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Mini Review

Chronic Psychological Stress Induced Inflammatory Mediators Leading to Malignant Changes in Lichen Planus and Oral Submucous Fibrosis

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Abstract

Potentially malignant disorders of the oral mucosa are lichen planus and oral submucous fibrosis. Chronic psychological stress is one of the etiological factors for lichen planus and oral submucous fibrosis along with arecanut. Chronic psychological stress induced release of catecholamines such as cortisol, ACTH and noradrenalin activate inflammatory mediators such as IL-1β, IL-6, TNF-α and COX-2, which further activates NF-KB and STAT-3 key transcription factors induced expression of inflammatory mediators involved in chronic inflammation, cell survival, angiogenesis, fibrosis, immune modulation, invasion and metastasis leads to malignant changes. This article highlights about the research findings of chronic psychological stress induced inflammatory mediators involved in malignant changes in lichen planus and oral submucous fibrosis.

Keywords: *NF-KB; STAT-3; Cortisol; ACTH; Noradrenalin; IL-1β; IL-6; TNF-α; COX-2*

Introduction

Lichen planus and OSMF are chronic inflammatory potentially malignant conditions of oral mucosa. Chronic psychological stress is the most important etiological factor for lichen planus and OSMF along with areca nut consumption. Oral submucous fibrosis is the most common oral potentially malignant condition. Lichen planus is a chronic inflammatory mucocutaneous potentially malignant condition affects skin and oral mucosa. There are various types of lichen planus, most common type is reticular type, other types are plaque, bullous and ulcerative type has more chances of turning to malignancy. Classical clinical presentation of oral lichen planus consists of white keratotic striae arranged in the form of reticular network like fashion known as "Wickham's striae". Oral submucous fibrosis is a chronic inflammatory condition of oral mucosa, most common etiological factors for oral submucous fibrosis isarecanut and chronic psychological stress. Chronic psychological stress is the main cause for tobacco addiction. Common clinical symptoms in patients with oral submucous fibrosis are burning sensation due to atrophy of oral mucosa, difficulty in mouth opening and tongue protrusion due to fibrosis [1-4].

Chronic psychological stress induced malignant changes in oral potentially malignant conditions are lichen planus and OSMF

Chronic psychological stress induced release of CRH (Corticotropin releasing hormone) from hypothalamus activate HPA-axis (Hypothalamic pituitary adrenal axis) through ANS (Autonomic nervous system) mediated release of catecholamines such as cortisol, ACTH and nor adrenaline activate inflammatory mediators such as 1L-1β, 1L-6, TNF-α and COX-2 from inflammatory cells such as neutrophils, macrophages, and mast cells, which further activates NF-KB and STAT-3 key transcription factors. IL-1β, TNF-α and COX-2 inflammatory mediators activate NF-KB a key transcription factor and IL-6 pro-inflammatory cytokine activate STAT-3 transcription factor. NF-KB and

STAT-3 both transcription factors work together involved in cell proliferation by activation of cyclin D, and E cell cycle regulatory proteins, cell survival by activation of anti-apoptotic proteins such as BCL-2 and BCL-XL, fibrosis by TGF-β pro inflammatory cytokine, angiogenesis by COX-2, IL-8, VEGF, genomic instability by ROS,RNS free radicals, iNOS, AID(Activation induced cytidine deaminase) enzyme, immune modulation by IL-4, IL-5, IL-10, IL-13, TGF-β, invasion and metastasis by UPA (Urokinase plasminogen activator), MMPs 2,9 (Matrix metalloproteinases 2,9).

NF-KB a key transcription factor induced expression of inflammatory mediators involved in conversion of Th1 lymphocytic type to Th2 lymphocytic type mediated by 1L-4, STAT6 transcription factor release 1L-4, 1L-5, 1L-13 pro-inflammatory cytokines, along with TH17 cells involved in chronic inflammation, tissue damage and immune modulation.

Altered induced regulatory T cells (I Tregs) formed from TH1 cells mediated by TGF-β inflammatory mediator release 1L-4, 1L-5, IL-6, 1L-10, 1L-13 pro inflammatory cytokines along with TH17 cells involved in immune modulation, otherwise normal regulatory T cell (n Tregs) involved in immune homeostasis and self-tolerance. Proteolytic enzymes such as UPA (urokinase plasminogen activator) and matrix metalloproteinases 2,9 (MMP'S 2,9) involved in extracellular matrix degradation induced tissue damage, tumor invasion and metastasis in lichen planus and OSMF considered as oral potentially malignant conditions. NF-KB a key transcription factor in chronic inflammatory microenvironment of potentially malignant conditions of oral mucosa antagonize p53 tumor suppressor gene, a guardian of the genome mutated in lichen planus and OSMF by inflammatory mediators such as NO (nitric oxide), ROS, RNS free radicals, AID (Activation induced cytidine deaminase) enzyme expressed by NF-KB transcription factor [5-10].

Conclusion

Chronic psychological stress induced inflammatory mediators activate key transcription factors such as NF-KB and STAT-3 involved in malignant changes in lichen planus and oral submucous fibrosis. Human clinical trials for thorough understanding of chronic psychological stress induced neurohormones activate inflammatory mediators and further activation of transcription factors involved in malignant changes in inflammatory micro environment of lichen planus and OSMF oral potentially malignant conditions helpful for future identification of biomarkers and therapeutic applications.

Conflict of Interest

No conflict of interest between authors.

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