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Virology & Immunology Journal
ISSN: 2577-4379

Viral causes of Vitiligo: A New Perspective for Vitiligo Pathogenesis

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Short Communication

Volume 2 Issue 8

Received Date: July 21, 2018

Published Date: August 02, 2018

Abstract

Vitiligo is an acquired skin depigmenting disorder due to loss of functional melanocytes in the epidermis. Several hypotheses have been proposed to explain its etiopathogenesis; however autoimmune pathomechanisms have been suggested to play an important role in the disease development. Previously, the viral causes of vitiligo have been suggested to be involved in vitiligo pathogenesis, however at present there are no such studies available to elucidate the role of viruses in inducing autoimmune mechanisms in vitiligo. The current article briefly summarizes all previous and currently available such studies involving viruses in vitiligo pathogenesis. The vitiligo being a complex autoimmune disorder and an important disease of research opens a new way to look at the virus based autoimmune mechanisms to cause vitiligo.

Short Communication

Vitiligo is an acquired, progressive, multifactorial, depigmenting disorder characterized by the appearance of circumscribed white macules in the skin due to chronic, progressive loss of functional melanocytes in the epidermis [1] (Figure 1). The selective destruction of melanocytes results in the development of depigmented patches. As such vitiligo is hardly a disease of medical significance but there is more of a social stigma attached to it because of cosmetic reasons. Although it might be viewed as minor disorder, these patches gradually increase in size and cause lot of psychological stress in the patient, self esteem and social interactions, particularly in patients with deeply pigmented skin [2]. The prevalence studies revealed that the worldwide prevalence of vitiligo ranges between 0.5 and 2% [3]. Based on a few dermatological outpatient records the prevalence of vitiligo in India is found to be 0.46% to 8.8% [4].

Figure 1: Patient with Vitiligo manifestation.

The exact aetiology and detailed pathogenesis of vitiligo is not fully understood, but autoimmunity has been strongly implicated in the development of the disease [5]. However, the involvement of microbial infections including the viruses cannot be avoided for vitiligo pathogenesis. The animal model studies showed that virus infection can trigger an autoimmune response. The viral peptide sequences may have molecular similarity with that of host cell antigens which in turn can activate the subsets of T-cells, resulting into autoimmunity. The virus may escape the detection after the onset of the disease [6,7].

Since, chronic viral infections have been suggested to trigger the development of autoimmune diseases; vitiligo may be triggered by viral infection in a genetically predisposed host [8]. It has been suggested that virus induced T-cells could act against melanocytes. The virus can also attract leucocytes and macrophages leading in turn to the 'oxygen burst' via NADPH-oxidase concomitant with the production of ROS (such as superoxide radicals, H2O2), thus generating ROS pool in vitiligo. The association of vitiligo with such virus and/or viral diseases has been shown in Table 1 [8-24]. However, few studies deny the involvement of virus in vitiligo pathogenesis [21,25].

Earlier studies have suggested that viruses may be involved in vitiligo pathogenesis. Viruses such as Cytomegalovirus (CMV) and Epstein Barr virus were detected in the epidermis of vitiligo patients [16,24]. The Herpes Zoster Virus was found in patients affected with segmental vitiligo [20]. The vitiligo was found to be associated with the Herpes Simplex Labialis Virus as well [22]. In addition, herpes virus connection was suggested in the expression of autoimmune vitiligo in Smyth line chickens [19]. Moreover, several studies have reported the association of vitiligo with HIV infection in AIDS patients either as a result of the infection itself or a complication of ART [8-15]. Tojo, et al. suggested that appearance of skin lesions in the early phase and their subsequent regression in the immunodeficient state indicate that certain immunological responses might be induced by HIV infection in the early course of this case [15]. Few studies have found that HIV infected persons led to development of psoriasis, alopecia universalis and alopecia areta suggesting that dermatological diseases including vitiligo may be due to autoimmunity caused by HIV virus in these patients [8,9,13]. However, one study has suggested that vitiligo was developed in AIDS patients after antiretroviral therapy [11].

The possible explanation for involvement of HIV in vitiligo development suggests that vitiligo could occur as a result of direct viral infection of melanocytes by HIV or by activated polyclonal B-cell directed against melanocytes surface receptor like melanin-concentrating hormone receptor 1 (MCHR1), and by excessive production of interferon-γ, or changes in the balance between helper and suppressor/regulatory T cells [10,26-29]. It has been observed that AIDS patients usually exhibit reduced numbers of $CD4^+$ peripheral T cells and which might favour the development of vitiligo; since increased $CD8^+$ cells and decreased $CD4^+$ cells have been observed in vitiligo patients [27]. Another study demonstrated that melanoma-derived Melan-A recognizing T-cell-lines were able to lyse T2 cells loaded with synthetic peptide sequences derived from viral origin; suggesting that T cells activated by virus could recognize self antigens and kill the host cells [30]. However, more research is needed to further understand the role of autoimmunity in AIDS.

Nevertheless, vitiligo has been found to be associated with chronic hepatitis C virus (HCV) infection and autoimmune hepatitis [17]. Akcan, et al. reported a low hepatitis B virus (HBV) sero-positivity in vitiliginous patients [18]. Moreover, it has been suggested that previous or concurrent cytomegalovirus (CMV) infections may induce the etiopathogenesis or deterioration of vitiligo [18,23]. In addition, the occurrence of cytomegalovirus DNA in skin biopsy specimens of vitiligo patients also suggested that viral infection could play a role in induction of vitiligo [24]. The involvement of other viruses such as Epstein-Barr virus, hepatitis E & C virus, herpes virus, herpes zoster virus, CMV, in addition to HIV is indicative of crucial role of viruses in development of vitiligo through modulating the immune system.

Virus Infection/Disease	Association with Vitiligo	References
HIV/AIDS	Yes (along alopecia areta)	[8]
HIV/AIDS	Yes (along with of psoriasis, alopecia universalis)	[9]
HIV/AIDS	Yes	[10]
HIV/AIDS	Yes (after antiretroviral therapy)	[11]
HIV/AIDS	Yes	[12]
HIV/AIDS	Yes (along with alopecia areta)	[13]
HIV/AIDS	Yes	[14]
HIV/AIDS	Yes	[15]
Epstein Barr Virus	Yes	[16]
Hepatitis C virus	Yes	[17]
Hepatitis B virus	Yes	[18]
Herpes virus	Yes (in Smyth line chickens)	[19]
Herpes Zoster Virus	Yes (in Segmental Vitiligo)	[20]
Herpes Simplex virus	No (in Serum)	[21]
Herpes Simplex Labialis Virus	Yes (in Post- Herpes Simplex Labialis Vitiligo)	[22]
Cytomegalovirus	Yes	[23]
Cytomegalovirus	Yes (in skin biopsy of patients)	[24]

Table 1: Association of vitiligo with virus/viral diseases.

Conclusion

The previous studies involving the virus infection and vitiligo development propose a significant role of viral mechanisms for destruction of epidermal melanocytes which may serve as possible risk factor for vitiligo. The animal model studies will be helpful in delineating the virus based autoimmune mechanisms for vitiligo pathogenesis. However, currently there is a lacuna in such studies and hence it opens yet another line of investigation on finding out the crucial autoimmune mechanisms induced by viruses to elucidate and confirm the involvement of viruses not only in vitiligo pathogenesis but other autoimmune diseases as well.

Acknowledgements

We are thankful to Uka Tarsadia University, Bardoli, Gujarat, India for providing necessary facilities needed for the preparation of this article. We are thankful to Mr. Hardik Dwivedi for providing his photograph to explain the vitiligo manifestation.

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