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Review Article

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INTRODUCTION

Vitiligo is an acquired idiopathic hypomelanocytic disorder, characterized by circumscribed depigmented macules. The cause is unknown. But, various theories such as the autoimmune, autocytotoxic, and neural hypotheses have been proposed. Extensive research has provided numerous answers regarding the pathogenesis, histopathologic evidence, and treatment of vitiligo. Vitiligo affects one or two percent of the population. About half the people who develop it, do so before the age of 20 and the incidence decreases with increasing age. Melanin, the pigment that determines color of skin, hair, and eyes, is produced in cells called melanocytes. If these cells die or cannot form melanin, the skin becomes lighter or completely white. Melanin is produced from tyrosine, a derivative of the essential amino acid phenylalanine. The density of melanocytes in skin does not vary among different races, but skin pigmentation in ethnic groups differs because of variations in the rate of melanin production by melanocytes.

Vitiligo is seen as acquired white or hypopigmented macules or patches. Progression of the depigmentation is variable. Generalized vitiligo is the most common presentation with bilateral, symmetric depigmentation of the face, neck, torso, extensor surfaces or bony prominences of the hands, wrists, legs, axillae, orifices, or mucosal surfaces. Most patients initially experience depigmentation in a sun-exposed site. Moreover, vitiligious lesions, known as the Koebner phenomenon, can develop at sites of trauma, such as abrasions, surgical scars, resolving psoriasis or eczema. Patients often associate the onset of their disease with emotional or physical stress, oral medications such as chloroquine and clofazimine. Patients with vitiligo have an increased risk of developing autoimmune diseases such as thyroid disease (Hashimoto's thyroiditis and Graves' disease), Addison's disease, pernicious anemia, Insulin-dependent diabetes mellitus, and Alopecia areata. Autoantibodies directed against these and other organ systems can also be present without clinical correlation.

Laboratory tests that may be helpful to detect the presence of associated systemic disorders may include but are not limited to test for

a. Adrenal insufficiency
b. Diabetes mellitus
c. Pernicious anemia
d. Thyroid disease.

One or more of the following tests may be useful:
A) Biopsy from the border stained with Fontana-Masson technique (for melanin) to differentiate vitiligo from some of the forementioned conditions.

B) Antinuclear antibody test.

TREATMENT MODALITIES

Older modalities include:

1. Topical and systemic corticosteroids.
2. Psoralen with exposure to ultraviolet A (PUVA) radiation therapy.
3. Depigmentation therapy with monobenzylether of hydroquinone.
4. Surgical treatments such as mini grafting, thin split-thickness grafting and micropigmenatation.

Newer modalities include:

1. Transplantation of cultured melanocytes.
2. Transplantation of non-cultured melanocytes.
3. Narrow band UVB therapy.
4. 308-nm excimer laser.
5. Vitamin D analogues.
6. Tacrolimus.
7. Depigmentation with Q-switched ruby laser.

Older modalities:

1. Topical and systemic steroids: Treatment of vitiligo with corticosteroids was initiated in 1959 and success was achieved by treating patients of vitiligo with oral psoralen and oral or topical steroids. Various topical steroid preparations were used and discovered that the face and neck responded better than other parts of the body, and that generalized vitiligo responded to treatment although segmental vitiligo did not. Corticosteroids cream is applied to depigmented skin once daily for 3 to 4 months. The response is monitored with Wood's lamp examination at 6-week intervals. Therapy is continued if repigmentation occurs, but stopped if there is no evidence of response after 3 months.

2. Psoralen-UVA: PUVA is a form of repigmentation therapy where a type of medication known as psoralen is used. This chemical makes the skin very

sensitive to light. Then the skin is treated with a special type of ultraviolet light called UVA. Treatment with PUVA has a 50% to 70% chance of returning color on the face, trunk, upper arms and upper legs. Hands and feet respond very poorly. Meladinine, a derivative of coumarin consisting of 8-methoxypsoralen and 8-isoamyleneoxypsoralen, was found to be an effective oral and topical treatment. But, how PUVA therapy stimulates these inactive melanocytes is still unknown.

Topical Therapy: Topical 8-methoxypsoralens can be used in patients with less than 20% total body surface area depigmentation. The procedure involves initially painting the affected area with 0.05% or 0.1% topical 8-methoxypsoralen, depending on the patient's skin type. The treated area is then exposed to an artificial UVA source 6 inches away from the depigmented region (two, 2-foot backlights in a fluorescent light fixture with a measured output of 1 to 2 J/cm-) initially for 30 seconds, increasing exposure time in 15- to 30-second increments up to 10 minutes, two to three times per week. Once 10 minutes is reached, a marginally higher strength of topical psoralen solution is prescribed (0.1% to 0.15%), and the same time intervals are followed. This is repeated until the time exposure cannot be increased because of burning, at which time the treated vitiligious area is exposed to the artificial light source two to three times per week for a specific amount of time. Shielding non-involved skin and especially the eyes with UV light-absorbing goggles is of the utmost importance. All patients are required to wash off the topical solution with soap and water immediately after treatment, and they should apply sun block and avoid sunlight.

Oral Therapy: Oral PUVA therapy is used in patients with extensive vitiligo. It is important to explain the chances of repigmentation and the associated short- and long-term side effects. After ingesting 0.5 mg/kg of 8-methoxypsoralen ultra 1½ hours before treatment (2 hours before, if using crystalline 8-methoxypsoralen) patients are started at 1 to 2 J/cm2 of light, increasing by 0.25 J/cm2 (for types I and II skin) or by 0.5 J/cm2 (for types III to V skin) per treatment, two to three times per week, until erythema results. Although 70% to 80% of patients will experience the induction of pigment with oral psoralen treatments, less than 20% of patients have total repigmentation. It is important to be selective when choosing patients for oral PUVA therapy. Darker pigmented patients respond better to PUVA therapy because of the increased tolerance to greater cumulative UVA dosage, and children also experience repigmentation to a greater extent than adults. Vitiligo on the trunk, proximal extremities and face respond well to PUVA therapy, although distal extremities and periorificial do not. The potential side effects of PUVA therapy include PUVA burn, nausea, erythema, pruritus, xerosis, fatigue, carcinogenicity, pigmented lesions, cataracts, and aging. It is contraindicated in pregnant women or women who are breast-feeding and children under the age of 12 years.

3. Depigmentation: For some patients with extensive involvement or those who have more than 50% involvement of the skin and have demonstrated therapeutic resistance to efforts at repigmentation, the most practical treatment for vitiligo is to remove remaining pigment from normal skin and make the whole body an even white color. That is usually done with 20% monobenzoether or hydroquinone applied to the skin once or twice daily for one to three years.This therapy takes about a year to complete. The pigment removal is permanent and irreversible, resulting in permanent photosensitivity.

4. Surgical treatment: If topical steroids or PUVA treatments fail to repigment, surgical alternatives exist.

Micropigmentation or (Tattooing): It involves the tattooing of vitiliginous skin, in an attempt to match the surrounding normally pigmented skin. Iron oxide pigment injected into the dermis is most often utilized. An exact match of pigment is difficult to obtain. Dark complexion cases show better results than fair complexion ones [1].

Dermabrasion and topical 5-fluorouracil: Vitiliginous skin is superficially dermabraded and 5% fluorouracil is applied twice Daily, under occulusion for 7 to 10 days. Complete, but darker, repigmentation may result. Undesirable effects include long recovery period, infection, scarring, and aggravation of vitiligo.

Newer modalities:

1. Transplantation of in vitro-cultured Epidermis: Melanocytes are harvested from a small fragment of pigmented skin from the patient. Blisters are formed by suction or liquid nitrogen at both donor and recipient sites, and the epidermis from the donor sites is removed. The epidermis is treated with trypsin, and the melanocytes are isolated and grown in cell culture for 3 weeks. The melanocytes adhere to Vaseline gauze that is divided and placed over the denuded area of recipient vitiliginous skin. A dressing is applied with an elastic bandage. A variant of this technique involves injecting in vitro-cultured melanocytes into suction blisters formed at the recipient site or applying melanocytes to dermabraded skin. With the in vitro transplantation

method, the repigmented site can be as large as 10 times the donor site, although continual passes with this method can yield a potentially large number of melanocytes to cover a large depigmented area. Variegated color in the recipient site can occur secondary to variable melanocyte concentration on the gauze, spotty graft failure, or relative instability of the recipient area. After 1 to 2 years of observation, the repigmented areas did not depigment. [2,3] With the epidermal grafting method, there is low incidence of scarring. Epidermal grafting using tops of suction blisters has been found to be the most effective surgical procedure.[4]

2. Transplantation of noncultured melanocytes: A method that resembles in vitro-cultured melanocytes, but instead noncultured melanocytes were isolated from skin samples obtained within a dermatome. The melanocytes were treated with trypsin, and with EDTA, placed in saline solution, and injected as a suspension into blisters in the recipient site created with liquid nitrogen. There was no significant difference between these two treatments.[2-3]

3. Narrow Band UVB (NBUVB): Amongst the several new treatments for Vitiligo this treatment appears to have have a higher success rate than previous therapies. A new device is used which can produce focused beam of narrow UV-B 311nm (microphoto-therapy) on vitiligo patches only, it is usually used two-three times per week with an initial dose of 100mJ/cm^2 the dose is gradually increased by 10%-20% per treatment for 20 treatments, and then by 2%-to 5% until at least 50% repigmenattaion is observed. Photographs of the patients are taken at the beginning of the therapy and then monthly and the response is measured in two comparable pictures using planimetry. Uptil now no side effects have been reported hence this could represent the treatment of choice for Vitiligo limited to less than 30% of the skin surface. [5-6] Repigmentation notably appears on the face, neck, throat, lower arm, chest, back and legs while it is usually less on the hand, feet and ankles.[7]

4. 308-nm Excimer laser: Recently narrow-band UVB (311nm) has been used successfully for the treatment of vitiligo patients, targeted photo therapy with single- wavelength laser light is a treatment alternative that has proved to be time efficient and effective therapeutic option for the management of vitiligo. More recently excimer laser with wavelength of (308nm) has been tried for targeted treatments of localized vitiligo with very good results, and may represent a new treatment modality for the management of stable vitiligo.[8-10]

5. Vitamin D Analogues: Some cases show poor clinical response to topical steroid ointments or PUVA therapy, such regimes are generally avoided in treating facial lesions due to undesirable side effects, hence such patients are treated with Vitamin D analogues i.e topical taclacitol, alpha 24{OH)2D3} with a good clinical response.[11]

6. Tacrolimus: 1% tacrolimus can be used in patients especially children with good results. It has proved to be as effective as 0.05% clobetasol propionate to restore skin color in lesions of vitiligo, since it does not produce skin atrophy or other adverse side effects. Tacrolimus is very helpful in treating younger patients and sensitive areas such as eye-lids. [12-15]

7. Depigmentation with Q- switched ruby laser: Bleaching creams which are often used in depigmentation therapy may lead to serious side effects. Q-switched (QS) ruby laser can destroy melanosomes in melanocytes and keratinocytes by selective photothermolysis. Patients with extensive vitiligo are first tanned and then QS ruby laser is used with good results, and has proved to be an effective and safe method of removing remnants of normal pigmentation in patients with vitiligo universalis. [16]

CONCLUSION

The exact cause of vitiligo is unknown, however, there may be an inherited component. Although many treatments are available there is no single cure. Research is ongoing and it is hoped that these new treatments will be adopted widely, but will not result in successful treatments in every situation. The ultimate judgment regarding the propriety of any specific procedure must be made by the dermatologist in light of all the circumstances presented by the individual patient.

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