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Vitiligo: Etiopathogenesis and Clinical Characteristics

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Abstract

Vitiligo is a skin disease which can occur at any age, it is characterized by melanocyte destruction, it is manifested in the form of well-circumscribed, milky white patches of varying numbers and sizes, and although it is acquired, it can also be rarely congenital. Vitiligo is a multifactorial disease associated with genetic and non-genetic factors. Generally accepted view is the functional loss of melanocytes in the skin and its histochemical demonstration. Three basic theories have been put forward about the destruction mechanisms of melanocytes in vitiligo as autoimmune, neural and auto destruction. The most common form of vitiligo is depigmented macules which are surrounded by normal skin, completely amelanotic, milky or chalk white in colour with varying diameters, sharply circumscribed, round or oval, linear or irregular shapes. In the initial and active periods, hypopigmented areas may not be selected better than depigmented areas. Lesions grow slowly or rapidly centrifugally over time. Vitiligo macules and patches have sizes ranging from millimetres to centimetres. In fair-skinned patients, lesions cannot be seen without Wood light examination. In dark-skinned patients, the difference in contrast between the skin with vitiligo and the normal skin surrounding it is very pronounced. Although vitiligo lesions are generally asymptomatic, itching may occur especially in active lesions.

Keywords: Vitiligo; Etiopathogenesis; Clinical Characteristics

Introduction

Vitiligo is a skin disease which can occur at any age, it is characterized by melanocyte destruction, it is manifested in the form of well-circumscribed, milky white patches of varying numbers and sizes, and although it is acquired, it can also be rarely congenital [1]. It can start at any age; however, in 50% of the cases, it starts between the ages of 10 and 30 [2]. Its prevalence is equal in both genders and all races [3].

Etiopathogenesis

Vitiligo is a multifactorial disease associated with genetic and non-genetic factors. Generally accepted view is the functional loss of melanocytes in the skin and its histochemical demonstration [4]. Three basic theories have been put forward about the destruction mechanisms of melanocytes in vitiligo as autoimmune, neural and auto destruction [2].

Neural Theory

Neural theory is based on the damage of neurochemical mediators released from nerve endings on pigment cells. The onset of vitiligo lesions after emotional stress, their spread on paralyzed extremity, the presence of segmental involvement and accompanying viral encephalitis, multiple sclerosis and Horner syndrome support this theory [5]. Changes in the catecholamine pathway of vitiligo lesions have been shown to increase catechol-O-ethyl transferase and monoaminoxidase activities and neuropeptide Y levels and a change has been observed in the balance of peptide and nerve growth factor receptors associated with calcitonin gene [1,3]. One study has reported that the levels of homovanillic acid, which is a dopamine metabolite, and vanillylmandelic acid, which is a metabolite of epinephrine-norepinephrine, are increased in the urine of early stage or active vitiligo patients [6]. It has been suggested that the increase of catecholamine metabolites in urine or plasma maybe a secondary phenomenon or cause of depigmentation [7]. Melanocytes originate from the neural crest, just like the nervous system. Increased sweating, prolonged haemorrhage time and increase in local temperature have been observed in vitiligo lesions when compared with the surrounding normal skin [5].

Autoimmune theory

Comorbidity of vitiligo and autoimmune diseases and inflammatory changes in the skin form the basis of the

autoimmune theory. Autoimmune diseases such as thyroid diseases, pernicious anemia, type I diabetes mellitus, Addison's disease, autoimmune hypoparathyroidism and multiple glandular deficiencies are common in vitiligo patients [5]. The relationship of melanocytes, whose main job is to protect the living things from UV rays, with the immune system, has been better understood recently [8]. Pathology has been found in both cellular and humoral mechanisms in vitiligo. Antibodies against normal melanocyte surface have been found in 80% individuals with generalized disease [5]. The presence of perilesional T cells supports cellular immunity in immunohistochemical studies. Recently, melan-A specific CD8+T cells have been identified in the peripheral blood of vitiligo patients. Melan A / MART -1 antigens, first identified in patients with melanoma, are specific melanocyte-bound antigens recognized by cytotoxic T cells. A few studies have suggested that tyrosinase is the first antigen. Other identified melanocyte differentiation antigens are gp100/ Pmel17 and tyrosinase dependent protein (TRP) 1 and TRP-2. While these differentiations are produced in melanosomes, requirement for target antigen production in the membrane has been determined in antibody-mediated killing. It has also been shown that TRP-1 can be expressed on mouse and human melanocyte cell surfaces. It is thought that this differentiation antigen will be a target for intracellular melanocyte destruction [8]. In various studies, the number of Langerhans cells in vitiligo skin was found to be normal, increased and decreased when compared to the pigmented skins of the same patients and the healthy controls [9,10]. Langerhans cells are cells that play a role in antigen presentation to T cells in the epidermis and it can be thought that any increase in their number may cause the immunological process in the melanocyte damage that occurs in vitiligo lesions [11]. While the debates about whether autoantibodies occur as a result of pigment cell destruction in vitiligo or whether they are present from the beginning and cause destruction in pigment cells are not clear yet, studies on animals suggest that antibodies against pigment cells are present in the environment without pigment loss [12].

Autotoxic theory

Tyrosine analogues and intermediates, which are highly toxic to melanocytes formed during melanin synthesis, can lead to vitiligo by causing changes in cell antigen [5]. Another theory on this subject is the decrease in the activity of thioredoxin reductase, which protects the outer part of the plasma membrane in the membrane of keratinocytes. Due to the decrease in thioredoxin reductase enzyme, free radicals generated by UV cannot be removed [13]. Passi et al. found that Vitamin E, reduced glutathione, ubiquinol, polyunsaturated fatty acids were significantly decreased and thus a lipoperoxidative process developed in the epidermis of active vitiligo patients when compared with the control group. For this reason, they advocated that the use of antioxidants such as Vitamin E, selenium, ubiquinol and methionine could increase the concentration in the circulation and epidermal pool and thus have a therapeutic role in patients with active vitiligo [14]. It was also found that hydroxydopamine, which occurs as a result of dopamine autoxidation, kills human melanocyte cells by generating free radicals [7].

Compound theory

Le Poole et al. brought together theories about vitiligo etiopathogenesis and suggested that many factors such as stress, accumulation of toxic compounds, autoimmunity, infection, mutation, altered cellular environment and impaired melanocyte migration could play a role in the etiopathogenesis [15].

Triggering factors

It is common for vitiligo lesions to occur after physical traumas such as pressure, heat and UV rays and mental traumas such as job turnover, accident, loss of a relative and illness which increase the stress burden [5]. Sunburn, inflammation, psychological stress, vitamin deficiency, pregnancy, oral contraceptives, recurrent infections and chemotherapy can increase vitiligo [12,16]. Situations such as major surgeries, malnutrition, emotional stress, unemployment, divorce, loss of a family member can start vitiligo. It has also been found that broad spectrum antibiotics, especially tetracyclines, are effective in the start of vitiligo. In a study including five thousand patients, triggering factors in vitiligo have been examined and as a result, they were found as nutrition in 51.4% of the patients, as recurrent infections in 34.2%, medication in 23.2% and emotional stress in 20.4% [16]. In another study, emotional stress was found to be the triggering factor in 60% of 233 patients between the ages of 21 and 30 [17].

Clinical Characteristics

The most common form of vitiligo is depigmented macules which are surrounded by normal skin, completely amelanotic, milky or chalk white in colour with varying diameters, sharply circumscribed, round or oval, linear or irregular shapes. In the initial and active periods, hypopigmented areas may not be selected better than depigmented areas. Lesions grow slowly or rapidly centrifugally over time. Vitiligo macules and patches have sizes ranging from millimetres to centimetres. In fair-skinned patients, lesions cannot be seen without Wood light examination. In dark-skinned patients, the difference in contrast between the skin with vitiligo and the normal skin surrounding it is very pronounced. Although vitiligo lesions are generally asymptomatic, itching may occur especially in active lesions [4]. Although the lesions may be seen in any part of the body, the most commonly affected skin areas are the face, dorsal parts of the hands, nipples, axilla, sacrum, ingunial and anogenital areas. Facial vitiligo typically appears around the eyes and the mouth. In the extremities, the knee, elbow, fingers, the flexor part of the wrist and the dorsal part of the foot are favourite involvement areas. Involvement in dorsal parts of the hands and feet due to recurrent traumas, and folds of the body, axilla, genital area perianal area due to friction are common [18]. For this reason, Koebner phenomenon is a positive finding for vitiligo and it is a characteristic finding seen in at

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least one third of the patients [12,19]. Vitiligo is divided into two main groups as localized and generalized in current classification according to the prevalence of involvement and the distribution of macules [4] (Table 1).

Table 1: Classification of Vitiligo.

Localized Vitiligo	Generalized Vitiligo
Focal	Vulgaris
Unilateral / Segmental	Acrofacial
Mucosal	Mix
	Universal

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