Autoantibodies Profile in Vitiligo

Kabir Magaji Hamid1,2,*, Zelalem Kiros Bitsue1 and Abbas Mirshafiey3

1Department of Immunology, Faculty of Medical Laboratory Sciences, Usmanu Danfodiyo University Sokoto, P.M.B 2346, Nigeria
2Department of Immunology, School of Public Health, Tehran University of Medical Sciences-International Campus (TUMS-IC) Tehran-14155, Box: 6446, Iran
3Department of Immunology, School of Public Health, Tehran University of Medical Sciences, (TUMS) Tehran-14155, Box: 6446, Iran

Abstract

Vitiligo is one of the disease which is yet to understand its pathogenesis, however many studies associate this disease as an autoimmune. Detection of autoimmune cells in the serum, lesional and perilesional area of vitiligo patients gives more insight on the disease mechanism. Presence of autoantibodies against melanocytes antigens in vitiligo patients indicates an autoimmune involvement in the aetiology of the disease. Identification and characterization of vitiligo autoantibodies would pave the way for developing new laboratory test for diagnosis. Studying the autoantibodies profile can give an impression on the disease condition of vitiligo patients. We realized the need of research emphasis in this area as more is yet to be discovered. In this review we give an account on different autoantibodies and their associated autoantigens in vitiligo as another effort of providing an updated data for detail analysis.

Keywords: Antibodies; Autoimmunity; Melanocytes; Pigmentation; Vitiligo

Introduction

Vitiligo is an acquired depigmenting disorder in which melanocytes are destroyed, resulting in patchy depigmentation on skin and mucosal surfaces [1,2]. The worldwide prevalence is range from 0.5–2% [3]. Clinically, vitiligo presents as round or oval white, hypopigmented macules with regular or raised red borders [4]. The disease was classified based on distribution patterns of vitiliginous lesions into focal vitiligo (isolated lesion), segmental vitiligo (unilateral macular lesions which generally cover a dermatome), non-segmental (generalized) vitiligo (most common form, disseminated macules of variable size, usually with a symmetric distribution and a certain predilection for extensor surfaces) [5,6] and universalis vitiligo (severe form that affects more than 80% of the body surface) [4].

The pathogenesis of vitiligo is unclear. although both genetic [7] and environmental factors are the ones implicated as the major cause [8], however, there are other several factors proposed in the pathogenesis of the disease (Figure 1), these include the following, physical trauma [9,10], psychological stress [11], infections [12], neural factors [11,13,14], biochemical factors [15-17], melanocytes growth factors [18], melanocortin hormones [19] and autoimmunity [20].

Most authorities favored the autoimmune causes due to the strong associations of vitiligo with multiple autoimmune diseases; the presence of autoantibodies [21,22] (Table 1), so that autoreactive T lymphocytes against pigment cells supports the theory that there is an autoimmune involvement in the aetiology of the disease [23]. However, even if the specific antibodies to pigment cells or secondary antibodies are not pathogenic, the identification and characterization of their target antigens could be a landmark for uncovering the pathogenic mechanism, formation of autoantibodies [24] and development of biomarkers. In this review we describe some autoantibodies and their associated autoantigens as potential biomarkers for laboratory diagnosis, treatment, monitoring and assessment of vitiligo.

Anti-Melanocytes

Melanocytes originate from neural crest and are responsible for the synthesis of melanin in melanosomes, membrane-bound organelles [25,26]. They are able to secrete a wide range of signal molecules, including cytokines, Pro-opiomelanocortin (POMC) peptides, catecholamines, and Nitric oxide in response to UV irradiation and other stimuli, for the regulation of variety of skin cells [27]. In active non-segmental vitiligo, melanocyte cytotoxicity is associated with increase in serum levels of immunoglobulin G (IgG) anti-melanocyte/vitiligo antibodies (V-IgG) and immunologic markers [28]. IgG anti-melanocyte antibodies were reported to induce melanocyte damage in vitro by a complement-mediated mechanism and antibody-dependent cellular cytotoxicity [29,30]. The melanocytotoxicity could be due to wrong presentation of vitiligo antigens to destructive cytotoxic T cells, this result from abnormal expressions of HLA-DR and increase expression of intercellular adhesion molecule-1 (ICAM-1) on melanocytes by IgG anti-melanocyte antibodies [29,31]. Antibodies to melanocytes occur at a significantly increased frequency in the sera of vitiligo patients when compared with healthy individuals [32]. Interestingly, correlations can also exist between the incidence and level of melanocyte antibodies and both the activity and extent of vitiligo [33]. Identification of anti-melanocyte or vitiligo antibodies against target antigens is useful in developing new diagnostic tests and serves as biomarkers for assessing the progress of the disease [23].

Anti-thyroid peroxidase (anti-TPO)

Anti-TPO antibodies are specific for the autoantigen TPO; found in active phase of chronic autoimmune thyroiditis; can be used in monitoring the disease progress in patients with these antibodies [34]. Most of the anti-TPO antibodies are produced by thyroid infiltrating lymphocytes and partly from lymph nodes and bone marrow [35]. In the past decades, many research teams reported the associations between vitiligo and other autoimmune diseases such as thyroid disease and anti-thyroid antibodies [36]. A previous study by Dave et al. reported 31.4% prevalence of thyroid-specific autoantibodies in patients with vitiligo [37]. A more recent study reported a mean prevalence of 20.8% in patients with vitiligo [38]. Again, Kasumagic-Halicov et al. found higher frequency of anti-TPO in vitiligo patients than control group [39]. Considering these findings vitiligo shows strong association with thyroid autoimmunity, therefore anti-TPO

*Corresponding author: Kabir Magaji Hamid, Department of Immunology, Faculty of Medical Laboratory Sciences, Usmanu Danfodiyo University Sokoto, P.M.B 2346, Nigeria, Tel: +998102159812; E-mail:kamhamid@hotmail.co.uk

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Detection in vitiligo patients could be useful markers for assessment of the disease. In this case, more in-depth studies are required to give detail information.

**Anti-melanocortin 1 receptor (MC1R)**

The melanocortin peptide α-melanocyte-stimulating hormone (MSH) is an important regulatory agent in skin pigmentation, inflammatory modulation and response to stress [19,40]. The α-MSH binds to MC1R on the melanocyte [41] to increase tyrosinase activity and eumelanin production; this action could lead to regulation of melanocytes, skin pigmentation, nitric oxide production and release of other signalling molecules from melanocytes [41]. Moreover, Pichler et al. reported that α-MSH levels were significantly lower in vitiligo patients compared to normal individuals [42]. Since the expression level of α-MSH in the melanocytes from lesion and perilesion area of vitiligo skin are lower than that from normal skin [43]. The proportion of α-MSH immuno-positive melanocytes is significantly reduced in the lesional and perilesional skin of vitiligo patients compared to controls [44]. Autoantibodies against MC1R are rare or absent in sera of vitiligo patients [45].

**Melanin concentrating hormones receptor (MCHR)**

MCHR1 has been identified as a B cell autoantigen in vitiligo; the
TH in melanocytes, existing knowledge indicates that the TH mRNA subsequently converts L-tyrosine to dopaquinone, a precursor of display technology [54]. TH was suggested to play role in melanin vitiligo with autoimmune disease [24]. Here the use of serological lamin A antibody may likely be a potential marker of non-segmented that 83% of vitiligo patients had the antibodies against VIT75 while disease or healthy controls [24]. Furthermore, previous study showed of the antibodies are higher than in the patients without autoimmune had at least one autoimmune disorder; the prevalence rate and titers clear. Interestingly, majority of vitiligo patients with anti-lamin A antibodies are detected in sera in a range of autoimmune diseases [52]; although in vitiligo remains unknown [24]. However, anti-lamin antibodies were not identified until recently, indeed, its immunopathogenic role in melanocytes. Antibodies against this antigen are used in the autoimmune mechanism in the vitiligo patients. Antibody against MART-1 requires further investigation, as it may potentially give an insight on an autoimmunity in the vitiligo patients. Antibody against MART-1 is indeed a good approach. The antibodies in vitiligo can serve as biomarker for development of new diagnostic test in vitiligo could be a good approach.

Other Antibodies

Circulating organ-specific autoantibodies particularly to the thyroid, adrenal glands, gastric parietal cells, and pancreatic islet cells are commonly detected in the sera of vitiligo patients [61]. Moreover, antinuclear antibody and IgM-rheumatoid factor have been detected at a significant frequency in vitiligo patients [32]. Anti-keratinocyte intracellular antibodies that correlate with disease extent and activity have also been detected in vitiligo patients [62]. Tyrosinase-related protein 1 (TYRPI) is a critical enzyme for the correct trafficking of tyrosinase to melanosomes [63]. In addition, autoantibodies against TYRPI are also suggested in vitiligo patients (Table 1).

Conclusion

It is obvious there is strong indication that autoantibodies are playing significant role in vitiligo pathogenesis. Although there are some disputed findings, however most of the studies indicate the presence of autoantibodies in vitiligo patients, therefore the use of these antibodies for development of new laboratory test for diagnosis is indeed a good approach. The antibodies in vitiligo can serve as potential biomarkers for monitoring and assessment of autoimmune diseases in vitiligo patients. In-depth researches in this area could likely give a good conclusion on the pathogenic mechanism of vitiligo in autoimmune diseases. Certainly, there are more to discover in vitiligo pathogenesis.
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