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VITILIGO: AN OVERVIEW

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ABSTRACT

Vitiligo is an acquired disorder of depigmentation affecting 0.1%-2% of the world's population without discrimination of race, age and gender. Vitiligo is a skin disorder in which white patches occurs on the skin may be in the form of lesions or on the whole body. These white patches occur due to destruction of colour producing cells melanocytes. Etiology is unknown and the several pathogenetic hypotheses do not account for the entire spectrum of the disease. Although no full therapeutic solution for Vitiligo is available, many options may lead to acceptable results in most patients. While not life threatening, the disorder is associated with serious psychological trauma. Currently no known cure is available and the precise etiology is unknown. There are many treatment options available for the disease. Standardized guidelines for treating this disease in Asian skin are not readily available which leads to no set criteria for treating this cosmetically disfiguring problem. Different drugs like methoxsalen, trioxsalen and psoralen are available for the treatment of vitiligo in oral capsule form or topical cream or lotion form. Psoralen with light therapy is also given which is also known as PUVA therapy. Treatment of vitiligo always poses a problem as the patient compliance is less.

Keywords: Vitiligo pathogenesis, Melanocytes, PUVA, Auto immune response, Treatment of vitiligo.

INTRODUCTION

Vitiligo is a skin disorder characterized by multiple patches of depigmentation causing significant social and psychological distress [1]. The histological picture shows loss of melanocytes and melanin in the white patches and an inconstant lympho-mononuclear infiltrate in the advancing margins of vitiligo. The disease is seen at a frequency of 1% of the world population [2, 3]. Disease can appear at any age but more frequently seen in individuals less than 20years of age. It affects about 0.1%-2% of general population and familial incidence is about 30%.2It does not include racial, sexual or regional differences among the population. Some reports suggest that incidence of Vitiligo in India, Egypt and Japan is higher. It is a common depigmenting skin disorder, [4-8] characterized by acquired, idiopathic, progressive, circumscribed hypomelanosis of the skin and hair, with total absence of melanocytes microscopically. The exact cause of the disease is not yet known, but several hypothesis suggest that genetic predisposition, autoimmunity and increased vulnerability of melanocyte to destructive effects of toxic metabolites play an important role in disease causation.6 Vitiligo is classified into four types based on the distribution of the hypopigmented lesions: non-segmental Vitiligo (NSV), segmental Vitiligo (SV), mixed NSV and SV and unclassified types including focal, multifocal asymmetrical non-segmental and mucosal at one site. Melanocytes synthesize melanin from the amino acid tyrosine in the presence of an enzyme called a melanosome.

Definition

Vitiligo is a non-contagious acquired pigmentation disorder characterized by sharply-defined white patches of variable shape and dimensions, increasing in size and number with time. Vitiligo can be a psychologically devastating disease, especially in darker skinned individuals, in whom it is more easily noticeable[4, 5].

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Classification

Vitiligo is currently classified into two major subtypes: segmental vitiligo (type B) and non-segmental vitiligo (type A). Type B is more rare, includes focal lesions and those restricted to a segment of the integument. It has a dermatomal distribution; after a rapid onset and evolution, it usually exhibits a stable course. Type A is more common, has a potential lifelong evolution, and is associated with Koebner phenomenon and frequently with autoimmune disease.17From another point of view, vitiligo is classified as segmental, acrofacial, generalized and universal, orby pattern of involvement as focal, mixed and mucosal types [6].

Epidemiology

Vitiligo is the most prevalent pigmentary disorder, occurs worldwide,15 with an incidence rate of between 0.1% and 2%,13–15,17,18 irrespective of age, race,15,17–19 ethnic origin or skin color. Vitiligo commonly begins in childhood or young adulthood,15,24 with peak onset of 10–30 years,15,25but it can develop at any age.15,20,26–28 The prevalence has been reported as high as 4% in some South Asian, Mexican and US populations.20–22 Although familial clustering of cases is commonly seen, inheritance occurs in a non-Mendelian pattern [6]. Occasionally, it is reported that vitiligo is determined by an autosomal dominant gene of variable penetrance. It has also been reported in monozygotic twins.1,23 Approximately 20% of patients with vitiligo have at least one first-degree relative with vitiligo, and the relative risk for first-degree relatives of vitiligo patients is increased by 7- to 10-fold.15 One study showed that a high proportion of patients with vitiligo were students or pupils or of a high socio-professional level.30 Most patients with vitiligo attribute the onset of their disease to specific life events (physical injury, sunburn, emotional injury, illness or pregnancy). With the exception of Koebner phenomena, there is no proof that these factors cause or participate in vitiligo.

Pathogenesis

The actual pathogenesis of vitiligo is not known but has been attributed to autoimmune (AI) causes, oxidative stress, and/or sympathetic neurogenic disturbance.8There are several pathophysiologic theories as explained earlier, but no one is exclusive, and it is likely that each of them partially contribute. The convergence theory explains that stress, accumulation of toxic compounds, infection, autoimmunity, mutations, altered cellular environment, and impaired melanocyte migration can all contribute to pathogenesis.9Autoimmune mechanisms are the likely cause of generalized vitiligo, while a more localized phenomenon as focal or segmental vitiligo is likely to be a result of neurohumoral mechanisms.10 New theories, such as melanocytorrhagy and decreased melanocyte survival, are also under consideration[7, 8] progressive with occasional flares. Hair is affected in later stages. There is a frequently associated personal or family history of autoimmune disorders.19Koebnerization and non-segmental subtypes are associated with disease progression in patients not receiving therapy[9]. Rare types of vitiligo include ponctue which manifests as discrete, confetti like amelanotic macules which occur on normal or hyperpigmented skin[11]. Trichrome vitiligo is also a rare type, represents a tan zone of varying n width between normal and depigmented skin [12].

Melanocytes synthesize melanin from the amino acid tyrosine in the presence of an enzyme called a melanosome. Vitiligo is a skin disorder in which the partial or complete loss of melanocytes from patches of skin produces irregular white spots. Due to the observed variation in clinical manifestations of the disease, it seems likely that etiology of vitiligo may differ among patients and is complex. Therefore; several theories on vitiligo etiopathogenesis have been combined to formulate a convergence theory of vitiligo[13]. Anecdotal reports of precipitating events by vitiligo patients may provide some clues that point to heritable biological properties that might make the melanocyte of some people susceptible to environmental triggers or other stressors, possibly resulting in melanocyte death by necrosis, apoptosis or pyroptosis, consequent presentation of tolerogens and loss of immune tolerance, and ultimately autoimmunity directed against melanocytes.

Symptoms

What are the symptoms of vitiligo?

These fall into two groups:

1. Natural sunlight causes sunburn of the white areas of skin.
2. Those affected by vitiligo may find it a cosmetic embarrassment, especially when it affects normally exposed skin. Vitiligo will stand out more obviously when the surrounding skin is tanned or in naturally dark-skinned individuals.

The most common symptoms include white patches of skin that itch. It can affect any area of the body but it is usually seen on the extremities, face or neck, and skin folds. It can also affect the areas around the lips, genitals, gums, and the colored skin that surrounds the nipple. Vitiligo generally strikes people between the ages of 10-30 years old, and it is common in females and males alike.

Causes

The exact cause of vitiligo is not known. It is an autoimmune disease that is believed to be hereditary. The proposed theories are that stress, thyroid dysfunction, skin injury, severe sunburns, chemicals, and medicines combined with the genetic tendency towards vitiligo can all contribute to the condition. However, these are theories

that have not yet been substantiated.

Diseases involving hypopigmentation

Vitiligo

Vitiligo is a chronic, idiopathic, acquired pigmentation disorder with an unpredictable course arising in association with melanocyte destruction in affected areas and characterized by hypoorachromic patches and macules in the skin and mucous membranes [2, 3]. The global prevalence irrespective of gender is reported at 0.5-4%, with a mean age at onset of 24 and equal prevalence between males and females [5]. Vitiligo was first described in Buddhist literature and sacred texts in approximately 1400 BC. Researchers have proposed several theories, however. These include genetic, immunological, ototoxic, neurohormonal, viral, cytotoxic, biochemical, oxidative stress, multifactorial, decreased melanocyte survival and melanocytorrhagy theories. The most popular theory in recent years is that vitiligo results from melanocyte destruction due to environmental factors against a genetic background. Environmental factors leading to the initial symptoms of the disease include puberty, pregnancy, major infections, dietary irregularities, stress and skin trauma. Vitiligo can develop as a result of all these hypotheses or pathological mechanism. This distinction is important in terms of treatment options and prognosis. Lesions can be seen in the form of white macules of varying shapes and sizes anywhere on the body[3]. Recent studies have reported that uveitis and sensorineural hearing loss can be seen in 13-16% of

Patients as a result of a decrease in melanocytes in the audio logical and ophthalmological system together with skin and mucosal involvement, or as a part of poly endocrinopathy syndrome. The most serious outcome of the disease is that it can compromise quality of life as a result of psychological impacts such as depression, social phobia and loss of self-esteem. Although various therapeutic options are available for vitiligo, resistance to treatment is common. The most generally employed of these therapeutic options are topical corticosteroids, topical calcineurin inhibitors and ultraviolet (UV) light therapy. UV therapies can be applied in the form of phototherapy (UVB) and photo chemotherapy (psoralen plus UVA). UV therapies are considered the most effective of these. Although systemic corticosteroids are effective in widespread and progressive cases, there are concerns over their reliability in long-term use. Several topical and systemic treatments are still being investigated. The effectiveness of TNF-α inhibitors due to increased TNF-α levels in vitiligo has also attracted attention [6, 7].

Diseases involving hyperpigmentation

Melasma

Melasma (chloasma) is an acquired pigmentation disease arising due to melanogenesis dysfunction. It is more common in females than in males. The disease is also known as the mask of pregnancy or chloasma. The cause is still unknown, although there are known to be triggering factors, such as pregnancy, menopause and oral contraceptive use. Clinically, brown macules with distinct and irregular margins are seen. These are generally symmetrical and often on the face when exposed to the Sun. There are two subtypes of facial melasma depending on the site of involvement, centrofacial and peripheral. It may also be seen in extra facial regions such as the arms, forearms or cervical and sternal regions. The course involves irregular, symmetrical hyper chromic skin discoloration. Involvement in these regions is generally seen in advanced age in patients undergoing the menopause or receiving hormone replacement. Diagnosis is generally clinical. Wood's light and histopathology may be employed on rare occasions. Treatment must primarily be directed toward the underlying cause. Additionally, local treatments such as hydroquinone, tranexamic acid, 4-n- butylresorcinol, oligopeptides, silymarin, an extract of the plant *Silybummarianum* and orchid extract can be used, as well as chemical peeling gents such as tretinoin, trichloracetic acid (TCA), glycolic acid (GA), kojic acid and the novel agent amino fruit acid, as well as Q switched (QS) laser therapies. One percent tretinoin used for chemical peeling has been found to achieve similar success to 70% GA. Peeling with TCA, which can be used at a level of 10-20%, produces results within 4 weeks, although recurrences can be seen after 12 months. Amino fruit acid peeling is a novel agent reported to represent an effective therapy with its powerful antioxidant and photo pigmentation-preventive effects.

Diagnosis of Vitiligo

The diagnosis of vitiligo is usually made clinically. Wood's lamp may be of use in determining extent and activity of vitiligo, as well as monitoring response to therapy and the progress of lesions over time[15].Recommended evaluation checklist for the management of patients with nonsegmental is as follows:

Checklist for assessment of Vitiligo patient

- Skin phototype
- Duration of disease
- Age at onset
- Premature hair greying
- Genitals involvement
- Type & duration of previous treatments and on-going treatments.
- History of auto immune disease in family including vitiligo.

Points regarding diagnosis of Vitiligo

There are two cases for diagnosis

1. **Special cases includes**

- Anti-thyroid peroxidase antibodies.

- Endocrinologist advice if multiple auto immune syndrome considered.
- TSH & other tests if needed to assess thyroid function.

2. Uncertain diagnosis includes

- Punch biopsy from lesional & non lesional skin.

Differential diagnosis of vitiligo is very difficult. To diagnose the exact vitiligo one should be able to differentiate between different conditions of the skin like complete depigmentation, hypo pigmentation and normal colour of the skin. Diagnosis of vitiligo is very difficult in patients having light complexion of the skin colour. Wood's light is very useful to diagnose the vitiligo in the patients having skin type I and II. Pure tone and speech audiometer, Sound treated room, Cochlear Emission Analyser Madsen, Immittance meter, Evoked Response Audiometer Nickolet Compact four, Wood's light lamp equipments can be used for the diagnosis of vitiligo.

Vitiligo is a specific type of dermatological condition characterized by loss of pigment of the skin that can affect almost any part of the body, including premature greying of hair. The exact cause of vitiligo is unknown but it is believed to be an autoimmune disease that can be caused by genetic and/or environmental factors. The relationship between HCV and vitiligo is controversial. Most studies have not been able to find a direct link between HCV and vitiligo, but some smaller studies have suggested a causal link. Still other studies have found a link between vitiligo and interferon therapy. The diagnosis of vitiligo is usually based on a combination of tests: physical examination, blood tests for autoimmune markers, skin biopsy, and obtaining a medical history of the individual's family. The diagnosis is usually easy to make by your GP or specialist. Occasionally, examination under an ultraviolet lamp is helpful, especially in light-skinned people. Once the diagnosis of vitiligo has been made, your doctor may want to take a blood sample to check for thyroid disease and for other autoimmune conditions. Clinical photographs may sometimes be taken by your doctor to monitor vitiligo and the effect of any treatment you receive. Among acquired disorders, post-inflammatory hypopigmentation, chemical leukoderma,1,15 tineaversicolor, pityriasis alba, lichen sclerosis et atrophicus,1,15,24 morphea,24 sarcoidosis,15 leprosy1 and tertiary stage of pinta24 are included in the list of differential diagnoses of vitiligo. In addition, nevus depigmentosus, hypomelanosis macules of tuberous sclerosis, piebaldism, Vogt–Koyanagi syndrome, Waardenburg's syndrome and Ziprkowski–Margolis syndrome are rare congenital disorders and syndromes in this list.

Treatment of Vitiligo

Etiology of the Vitiligo is still unknown. But it involves some theories like Auto immunity, cytotoxicity, triggering, neural, free radicals and genetic. It can be treated by oral or topical formulations of the drug alone in mild cases but in severe case of Vitiligo Light therapy is also given with the consumption of medication to increase the pigmentation of the skin. The treatment of leukoderma or Vitiligo requires not only a deposition of pigment in the areas of depigmentation, but it also requires a redistribution of pigment from hyper pigmented borders, so that the result will be an even distribution of the normal amount of cutaneous colouring. It also depends on the presence of the type of the cell. Possibility of formation of melanocyte in inter-follicular epidermis is decreased by the presence of keratinocyte stem cells in the similar location.

There is no standardized treatment for vitiligo. Treatment is usually individualized and can include phototherapy (light therapy), steroids, and various topical ointments. In severe cases of vitiligo skin grafts have been found to help as well as tattooing the skin in people with dark skin. The skin can also be dyed or artificially tanned although it is difficult to match the dyed or tanned area to the pigmentation of the surrounding or healthy skin. Sun protection of the vitiliginous areas with sunblock's is important[14]. which help prevent sunburn and thus may lessen photo damage as well as the chance that a Koebner phenomenon will occur. Sunscreens also decrease tanning of the uninvolved skin and therefore lessen the contrast with vitiliginous lesions[15]. The substantial disfigurement associated with vitiligo can cause serious emotional stress for the patient, which necessitates treatment. Although it is relatively resistant to most of the treatments, spontaneous repigmentation occurs in more than 1–25% of cases[16].

Treatment of vitiligo with herbal medicines

From the list of Chinese herbs acting for the treatment of vitiligo decoction of *Xiaobailing changyee* powder and three yellow powders are most effective. These medicines include *Xanthum stramanum*, *Sophora flavescens, Atractylodes japonica*, *Arisaema amurense*. Some other herbs include *Carthamus tinctorius*, *Eclipta prostrate*, *Pleuropterees multiflorees, Salvia miltiorrhiza, Sesamum indicum, Spatholobus suberectus, Rehmania glutinosa*. Applying these medicines onto skin improve skin coloration and treat the vitiligo. There are a number of treatment options that can be discussed with your GP or dermatologist. Often no treatment may be required other than good sun protection, especially in pale-skinned individuals and cosmetic camouflage.

Sunscreens

Areas of vitiligo will burn easily in the sun. The use of a sunscreen with a high sun protection factor (SPF) of 30 or higher helps to protect skin affected by vitiligo, and also, when applied more widely, reduces the contrast between the areas of vitiligo and the surrounding normal skin. Other standard sun protection measures, such as appropriate protective clothing and sun avoidance should also be employed (see the 'top sun safety tips' below for

more information).

Topical corticosteroids

The application of a potent or very potent corticosteroid anti-inflammatory cream or ointment to areas of vitiligo may restore some pigment. Side effects, such as thinning of the skin and stretch marks, are a risk with continued use.

Other topical preparations

Other types of anti-inflammatory creams and ointments, such as the calcineurin inhibitors Tacrolimus ointment and Pimecrolimus cream and vitamin D analogues such as Calcipotriol, may also restore pigment in some patients. These topical treatments will help avoid the corticosteroid side effect of skin thinning. Photosensitizing agents involve *Psoralea corylifolia*, *Semicarpus anacardium* and *Ficus hispida*. They are administered locally as well as systemically with the sun exposure. Blood purifiers include curcuma longa, *Eclipta alba*, *Tinospora cardifolia*, *Hemiclascus indicus*, *Acasia catechu* and *Acaranthus aspara*. Exact mechanism of the herbs is unclear but it involves some mechanisms like phototoxic reactions, melanocyte proliferation, promoting anti-inflammatory activity and trigger reduction.

Phototherapy

This involves exposing affected skin to artificial ultraviolet light. Phototherapy may be helpful in a proportion of patients with vitiligo. However, treatment often needs to be prolonged (lasting at least several months). Full repigmentation is unusual and cosmetically sensitive areas such as the fingertips and the skin around the lips are less likely to improve (see Patient Information leaflet on Phototherapy). Ultraviolet light has been used to treat patients with vitiligo since many years. The exact mechanism of action is not known. It acts via both immunosuppressive and melanocyte stimulatory effects. Phototherapy should be reserved for patients who fail topical therapy or who have extensive vitiligo at the onset.

NB-UVB

NB-UVB is indicated for generalized NSV. 311-nm NBUVB phototherapy has outdated PUVA phototherapy in the treatment of vitiligo because it was shown to be clinically more effective. NBUVB induces tyrosine, an enzyme required for melanin production, and increases the presentation of HMB45 on the surface of melanosomes.

Surgical treatment

This process involves transplanting small islands of normal skin into areas of stable vitiligo. This method of treatment is still being developed and is not yet in general use.

Laser treatment

Some people have benefited from treatment with a laser called the Excimer laser. This treatment appears to work best on vitiligo that has not changed for a long time and affects relatively small areas of skin.

Removing the remaining pigment

If vitiligo has spread very widely (more than 50% of the body) or involves large areas of the face or hands, it may in exceptional circumstances be reasonable to consider removing the small amounts of pigmented areas of skin using a bleaching chemical such as hydroquinone. The emotional, social and medical implications must be carefully discussed before this treatment is used.

Psychological treatments

Professional help with developing coping mechanisms may be helpful in some cases of vitiligo.

Skin camouflage

Advice from experts about skin camouflage is now widely available. There are good quality camouflage products in a range of colours that are hard to rub off, and can be waterproof. Your GP or dermatologist can arrange instruction in this technique. Careful use of fake suntans can effectively disguise vitiligo.

Yoga therapy

Kapalbhati is helpful in the treatment of vitiligo. Because Of inhalation and exhalation kapalbhati provides aeration to blood and purifies blood circulation. This is beneficial in different skin diseases like vitiligo, psoriasis and other allergies.

Photo chemotherapy

Application of photochemical reaction is an advantageous for the treatment of vitiligo. Photo chemotherapy is Traditional therapy for Vitiligo. This therapy is based on ancient Atharva Veda observations. Psoralen is having very good photochemical response to ultraviolet B as well as ultraviolet A. Because of this reason the treatment includes topical/oral psoralen treatment, followed by exposure to ultraviolet light or Sunlight. This combined treatment is known as PUVA therapy (Psoralen Ultraviolet A therapy).Oral PUVA is being currently used in adult patients with generalized vitiligo as a second line therapy. UVA phototherapy is almost always given in combination with the photosensitizer psoralen. PUVA phototherapy induces hypertrophy of melanocytes and hyperactive melanosomes. Clinically, this results in perifollicular repigmentation.68 PUVA is approved by the FDA for the treatment of vitiligo, but high doses of UVA alone (15 J/cm2) has also induced repigmentation in various trials on vitiligo patients.

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CONFLICT OF INTEREST
None.

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