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PROFILE OF TH17 PATHWAY IN THE PATHOGENESIS OF VITILIGO

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Abstract

Background: Vitiligo is caused by a confluence of hereditary predispositions and environmental stimuli. Its etiology is yet unknown, though. Recent research suggests that cell-mediated cytotoxicity, oxidative stress, neurohumoral factors, and autoimmunity are all involved in the pathophysiology of vitiligo. According to the autoimmune theory, the continuous production of autoantibodies and the significant infiltration of cytotoxic (CD8+) T-cells at the site of inflammation in the skin region result in the targeted killing of melanocytes.

Material and Method: This study was conducted in the Dept. of Dermatology. This is a case–control study. Clinically diagnosed vitiligo patients were grouped as cases while healthy volunteers were grouped as controls. Both the groups comprised age and gender-matched individuals. Whole blood samples collected from both groups were used to estimate the selected cytokines (IL6, IL23, IL10, and IL17) level.

Result: The clinical and demographic details of the study participants are summarised in Table 1. The majority of the patients showed the non-segmental type of vitiligo (86.7%). Some patients (10%) reported a familial history of vitiligo.

Conclusion: The plasma's cytokine concentrations were examined. In vitiligo, IL6 and IL17 plasma levels were 2.3 and 1.6 times higher, respectively, than in controls. In contrast, vitiligo patients had 2.5-fold lower plasma levels of the suppressor cytokine (IL10). Plasma IL23 levels did not significantly differ between the groups, though. In addition, vitiligo patients had larger ratios of inducers to suppressors (IL6/IL10 and IL23/IL10) than controls. These findings suggested that the cytokine profile in vitiligo is proinflammatory.

Keywords: IL6, IL23, TH17, Vitiligo and Autoimmune

Introduction

A non-infectious autoimmune condition called vitiligo causes the skin to become less pigmented as a result of the death of melanocytes. Around 4% of people in India and 1% of people globally have vitiligo. Although vitiligo does not typically result in any severe disabilities, it has a significant influence on sufferers' social lives and is still stigmatized in India. Recent improvements in vitiligo therapy merely lessen the severity of the condition; they do not cure it. In order to create targeted medication therapies and treat the illness, current research is focused on understanding the autoimmune systems involved in causing vitiligo.[1]

Vitiligo is caused by a confluence of hereditary predispositions and environmental stimuli. Its etiology is yet unknown, though. Recent research suggests that cell-mediated cytotoxicity, oxidative stress, neurohumoral factors, and autoimmunity are all involved in the pathophysiology of vitiligo. According to the autoimmune theory, the continuous production of autoantibodies and the significant infiltration of cytotoxic (CD8+) T-cells at the site of inflammation in the skin region result in the targeted killing of melanocytes. However, the mechanism that initiates autoimmunity is unknown. Recent research has shown that the Th17 pathway is involved in triggering autoimmunity in several autoimmune disorders, including psoriasis, psoriatic arthritis, inflammatory bowel disease, systemic lupus erythematosus, and others.[2]

The development and control of naive T cells into T-helper 17 cells (Th17) are regulated by the Th17 pathway. Dendritic cells (DCs) release inflammatory cytokines such IL6, IL23, and TGF-beta (TGF), which bind to their respective receptors on naive T cells and start the Th17 pathway, to trigger this process. Three main elements make up the Th17 pathway: effectors, mediators, and inducers. Pro-inflammatory cytokines including IL6, IL23, and TGF-beta (TGF) that work as positive regulators to support the activation process are known as inducers.[3] The expression of Th17 pathway genes including IL17A, IL17F, IL22, and IL26 is increased as a result of the activation of transcription factors (mediators) such STAT3 and RAR-related orphan receptor C (RORC) by these inducers. These chemokines are released from resident cells such fibroblasts, Antigen Presenting Cells (APCs), and keratinocytes (in the case of skin) by these secretory pro-inflammatory cytokines (effectors). Cytotoxic T cells are then stimulated by chemokines to go toward the infection site. Being a part of innate immunity, this pathway's unchecked activation can result in persistent inflammation and the mutilation of nearby tissues, which can cause autoimmunity. However, it is still unclear whether the Th17 pathway contributes to autoimmunity in vitiligo.[4,5]

Aim

The aim of this study was to determine the status of the Th17 pathway in vitiligo.

Material and Methods

This study was conducted in the Dept. of Dermatology. This is a case–control study. Clinically diagnosed vitiligo patients were grouped as cases while healthy volunteers were grouped as controls. Both the groups comprised age and gender-matched individuals. Whole blood samples collected from both groups were used to estimate the selected cytokines (IL6, IL23, IL10, and IL17) level.

Inclusion Criteria

Patients clinically diagnosed with vitiligo

Both male and female patients of age ≥ 18 years

Patients not under topical treatment for vitiligo or any other inflammatory conditions for 1 month before sample collection

Exclusion Criteria

Pregnant and lactating women

Patients undergoing immunosuppressive therapy (for example with drugs like methotrexate or cyclosporine)

Results:

Table 1: Clinico-demographic details of the study participants

Parameter	Vitiligo (n=30)	Control (n=30)
Demographic details		
Gender (Male/ Female)	18/12	15/15
Age (Mean ± SD)	34.32 ± 14.60	35.28 ± 13.88
Clinical Variants of Vitiligo		
Non-segmental	26	-
Segmental	4	-
Family History		
Yes	3	-
No	27	-

The clinical and demographic details of the study participants are summarised in Table 1. The majority of the patients showed the non-segmental type of vitiligo (86.7%). Some patients (10%) reported a familial history of vitiligo.

Table 2: Level of IL6, IL23, IL10 & IL17 in Vitiligo and Control group

Parameters	Vitiligo (Mean ± SD)	Control (Mean± SD)	P Value
IL6 (Pg/ml)	13.21 ± 8.79	5.62± 2.25	P<0.001
IL23 (Pg/ml)	361.1 ± 152.4	331.1 ± 247.6	P = 0.57
IL10 (Pg/ml)	166.71 ± 52.7	410.2±83.4	P<0.001
IL17 (Pg/ml)	34.12 ± 5.12	23.62 ± 8.17	P<0.001

Table 2 shows the Significantly increased level of IL 6 and IL 17 in Vitiligo Patients as compare to Control groups while IL23 is non-significantly increased in Vitiligo patients.

Discussion

The literature study earlier noted that both inducer (IL6 and IL23) and suppressor (IL10) cytokines are modulatory elements of the Th17 pathway. The Th17 pathway's main inducer is IL6.[6] Consistent with its role, this study observed elevated plasma levels of IL6 in vitiligo. Similar observations were also reported by Singh et al.[7] and Sushama et al.[8] The differentiation of naive T cells into Th17 cells cannot be induced by IL23, but it is involved in maintaining the phenotypic, growth, and survival of Th17 cells.[9] This is due to the fact that IL23R is only expressed once naive T cells have begun to differentiate into Th17 cells.[10] The current investigation did not find any significant changes in plasma IL23 levels between the vitiligo and control groups, which is consistent with its function and suggests that IL23 may not be involved in the hyperactivation of the Th17 pathway.

The balance of inducers and suppressors is crucial for controlling the Th17 pathway. The ratios of the modulatory cytokines show the balance between them. In comparison to the control group, the IL6 to IL10 ratio was greater in the vitiligo group. Even while there was no difference in plasma IL23 levels between the research groups, it is interesting to note that the ratio of IL23 to IL10 was likewise higher in vitiligo. These results suggest that whereas the balance between inducers and suppressors is anti-inflammatory in the control group, it is pro-inflammatory in vitiligo.

Conclusion

An autoimmune condition called vitiligo develops when melanocytes are destroyed by the Th17 pathway. The Th17 pathway's primary physiological role is to deliver an innate immune response against infectious pathogens. On the

other hand, unchecked or persistent activation of the Th17 pathway can cause excessive inflammation and harm to nearby tissue. Similar persistent Th17 pathway activation and melanocyte destruction have been seen in the lesions of vitiligo patients. These findings have given rise to the theory that excessive responses of the Th17 pathway may result from variances and changes in gene expression. The purpose of the study was to assess the function of the Th17 pathway in vitiligo using a mix of protein, gene, and genetic analyses. By choosing appropriate markers for the pathway's three inducer, mediator, and effector components, the study's theory was put to the test.

The plasma's cytokine concentrations were examined. In vitiligo, IL6 and IL17 plasma levels were 2.3 and 1.6 times higher, respectively, than in controls. In contrast, vitiligo patients had 2.5-fold lower plasma levels of the suppressor cytokine (IL10). Plasma IL23 levels did not significantly differ between the groups, though. In addition, vitiligo patients had larger ratios of inducers to suppressors (IL6/IL10 and IL23/IL10) than controls. These findings suggested that the cytokine profile in vitiligo is proinflammatory.

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