Reduced expression of local estrogen synthesis enzymes in vitiligo lesional skin suggests a dysregulation in estrogen signaling, potentially contributing to vitiligo pathogenesis.[11] Moreover, estrogen synthesis enzymes are mainly found in keratinocytes, while estrogen receptors are primarily present in melanocytes.[11] Specifically, 17β-hydroxysteroid dehydrogenase 1 (HSD17β1) is highly expressed in keratinocytes, whereas G protein-coupled estrogen receptor 1 (GPER1) is the predominant estrogen receptor.[11] Notably, decreased levels of HSD17β1 protein are observed in the lesional skin of vitiligo patients in progressive states compared to healthy controls or normal skin samples.[11] The multifactorial nature of vitiligo involves genetic and non-genetic factors, including cytotoxic, autoimmune, and oxidant- antioxidant mechanisms, leading to progressive melanocyte loss and skin depigmentation.

Although spontaneous remission due to the natural disease course or reduced psychosocial stress following treatment discontinuation are potential contributing factors in vitiligo, they were not identified as primary drivers in this case. The patient's re-pigmentation occurred several years after treatment cessation and coincided more closely with pubertal hormonal changes than with changes in stress or disease stability.

This case highlights the potential role of estrogen in spontaneous re-pigmentation of vitiligo following menarche. Yet, it is important to acknowledge that the association observed between menarche and vitiligo re-pigmentation does not establish a direct causal relationship. While the exact relationship between menarche and vitiligo is not yet fully understood, the immunomodulatory effects of estrogen, combined with its local synthesis in keratinocytes and its protective role against oxidative stress, are promising routes for further research. Understanding hormonal factors' impact on melanogenesis and immune response mechanisms could pave the way for innovative therapeutic strategies and enhanced treatment outcomes.

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