Inflammatory theory in Vitiligo

Ibrahim Galadari, MD

***Abstract*:**

The aetiology of vitiligo is still unresolved, and there is still different speculation that can be considered. Autoimmune, self destruction, neurologic, genetic, environment and others. I have reported 22 cases of vitiligo, that inflammatory theory should be strongly considered.

Introduction:

Vitiligo is a relatively common disorder that affects 1-3% of the population. It is manifested by cutaneous depigmentation which causes cosmetic problems. Few cases of Vitiligo were reported presenting with raised inflammatory borders[1] together with an enhanced cholinergic activity[2]. The disease might be associated with other diseases as ocular abnormalities, alopecia totalis, psoriasis and necrobiosis lipoidica

Diagnosis:

It is sometimes difficult to be sure, whether a depigmented macule represents true vitiligo or simply post - inflammatory depigmentation. In such cases, the history and subsequent progress of the case may provide the clue. In the recent cases reported, however, it can be clearly noted that the depigmentation was associated with the resolution of papular satellites, discrete papules, raised inflammatory border or migrating edge. Further spontaneous spread of de-pigmentation beyond the papular satellites or the inflammatory edge and beyond the biopsy scar in previously recognized cases of vitiligo and the presence of other typical vitiliginous macules in almost all of the reported cases, defeat suspicion that the depigmentary process in discussion might be simple non- specific inflammatory depigmentation and not true vitiligo. Furthermore, with exception of the papular lesions the inflammatory processes which in all other cases did not conform with a definite clinical diagnosis or show what favours the diagnosis of a post inflammatory hypopigmentation. It is very unlikely to suggest or consider the coincidence of an inflammatory process unrelated to Vitiligo to be restricted to the edge of Vitiligo lesion.

Correspondence:
Ibrahim Galadari, MD
UAE University
P.O. Box: 8716
Dubai, UAE.

Clinicopathologic Interpretations:

It is note worthy that lichen nitidus like histologic features were seen in some cases (cases No. 3,4 & 5), these features were absent in other cases and even in a second biopsy from the same patient (case No .3) where the histologic features of the second biopsy suggested non-specific dermatitis rather than lichen nitidus like.

The clinical resolution of discrete papules into vitiliginous macules have been repeatedly observed (cases 1,2,3 & 5). It is therefore, tempting to consider that despite the histologic resemblance of some of the described papules to lichen nitidus the possibility of mere coincidence of the two conditions is very -unlikely because of the evanescent nature of these papules ultimately resulting in most of the reported cases, into skin that usually follows the spontaneous resolution of lichen nitidus when it occurs. Moreover, other characteristic features of lichen nitidus are lacking viz: the distribution, the colour of individual papules (flesh-coloured or slightly darker than surrounding skin) and the known chronicity of the lichen nitidus. Furthermore, the presence of perivitiligo papular satellites and inflammatory edges in different Vitiligo lesions; of the same patient, probably speaks for identical or at least related inflammatory processes.

Comment:

Vitiligo is a complex disorder, the exact cause of which is unknown. It involves dysfunction and defectiveness of melanocytes [14] and defective keratinocytes Calcium uptake in Vitiligo[15]; some cell surface antigens are selectively expressed on pigmented cells with or without an auto-immune reaction and it is possible that the immune system will respond to these antigens. Acetylcholine might play a role because acetylcholine esterase activity was found to be lower in vitiliginous skin but become positive during repigmentation [16].

The auto immune theory as a cause of vitiligo is gaining an increasing support particularly when Vitiligo association with multiple with multiple autoimmune disease is noted [17]. Added to that, organ specific antibodies were found by some worker. Moreover, T-cell abnormalities were detected in Vitiligo as high levels of CD4 positive lymphocytes with increased CD4/CD8 ratio. These T-cell abnormalities were found in Vitiligo patients relatives [18]. These T-cell changes are more

striking in active Vitiligo than in static Vitiligo which indicate a possible role for cell-mediated immunity in the pathogenesis of the disease [19]. Added to this, natural killar cell activity was found to be abnormal (more marked in static Vitiligo) [20]. Auto-reactivity to pigmented cells was also detected. Further support to the autoimmune theory of the disease is the finding of antimelanocyte antibodies in affected area of patients with Vitiligo [21].

These antibodies can lyse melanocytes by both complement cascade activation and antibody dependent cellular cytotoxicity [22]. Vitiligo antibodies level is directly propotional to the extent of the disease. Another finding is that epidermal dendritic cells (Langerhan's cells and intermediate cells) are absent in some patients with Vitiligo (possibly destroyed by cytotoxic factors)[23], while in other patients there was functional impairment of langerhan's cells in vitiliginous skin while the number of these cells was not affected [24]. In another study Langerhan's cells were found to be normal in number during depigmentation and increased in number after depigmentation, so this casts some doubts about the role of langerhan's cells in Vitiligo [25]. An interesting association was found between Vitiligo and chronic urticaria with total absences of eosinophils [26], and in this contest the inflammatory theory as a cause of Vitiligo remains to be studied. The association of human leukocyte antigens (HLA) with autoimmune disease is interesting. Vitiligo was found to be associated with HLA-DR4 [27]; Moreover, a relationship was found between the age of onset of Vitiligo and HLA supratypes.

Another tempting theory is the viral theory. A viral infection might be the trigger for the development of some auto-immune diseases, Vitiligo was reported to develop in patients with acquired immuno-deficiency disease and hepatitis, so the viral infection might be the trigger in genetically predisposed individuals [28].

The inflammatory theory is a possible alternative; inflammatory borders to the lesions were reported long time ago but later other authors reported more cases with Vitiligo associated with raised inflammatory borders [29] of inflammatory reaction seen histologically in some cases. Regardless the paucity of the reported cases with inflammatory element, similar cases with minor degree of inflammatory process could be easily overlooked. Some workers favoured an inflammatory origin for Vitiligo even in the absence of erythema and they thought that the response from topical steroids in these cases was due to the anti inflammatory effect of these drugs [29,30].

The associated perilesional hair loss seen in some cases may be attributed to an inflammatory process comparable to that seen microscopically in early lesions of alopecia areata. Also graying of hair in some cases of alopecia areata might represent a type of Vitiligo, and it is felt that the association of Vitiligo and alopecia areata is far from being accidental. Some cases of alopecia areata in their progress to alopecia totalis undergo gradual dilution of skin colour and develop total Vitiligo[31].

More interestingly, alopecia areata was reported to develop around a nevus pigmentosus of the scalp which is probably comparable to perinevoid Vitiligo (32), and actually Uda et al have also suggested the presence of at least two etiological varieties of Vitiligo, the common variety and the one associated with halo nevus. So all these observations collectively point out the importance of the inflammatory cause for Vitiligo.