A Case Report of Extensive Vitiligo

Tien-Ahn Wee MD, Medical Resident
Department of Medicine, University of Hawaii

This is a case presentation and discussion of extensive vitiligo in a 44-year-old woman who was treated with monobenzone who had previously failed repigmentation therapy with psoralen-ultraviolet A therapy.

Case Report

The patient is a 44-year-old woman of Portuguese descent who first started experiencing depigmentation of her skin at age 14. The patient was treated with oral psoralen-UltraViolet-A(PUVA) treatment for 2 years with partial repigmentation of the affected areas. Additional therapy was performed intermittently between the ages of 23 to 25 years with limited response. Due to pregnancy, the patient discontinued treatment when she was 26. During this time her vitiligo continued to worsen. Two years after her pregnancy the patient began to experience a rapid progression of her vitiligo. The patient was then evaluated for further PUVA therapy. On examination it was noted that her vitiligo was extensive, involving more than 60% of her body. This included highly visible areas around her eyes, cheeks and mouth, in addition to her body and extremities. Furthermore, the patient reported that sites of old repigmentation were irregular and hyperpigmented even 15 years after initial treatment. The patient reported her condition caused her severe emotional distress. In light of the unsatisfactory results to her prior repigmentation therapy and the extensive areas of involvement, the patient desired depigmentation therapy. Of note is the absence of any family history of vitiligo or autoimmune disorders.

The patient was photographed for documentation and then started on 20% monobenzone cream with frequent follow up examinations for progression of her therapy. The patient received 3 years of treatment with highly satisfactory results and no side effects. However, soon after termination of monobenzone treatment, the patient noticed some repigmentation on her arms after sun exposure. This progressed to involve areas on her chest and face. Unfortunately soon after this, the pharmaceutical manufacturer stopped supplying monobenzone and no further supplies have been available in America. The patient was then treated with hydroquinone without satisfactory response. Numerous attempts have been made to find alternative sources of monobenzone. So far this has been unsuccessful.

Discussion

Definition

"Vitiligo is a disease of unknown origin which causes destruction of melanocytes in the skin, mucous membranes, the eyes, and occasionally in hairbulbs and in the ears. The loss of melanocytes alters both structure and function of these organs."[1]

Incidence

Vitiligo affects between 0.066% to 8% of Americans.[2-4] It occurs in all ethic groups and equally in males and females. Vitiligo tends to be more noticeable in darker skinned ethnic groups. However, there is no evidence to conclude that the incidence is any greater in darker skinned people. Of additional interest is the age predominance in vitiligo; 25% of patients develop vitiligo before 10 years of age, 50% develop it before 20 years of age and 95% before the age of 40.[1] There is no literature to suggest any significant difference in the incidence of vitiligo in Hawaii compared with the rest of the country.

Pathophysiology

There are three widely accepted theories as to the etiology of vitiligo, however, the precise pathophysiology of vitiligo is still unknown and the subject of current research. The neural theory supports the notion that depigmentation is due to melanocyte destruction or inhibition of melanin production when a chemical mediator is released at the nerve endings. Another theory explains vitiligo as the result of destruction of melanocytes by tyrosine, dopa and 5,6-dihydoxyindole which are all involved with the normal production of melanin. It has been postulated that melanocytes have a protective mechanism against their destruction, however, when this is lost, the result is melanocyte damage and depigmentation. The final theory ascribes vitiligo to an autoimmune dysfunction. Of particular interest is the finding that there is a ten fold increase in vitiligo in patients with autoimmune diseases.[5-13] In addition, studies by Naughton et al., and Gilhar et al., have demonstrated antibodies against melonocytes in vitiligo patients.[7,14]

Differential Diagnosis

There are a number of other conditions of depigmentation that may be confused with vitiligo. Usually a careful physical examination and history is sufficient to distinguish vitiligo from other causes. One of the most common of these is tinea versicolor, i.e., kane in Hawaiian. This can be readily ruled in or out by performing a potassium hydroxide test on skin scrapings and looking for the characteristic fungal hyphae under the microscope. Tinea, if diagnosed, can be readily treated with any number of the antifungals available to the clinician. Scleroderma and morphea can also be readily ruled out by simple palpation of the lesions. Listed below are some additional, conditions that the clinician should be aware of in the differential diagnosis.

Diagnostic Criteria

Clinical Features

The diagnosis of vitiligo is almost exclusively made by examination of the patient. Vitiligo is often first detected by patients when they notice areas of depigmentation contrasting with normal darker areas of their skin. In addition, hypopigmentation may also be present. These patterns generally have well demarcated borders. Commonly affected areas are the hands and body openings such as the eyes, nostrils, mouth, nipples, umbilicus and genitalia. These areas of vitiligo are usually bilateral and symmetrical. However, the converse is also observed and any part of the body may be affected. Other areas affected that have been reported are previous sites of trauma and scarring.[9,14] In particularly fair skinned patients(type I/

Table 1.—Differential Diagnosis
1. Discoid lupus Erythematosus
2. Idiopathic guttate hypomelanosis
3. Lichen sclerosus et atrophicus
4. Morphea
5. Nevus anemicus
6. Piebladism
7. Pityriasis alba
8. Woolf's syndrome
9. Tinea versicolor
10. Turberous sclerosis
11. Scleroderma
12. Waardenburg's syndrome
13. Ziprkowski-Margois syndrome
14. Leukoderma
15. Hanson's disease
16. Mycosis Fungoides

Table 2.—Repigmentation Therapies
Medical
1. Topical psoralen photochemotherapy
2. Oral psoralen photochemotherapy
3. Topical steroid therapy
4. Oral steroid therapy
5. Intralesional therapy
6. Cosmetics
7. Khellin and UVA
8. L-Phenylalanine and UVA
9. Immune modulators(cyclosporine, Anapsos, Isoprinosine)
Surgical
1. Dermabrasion and topical 5-FU.
2. Autologous epidermal grafts.
3. Tattooing
4. Autologous melanocyte transplants.

Table 3.—Depigmentation Therapy
Medical
1. Monobenzylether of hydroquinone

II) who may not have greatly contrasting areas of depigmentation, a Wood's lamp may prove helpful in assessing the involved areas. While the diagnosis of vitiligo can generally be made by the history and physical examination, further diagnostic tests may be helpful in differentiated this condition from other disorders that are similar in presentation. In addition, associated disorders such as thyroid disorders, pernicious anemia, diabetes, or Addison's disease may be also detected by additional diagnostic tests.

A biopsy may be helpful in differentiating vitiligo and other similarly presenting diseases — the histological features of vitiligo are discussed in the next section. However, most patients do not require a biopsy.[1] Thyroid function tests may be helpful in ruling out an associated thyroid disorder. Further tests include antiparietal cell, antithyroid(thyroglobulin and microsomal), and antinuclear antibodies to rule out commonly associated autoimmune disorders.

Histology

In early vitiligo the only abnormality may be a decrease in the number of melanocytes. In late stages there is a complete absence of melanocytes. Additional features may be basilar vacuolopathy, exocytosis of lymphocytes, spongiosis, and lymphohistiocytic infiltrates.[1,14-16] However, often times these are not observed.

Current Treatment Modalities

There are two major ways to treat this disfiguring ailment. The more preferable and widely used therapy is repigmentation. An alternative in extensive vitiligo (>50%) or vitiligo that has failed repigmentation therapy is depigmentation of the remaining melanocytes.[1,9,15] These various methods have been well described in numerous articles. In addition, on going research holds the promise of additional treatment therapies.[1,16,18,19]

Repigmentation Therapy

This can be done by a variety of methods. However, the most widely used and successful is PUVA(Psoralen UltraViolet A) therapy.[1,16] The precise mechanism of action of psoralen is unknown. However, PUVA therapy has been observed to result in melanocyte hypertrophy and proliferation in the residual follicular melanocytes in the vitiliginous areas. Furthermore, melanocytes in pigmented areas surrounding these lesions undergo similar changes. This results in repigmentation when these stimulated melanocytes migrate to the depigmented areas. Treatment may require up to 18 months and more than a hundred visits.[9,16] This requires considerable patient motivation. However, 16-24 treatments will usually produce some new pigmentation.[16] Suitability of this treatment is based on the patients motivation, concern for appearance, race, age, and access to phototherapy facilities. In addition, eye disease, skin cancer, lupus erythematosus, hepatic and cardiovascular diseases are also screened for in the evaluation of appropriateness of PUVA therapy for the patient. In general topical PUVA is used in patients with less than 20% involvement of their skin. For patients with more than 20% involvement, resistant to topical PUVA or children younger than 10 years old, oral PUVA is used instead.[1,9,16] A common side effect of both topical and oral PUVA is photosensitivity. Severe blistering may occur with sun exposure and the patient must ensure adequate protection with a broad spectrum(UVA and UVB) sunscreen. With good patient motivation and compliance PUVA can produce excellent results with a minimum of side effects. The long term effects of PUVA are excellent and the vast majority of patients are able to avoid additional therapy.[15] Artificial sources of UVA are generally more preferable over natural sunlight. UVA machines have better reliability and consistency compared with natural sunlight UVA which varies according to atmospheric conditions, the season, time of day and various other factors. In addition, the risk of overexposure and toxic side effects are greater with natural sunlight UVA. Topical PUVA is a contraindication for natural sunlight PUVA.[1] PUVA therapy is not indicated for children under 2 years of age. Unfortunately, despite generally good results, some patients are resistant to PUVA. Another therapy option is steroids. Topical, intralesional, and oral steroids all have been used with partial to complete repigmentation ranging between 10% and 82%.[16] Topical steroids are usually considered for the initial treatment of vitiligo. They are also useful in the treatment of children less than 2 years old. Low potency steroids are used in younger children whereas mid to high potency steroids are used in older children and adults.[16] Results may take several weeks to appear and side effects of the treatment include atrophy, striae, and telangiectasias. Moreover, the risk of immunosuppression and infection is a concern with steroid therapy. In patients who are resistent to repigmentation or

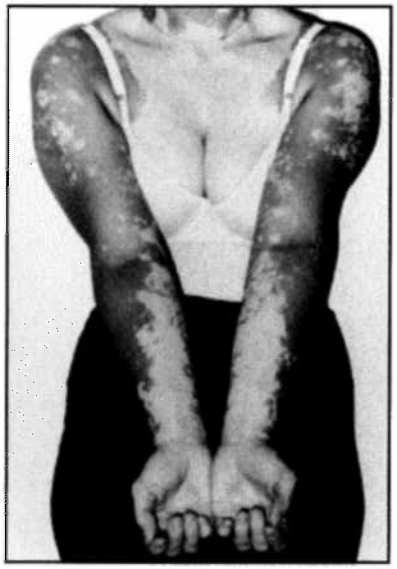

Fig 1.—Pretreatment with monobenzone: This demonstrates extensive depigmentation of the arms, chest and neck.

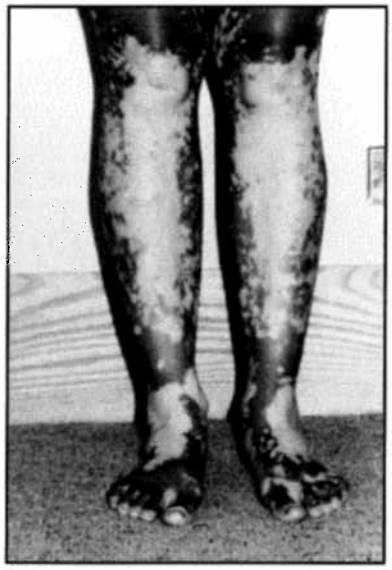

Fig 2.—Pretreatment with monobenzone: This shows extensive involvement of the anterior surfaces of the lower extremities.

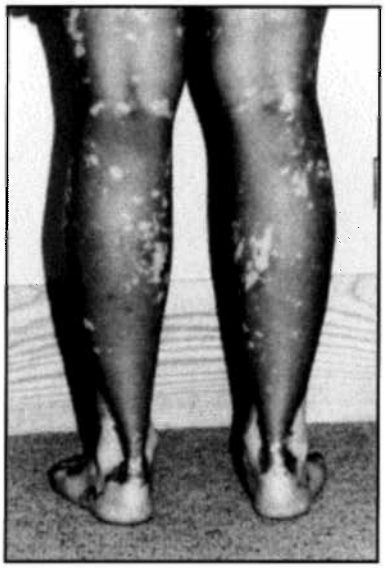

Fig 3.—Pretreatment with monobenzone: This shows extensive involvement of the posterior surfaces of the lower extremities.

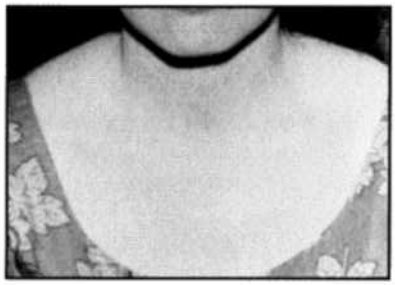

Fig 4.—Pretreatment with monobenzone: This shows the results of depigmentation with monobenzone to the neck.

Fig 5.—Post-treatment with monobenzone: This demonstrates the results of depigmentation of the right arm following treatment.

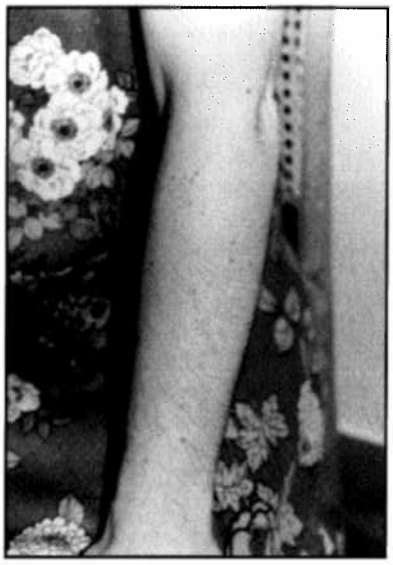

Fig 6.—Post-treatment with monobenzone: This demonstrates the results of depigmentation of the left arm following treatment.

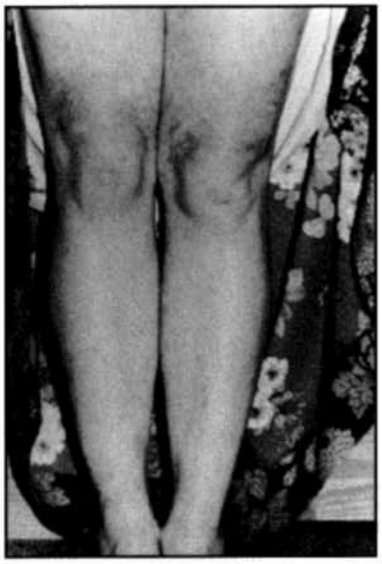

Fig 7.—Post-treatment with monobenzone: This demonstrates the results of depigmentation of the lower extremities (anterior surface).

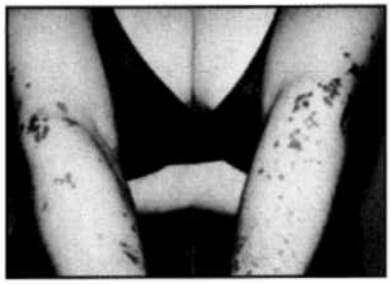

Fig 8.—Repigmentation: This photograph demonstrates spontaneous repigmentation of the arms following cessation of monobenzone therapy.

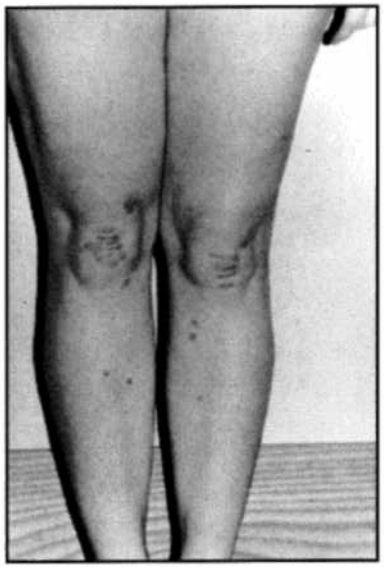

Fig 9.—Repigmentation: This photograph shows several small areas of repigmentation to the anterior surfaces of the lower extremities following cessation of monobenzone therapy.

with such extensive lesions that neither PUVA nor the other repigmentation therapies are appropriate, depigmentation of their remaining melanocytes is another option.

Depigmentation Therapy

This is the treatment of choice in patients resistance to repigmentation or with extensive(greater than 50% involvement of skin) vitiligo. The only recommended treatment in depigmentation therapy that has been shown to work effectively and produce cosmetically acceptable results is monobenzone.[1,9,16] Treatment is usually started with 10% monobenzone twice a day. However, therapy should be tailored to the individual patient. After 2 to 3 months the concentration is increased to 20% if no irritation occurs. Initially the face and upper arms are treated first to limit systemic effects. This is followed by application to the other affected areas. Depending on the patient's reaction to the treatment this may take up to 2 or 3 years. After treatment is complete the patient is completely depigmented and must take precautions against sun exposure. Dermatitis and pruritus are the most commonly reported side effects. However, they can be effectively controlled with corticosteroids. In addition, serosis, alopecia, premature graying, and ocular changes have also been reported in some patients.[16] While it is important to note that this treatment is generally considered to be permanent, repigmentation can occur. Additional applications of monobenzone to the repigmented areas are usually sufficient to remove them.

Conclusion

For extensive vitiligo(involving more than 50% of the patient's body) or vitiligo unresponsive to repigmentation therapies, depigmentation provides an excellent alternative treatment.[9,16] The side effects are easily controlled and the results can be highly satisfactory. Unfortunately, the only effective medication, monobenzone, is no longer available in the United States. Reintroduction of this drug to help this selective group of vitiligo patients would be highly desirable.

Addendum

Shortly after submission of this manuscript there was news that 20% benoquim(monbenezone) might soon be reintroduced to the American market.

Credits

Special thanks to Dr Norman Goldstein for his assistance.

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