ORIGINAL ARTICLE

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Disorders of Hypopigmentation

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ABSTRACT

Hypopigmentation and depigmentation of the skin can be due to multiple causes and has a broad differential diagnosis. The most common cause of depigmentation worldwide is vitiligo. This disorder affects 1-2% of the world's population and is seen in all races. Vitiligo is an autoimmune disorder in which the predominant cause is an attack by CD8+ cytotoxic T cells on melanocytes in the epidermis. This condition can have a significant negative impact on the quality of life of affected individuals. Treatment options currently include psychological counseling, topical therapy, systemic therapy, phototherapy, surgical therapy, and depigmentation. In patients with stable, refractory disease, successful repigmentation has been achieved using mini-punch grafting, blister grafting, and non-cultured epidermal suspension (NCES) grafting. Emerging therapies include the Janus kinase (JAK) inhibitors ruxolitinib and tofacitinib. Further studies exploring the pathogenesis of vitiligo are warranted in order to optimize treatment for affected patients.

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INTRODUCTION

Hypopigmentation and depigmentation of the skin can be caused by multiple disorders. These include seborrheic dermatitis, mycosis fungoides, tinea versicolor, pityriasis alba, nevus depigmentosus, leprosy, and vitiligo (Figure 1).[1,2] The most common cause of depigmentation worldwide is vitiligo. This disorder affects 1-2% of the world's population and can be seen in all races.[3] Vitiligo can have a significant impact on the quality of life of affected individuals.[4] Although the disease course is often unpredictable, a few clinical signs that indicate increased disease activity have been identified. Confetti-like lesions, trichome lesions, and evidence of the Koebner phenomenon all indicate the need for immediate treatment (Figure 2).[5,6]

Vitiligo is caused by a disorder in the immune system in which CD8+ cytotoxic T cells attack melanocytes in the epidermis causing apoptosis and subsequent depigmentation.[3] Although there are no current biomarkers to measure activity of vitiligo, certain clinical findings have a bearing on prognosis and likelihood of repigmentation. Patients who tend to respond well to treatment include younger patients, darker skin types, a short history of disease (<2 years), and those with depigmentation of the face, ears, neck, axillae, and other hair bearing areas with pigmented hairs. Features that characterize a poor prognosis include older patients, lighter skin types, long history of disease or rapidly spreading disease, and involvement of the scalp, lips, hands, elbows, genitalia, feet, or knees. Additionally, evidence of leukotrichia within depigmented lesions is a sign of poor prognosis (Figure 3).

Treatment options for vitiligo include psychological counseling, topical therapy, systemic therapy, phototherapy, surgical therapy, and depigmentation.[7] The current mainstay of treatment is phototherapy although treatment courses are often prolonged, lasting 6-18 months.[7] Narrow band-UVB, PUVA, PUVASOL, UVA, sunlight, and solarium therapy can all be utilized based on treatment availability. However, the most successful phototherapy type remains NBUVB, which is effective due to its immunosuppressive effects and ability to induce melanocyte differentiation and melanin production.[7,8] Studies have shown that home phototherapy is more efficient and cost effective than in-office phototherapy.[9] In patients with the signs of active disease discussed above, a short course of an oral corticosteroid, such as dexamethasone, may be warranted.[7,10] Due to their

FIGURE 1. Visual differential diagnosis of hypopigmentation. Included in the differential diagnosis of hypopigmented and depigmented lesions are hypopigmented mycosis fungoides **(A)**, vitiligo **(B)**, tinea versicolor **(C)**, and nevus depigmentosus **(D)**. Other items on the differential diagnosis, but not included in this image, include seborrheic dermatitis, pityriasis alba, and leprosy.

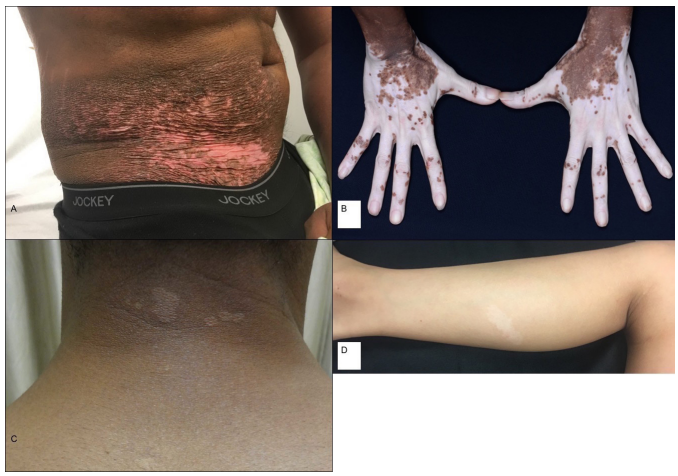
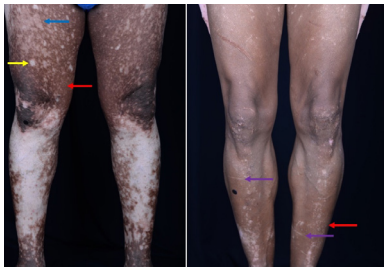


FIGURE 2. Signs of activity in vitiligo: confetti, trichome and Koebner phenomenon. Common signs of activity in vitiligo include trichrome (blue arrow) and confetti-like (red arrows) depigmentation as well as Koebner phenomenon (purple arrow). An example of a vitiligo lesion, for comparison, is indicated by the yellow arrow.



antioxidant properties, vitamins C, E, and alpha lipoic acid may also be useful in reducing triggering factors that lead to depigmentation when used in combination with topical and systemic treatments as well as phototherapy.[11]

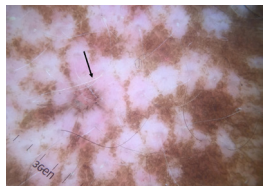
Emerging therapies for vitiligo include topical and oral Janus kinase (JAK) inhibitors. Topical ruxolitinib and oral tofacitinib have both been found to be potentially effective in achieving repigmentation in small pilot studies.[12,13] These medications interrupt IFNγ signaling via the JAK STAT pathway, which is crucial in the pathogenesis of vitiligo.[13] Other potential therapeutic targets include IFNγ, CXCL9/10, and CXCR3.[3,13]

In patients with resistant depigmentation that has been stable for 6 months to 2 years, surgical therapy may be considered.[7] Mini-punch grafting, blister grafting, and non-cultured epidermal graft suspension (NCES) are all viable options for patients.[7] The choice of procedure is dependent on the body area involved, surface area of depigmentation, and affordability. NCES has been proven to be most efficacious, however mini-punch and blister grafting techniques are less expensive and easier for practitioners to master.[7] In patients with widespread vitiligo (>50% body surface area involvement) that is refractory to therapy, depigmentation of the remaining pigmented areas with monobenzylether of hydroquinone may be considered.[7] Patients should be educated that this process is irreversible and be comfortable with the permanent nature of this treatment prior to initiation.[7]

CONCLUSION

In summary, vitiligo is a common autoimmune disorder that causes depigmentation and significantly impacts the quality of life of affected individuals.[3,4] A careful history and physical examination should be performed in order to differentiate vitiligo from other conditions that may cause hypopigmentation or depigmentation. Physicians should be wary of signs of activity that mandate prompt treatment.[5,6] Current mainstays of treatment include topical corticosteroids and phototherapy.[7] Emerging therapies that may be life changing for patients with refractory disease include the JAK inhibitors ruxolitinib and tofacitinib as well as new JAK inhibitors that are being studied. Further studies exploring the pathogenesis of vitiligo are warranted in order to optimize treatment options for patients.

FIGURE 3. Leukotrichia in vitiligo. Leukotrichia (black arrow) as seen on dermoscopy. In patients with vitiligo, leukotrichia within depigmented lesions is a sign of poor prognosis.



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