Vitiligo in a young woman

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Vitiligo is common and can be distressing for patients, particularly those with a darker skin type in whom the depigmentation is more obvious.

Case history

A 26-year-old woman had a three-year history of irregular white macules appearing gradually and symmetrically on her face (eyelids and perioral area), neck, dorsal hands and fingers, arms and legs, with a few on her trunk and buttocks. Her complexion was olive, making the macules more unsightly.

There was no family history of similar problems, nor any personal or family history of thyroid problems, pernicious anaemia, diabetes mellitus or other autoimmune diseases. She worked in an office and gave no history of exposure to relevant chemicals.

Diagnosis

A diagnosis of vitiligo was made.

Treatment

The patient was treated with narrow band UVB phototherapy, methylprednisolone aceponate cream twice daily and, on the sites she found of most cosmetic concern (hands, face and neck), pimecrolimus cream twice daily, which was applied half an hour before the methylprednisolone aceponate. As the vitiligo was extensive, it was explained to her that there was a significant chance the treatment would not work well enough to achieve cosmetically useful repigmentation, and as such the treatment would be a trial for three to six months.

Comment

Vitiligo is generally easy to diagnose because it causes complete loss of colour in the affected areas (Figures 1a to 1d). Partial depigmentation (hypopigmentation) may occur, particularly for early lesions, but this usually progresses to complete depigmentation or a mix of complete and partial depigmentation ('trichrome vitiligo'). Vitiligo is most often symmetrical – the patient in this case had a typical distribution of colour loss.

Onset most commonly occurs in childhood to early adult life (average age of onset is 20 years) but can be at any age. New lesions gradually appear and old ones may enlarge, eventually becoming confluent and often leaving permanently depigmented areas. If hair-bearing skin is affected, the hair is often white (poliosis). There is substantial variability in the extent, rate of progression, age of onset and sites affected. Repigmentation may occur spontaneously and while new areas are appearing elsewhere, but it is rarely complete. Unilateral (segmental) vitiligo is an uncommon form in which the depigmentation is on one side only, is limited in size and, if on the trunk, face or neck, has a distinct cutoff at the midline.

Vitiligo is common, having a prevalence of 0.5 to 2% worldwide. Pathology shows total or near total loss of melanocytes in affected areas, usually with no or minimal evidence of inflammation. The aetiology is probably at least in part an autoimmune attack against melanocytes, although it is not known why only some areas of the skin are affected. In line with this, there are reports of vitiligo being transferred by allogenic bone marrow transplantation.[1] Genetic factors (partly via human leucocyte antigen [HLA] associations) also play a role but only around 10% of patients give a family history of vitiligo.

Other explanations for vitiligo have also been investigated, including melanocytotoxic effects of a breakdown of defences against free radicals, deficiencies in melanocyte growth factors, dysregulation of melanogenesis (with a role of the melanocortin receptor), neural factors (particularly for segmental vitiligo) and intrinsic melanocyte defects leading to their early death or apoptosis. It may well be that different factors in different patients lead to a common phenotype. The occurrence of the segmental form of vitiligo also suggests genetic factors; here the mutation presumably occurs during embryogenesis and thus only affects a limited amount of skin.

Vitiligo can be a distressing condition, particularly in people with a darker skin type in whom the depigmentation is more obvious.[2,3] That it more often occurs at a young age and frequently affects cosmetically sensitive areas such as the head, neck and distal limbs adds to its impact. Patients' responses to the condition vary from indifference to intense embarrassment and, on occasions being housebound.

Associations

There is a higher frequency of other autoimmune diseases in patients with non-segmental vitiligo than in people without the condition. Hashimoto's thyroiditis and Graves' disease are particularly associated, alopecia areata less commonly, and pernicious anaemia, Addison's disease and diabetes mellitus rarely. It is prudent

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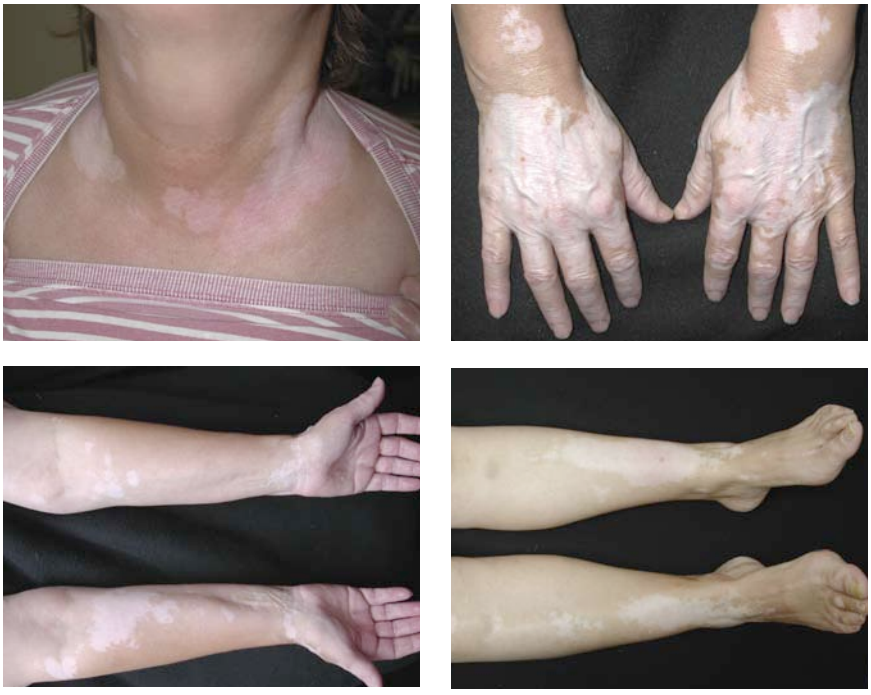

Figures 1a to d. Vitiligo on various sites of the body (not the case patient).

to perform thyroid function tests periodically in patients with vitiligo.

Differential diagnoses

Halo naevus

Halo naevus is a melanocytic naevus with surrounding vitiligo-like depigmentation. It most often occurs in teenagers (prevalence, 5%), and more than one mole may be affected. Sometimes patients also develop vitiligo elsewhere. It is probably a vitiligo-like process against naeval melanocytes. Rarely, a similar process can occur against a cutaneous or ocular melanoma, and this sometimes heralds regression of the melanoma.

Pityriasis alba

The most common cause of inflammatory depigmentation is pityriasis alba, a low grade form of atopic dermatitis where the inflammation disrupts the passing of melanosomes from melanocytes to epidermal keratinocytes. There is usually mild eczema or dry skin prior to the partially depigmented patches appearing. It occurs most often on the face but sometimes on the limbs or elsewhere, and it is more obvious in darker skinned people. Treatment settles the dermatitis but the pigment takes a long time to spontaneously reappear.

Other causes of inflammatory depigmentation include lichen sclerosus, morphoea, discoid lupus erythematosus, psoriasis, sarcoidosis and the uncommon depigmenting form of cutaneous T-cell lymphoma.

Guttate hypomelanosis

(Idiopathic) guttate hypomelanosis is common. These small partial or completely depigmented macules usually occur on sun exposed sites on the limbs or trunk, and rarely on the face. They do not coalesce and they persist for life. Substantial sun exposure is probably the main cause.

Chemical leukoderma

Chemical leukoderma causes vitiligo-like depigmentation. Many chemicals have been reported to cause it, particularly those used in rubber manufacture (usually it is workers involved in the manufacture of rubber that are affected but occasionally people can be affected by wearing rubber items). Other causative chemicals are monobenzyl ether of hydroquinone (which is used in depigmentation therapy for vitiligo – see later section on treatment) and also monomethyl ether of hydroquinone, p-tert-butyl catechol, p-tert-butyl phenol, sulfhydryl chemicals, arsenic, mercury and many more. Medicaments including hydroquinone and injected corticosteroids are an occasional cause.

The depigmentation occurs at sites of skin contact. However, some causes (e.g. the hydroquinone ethers) may also cause depigmentation well away from contact sites.

The decline of manufacturing industries in Australia means chemical leukoderma is rarely seen here.

Leukodema from skin injury

A common cause of leukodema from skin injury is cryotherapy as melanocytes are particularly sensitive to cold injury. Other causes include burns, wounds, lasers (including therapeutic ones) and ionising radiation. It should be remembered, however, that vitiligo may occur at sites of injury (Koebner reaction).

Infectious causes of depigmentation

By far the most common infectious cause of depigmentation is pityriasis versicolour, in which the yeast *Malassezia* causes partial depigmentation of particularly the upper trunk, neck and arms. The organism is commensal and thrives in a humid environment, so the infection is often worse in summer. In people with lighter skin, active disease is reddish brown with light scaling; in olive skinned people, it may be just light scale with hypopigmented skin. The hypopigmentation persists for months after effective treatment.

Herpes zoster may also be an infectious

cause of depigmentation, the scars from it occasionally being hypopigmented. Other infectious causes include leprosy, onchocerciasis, post kala-azar leishmaniasis and treponematoses such as secondary syphilis, pinta, bejel and yaws, but these are rarely seen in Australia.

Naevus depigmentosus

Naevus depigmentosus causes partial, sometimes complete, depigmentation in a naevoid distribution like segmental vitiligo. It is often present at birth, but may develop later. More extensive forms merge clinically with hypomelanosis of Ito syndrome (30% of children with this syndrome have a range of developmental problems, some neurological).

Genodermatoses

Various genodermatoses include depigmented skin as part of their presentation, such as albinism, piebaldism, tuberous sclerosus, phenylketonuria and Waardenburg's syndrome.

Treatment

The goal of treatment of vitiligo is to achieve a cosmetically acceptable amount of repigmentation and to halt progression of the disease. Unfortunately, the treatments are slow to work (take many months) and there is a relatively low chance of achieving complete or substantial repigmentation. Also, the vitiligo may continue to appear once areas have repigmented. Vitiligo on the fingers, lips and nipples often responds poorly to treatment.

The main treatment options are topical corticosteroids, topical calcineurin inhibitors, phototherapy, melanocyte grafting techniques, camouflaging techniques and chemical depigmentation of nonaffected skin.[4] Most often used are the topical therapies, with or without phototherapy, and partial repigmentation is usually achieved.[5] Little dots of perifollicular pigmentation (the hair follicle can be a reservoir of viable melanocytes) may slowly join to repigment a larger area but ultimately the amount of repigmentation may be too patchy to be cosmetically useful. Segmental vitiligo tends not to respond as well to medical treatments or phototherapy as nonsegmental vitiligo.

Topical corticosteroids

For small areas of vitiligo on the trunk, limbs or neck, a potent topical corticosteroid, such as betamethasone dipropionate 0.05% cream, ointment or lotion (Diprosone, Eleuphrat), may be used. Prolonged use of potent corticosteroids may cause skin atrophy with striae distensae and telangiectasiae. A compromise is to use somewhat weaker ones, such as methylprednisolone aceponate cream, ointment or lotion (Advantan) or mometasone furoate cream or ointment (Elocon, Novasone) twice daily, which are likely to be less effective but also less prone to atrophy.

Topical corticosteroid induced rosacea can be an issue on the face. Weaker products can be tried for this site, such as desonide lotion (Desowen) or 1% hydrocortisone cream, although in practice I often use methylprednisolone aceponate and monitor the patient's response.

Topical calcineurin inhibitors

The topical calcineurin inhibitors pimecrolimus cream (Elidel) and tacrolimus 0.03 to 0.1% cream (available through some compounding pharmacies) have recently become available.[6] Anecdotally, tacrolimus seems more effective. The PBS covers only pimecrolimus and only for atopic dermatitis; both are expensive, particularly tacrolimus. Small studies suggest response rates for monotherapy with a topical calcineurin inhibitor are as good as or better than with topical corticosteroids, and they may increase the success rate when used with topical corticosteroids.[7] Their safety profile is good, although they may cause burning irritation in the first week or two of treatment.

Calcipotriol

Small studies also suggest that calcipotriol cream or ointment (Daivonex) applied twice daily may add to the effectiveness of topical corticosteroids or phototherapy. The mechanism of action is unknown.[8]

Phototherapy

Various forms of phototherapy can be effective and are often given in conjunction with topical therapy. Most often used is narrow band ultraviolet B, which does not require oral or topical psoralens.[9] Treatments are given three times a week for more than three months. Response rates of over 60% have been reported but in practice the useful response rate is probably considerably lower with more extensive vitiligo.

Response rates of around 50% have been reported with psoralen ultraviolet A (PUVA) therapy but this therapy is more difficult to deliver, more prone to cause burning and causes more pigmentation of unaffected skin than narrow band ultraviolet B therapy. The psoralens can be delivered topically or orally. Topical psoralens can also be applied by the patient, with graduated exposure to natural sunlight, but this therapy is more uncontrolled and is infrequently recommended as it is notorious for causing severe sunburns.

Excimer lasers also deliver UV light and can be effective for localised vitiligo, with the advantage of causing little pigmentation of surrounding unaffected skin.[10] However, this treatment is not currently available in Australia.

Long term photodamage and photocarcinogenesis are issues for all forms of phototherapy.

Melanocyte grafting

Melanocyte grafting techniques have been successfully used for localised and segmental vitiligo.[11-13] However, few practitioners perform this therapy in Australia. It is best contemplated when

the vitiligo is stable and it is generally used for specific sites.

Several methods have been employed to harvest melanocytes or melanocyte bearing skin and to prepare the application site. Techniques used include mini punch grafts (perhaps more prone to later depigmentation) and suction blister or sheet grafts (donor site may depigment). Autologous culture techniques, with or without concentration of melanocytes, can be useful, and some dermatologists in Australia have tried ReCell – the cell culture technology used in some burn victims from the Bali bombings of 2002. In ReCell, the melanocyte concentration is not high and the results have been variable.

Camouflaging

Camouflaging can be achieved with dihydroxyacetone fake tan lotions, applied by the patient or a beautician. The number of applications will alter the intensity of the colour. Some beauticians specialise in cosmetic camouflage using various make-ups requiring accurate colour matching. Available brands include Covermark and Dermablend.

Microtattooing using iron oxide can be successful for stable disease.[14] This is performed by some beauticians or by dermatologists (as, for example, at the Skin and Cancer Foundation in Sydney).

Chemical depigmentation

If large areas of skin are affected or repigmentation techniques fail, depigmentation therapy to give a uniform colourless skin may be considered, but is rarely performed. Certain lasers and monobenzyl ether of hydroquinone may be used. The latter requires repeated application for nine to 12 months and may cause loss of colour elsewhere (through systemic absorption) or only partial depigmentation on the treated area (this can be managed by increasing the concentration of the chemical or also using a depigmenting laser). Irritation or contact allergy is not uncommon. Although the effects are permanent, later sun exposure may cause ugly perifollicular repigmentation.

Summary

Vitiligo is a common condition and can be distressing for the patient in that it often occurs at a young age and often affects cosmetically sensitive areas such as the head, neck and limbs. Treatment options include topical corticosteroids and calcineurin inhibitors, phototherapy, melanocyte grafting and camouflaging techniques and chemical depigmentation of nonaffected skin. Unfortunately, they are slow to work and there is a relatively low chance of achieving complete or substantial repigmentation. MT

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DECLARATION OF INTEREST: None.

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