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The Significance of Level of IFN-Y and Il-4 in the Body as a Causative Factor for Lichen PLANUS

Kaustubh Kumar
BDS
King George's Medical University, Lucknow (UP)

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I. Introduction :

It is a chronic mucocutaneous debilitating inflammatory disease affecting skin, nails, mucosa. It is histologically characterized by infiltration of T cell response in epidermal keratinocyte apoptosis.

It is CD 8+ cell mediated cytotoxic response through MHC Class 1 induction in a co culture model. JAK-2 and signal transducer and activator of transcription factor (STAT 1) ,but not JAK 1 or STAT-2 signaling. Using drug prediction algorithms identification of JAK inhibitors served as promising therapeutic agents in LP and demonstrate that JAK ½ inhibitor baricitinib fully protects keratinocyte cytotoxic responses .

SERUM AND SALIVARY IFN-y AND IL-4 LEVELS IN PATIENTS OF ORAL LICHEN PLANUS :

The signature cytokines of district T-Cell differentiation are indicated to be of fundamental importance in mucosal immunity . A component of mucosa T-Cell response is mediated by CD4+ T-Lymphocytes that can differentiate into functionally distinct subsets. Th1 cells secrete cytokines IFN-y and TNF-a , Th-2 cells secrete IL-4, IL5, IL9, IL-13 . The mutually antagonistic effects of IFN-y and IL-4 , the principal cytokines TH1 and IL4 , The principal cytokines TH1 and Th2 cells respectively, regulate TH1 and TH2 balance and subsequent polarization.

Cytokine but not the cytokine -secreted cells drive and maintain in -vivo immune response . The IFN-y and IL-4 the most characteristics TH1 and TH2 cytokines respectively, regulate the T-cell differentiation and TH1/TH2 Balance involved in physiological and pathological immune processes .

IFN-y involved in the maturation and activation of CD8+ cytotoxic T-cell response and maintaining the expression of MHC -2 Molecules thus participating in keratinocyte apoptosis and disease chronicity of OLP. Higher expression of IFN-y has been reported in the isolated T-Cell lines from OLP biopsies .

It's expressions have been located on the CD4+ TH cells in OLP lesions. It is suggested that the high expression of IFN -y at the advanced stage of OLP development may be involved in the activation of CD8+ T cells and help in maintaining the expression of major histocompatibility class on the keratinocyte growth factor. The increased expressions of IFN-y in OLP influence the clinical outcome and has been associated with clinical manifestations of OLP lesion. Furthermore IFN-y enhance TH1 responses by activating NK cells and macrophage. It also promotes the specific cytotoxic immunity via T- cell and APC interaction . So it has been suggested that IFN- y (874A/T) polymorphism may be a risk factor for OLP development. IL-4 on the other hand, necessary for the TH2 cell differentiation plays an important role in regulation of antibody production and humoral immune response . As IFN-y inhibits the expression of TH2 Cytokines such as IL4 , the IFN-y /IL4 Cytokine ratio is considered to be simple and direct indicator of TH1/TH2 balance.

Based on the expression of TH1 cytokines (IFN-y and TNFa but not the IL4 AND IL10) by the T cells in the lymphocytic infiltrate of OLP lesion and the pathological hypothesis of OLP that intra epithelial TH1 -activated auto cytotoxic CD8+ T cells trigger the keratinocyte apoptosis.

There were strong correlations of IFN-y and lL4 levels and the ratio between serum and saliva from OLP patients . It is suggested that cytokine expression in OLP was consistent in saliva and SERUM, detection of salivary cytokines would reflect systemic cytokine expression profile in OLP. Furthermore it is observe that the salivary concentration of the cytokines from patients with OLP were higher than their serum partners , probably due to production of cytokines from the inflammatory infiltration and keratinocytes in OLP lesions and dysfunction of the structural barriers in the oral mucosa.

The previous investigations indicated that erythromatous ulcerative subtype seemed to cause more severe symptoms like pain and bleeding, be at risk for future malignant transformation compared with the

reticular subtype . In the current study , though the expression of both the cytokine was significantly different in the cases suffering from OLP and controls, only IL4 level (both in the serum and in saliva) showed significant differences in between subtypes of OLP . These results indicated IL4 might be detrimental for OLP clinical outcome and a fine biomarker of severity of OLP.

TGF-B Plays highly significant role in the immune system . It regulates the IFN-y production by NK cells . It can help accumulate the proinflammatory macrophage to anti-inflammatory type . On the other hand inhibition of TGF-B pathway in lymphocytes , contributes to the chronic inflammation in the OLP lesions which is partly attributed to the over productions of IFN-y leading to the blockage of phosphorylation of SMAD-3. The balance between TGF -B and IFN-y signaling determines the immunological status and can be a therapeutic target in OLP patients.

Keywords:
IFN y : interferon gamma
TH : helper T cell
MHC : Modified histocompatibility complex
IL : interleukin
OLP : oral lichen planus
TNF A : Tumor necrosis factor alpha
TGF B: Transforming growth factor beta
SMAD : family of structurally similar proteins