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AUTOIMMUNITY: MOLECULAR PATHOGENESIS AND ASSOCIATED ORAL DISEASES.

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ABSTRACT

Autoimmunity can be defined as an immune response against self –antigens so called self-tolerance. The etiology is considered as multifactorial. Humoral or cellular immune mechanisms are responsible for various systemic and organ specific autoimmune diseases. Advances made in this field to know the immunopathology of autoimmune diseases affecting the oral tissues.

KEY WORDS : Autoimmunity, Self-antigen, Self-tolerance, T- lymphocytes, B- lymphocytes

INTRODUCTION

The unique feature of immune system is its capacity to distinguish between self and non -self antigens. The lack of immune response to the own tissue components is termed as self-tolerance. When the self-tolerance breaks down, auto antibodies and activated T-lymphocytes acts against self determinants results in autoimmune diseases¹. Various factors involved in the pathogenesis of auto immunity, which include down of physiological mechanisms break responsible for maintaining central or peripheral tolerance to self antigens, release of sequestered antigens, role of genetic factors, antigenic alteration by physical, chemical and biological factors, abnormal T- cell function, polyclonal B-cell activation, abnormal immunoregulaton/ breakdown of suppression, molecular mimicry and defects in idiotypic and anti-idiotypic network²⁻⁵. Its relevant oral diseases include pemphigus pemphigoid, dermatitis herpetiformis, linear IgA disease, lupus erythematosis and epidermolysis bullosa acquisita.6,9

Molecular pathogenesis of autoimmunity:

1. Break down of central T or B-cell tolerance: Central tolerance is due to clonal

unresponsiveness deletion or of the developing T or B-lymphocytes when they encounter the self- antigens in the generative lymphoid organs such as thymus and bone marrow. This tolerance is by either negative selection or apoptosis or clonal anergy. Those T or B- lymphocytes that bind to self antigens with high avidity are deleted in negative selection. Clonal energy is defined as functional unrespon- siveness of T or Blymphocytes without cell death. Failure of any of these mechanisms results in auto immunity^{2,3}.

2. Breakdown of peripheral tolerance: This phenomenon involves mechanism of action on matured lymphocytes which have left the generative organs and encounters self antigens in peripheral tissues. The mechanisms include passive or activation induced apoptosis, anergy, ignorance and suppression of auto reactivity by regulatory lymphocytes. Activation induced and passive cell death is defined as apoptosis of T or Blymphocytes with and without antigenic stimulation. Activation induced cell death is mediated by interaction between Fas and Fas ligand (Fas L). Activation of T-lymphocytes upregulates the number of Fas molecules and induces denovo expression of Fas L. Engagement of Fas by Fas L leads to activation of Caspase 8 results in death of the cell. Self-antigens lacking costimulatory molecules or anatomically sequestered antigens are ignored by T- lymphocytes and this is termed as **ignorance.** Failure of the above mechanisms results in autoimmunity^{2,3}.

- **3.** Uncovering of sequestered antigens: Sequestered antigens are present in closed systems and are not accessible to the immune apparatus. Immunological tolerance to these antigens is not established during fetal life, if they are released in later life results in auto immunity. Examples – lens antigen of the eye and sperm antigen⁴.
- **4.** Altered antigens or neoantigens: Alteration occurs as a result of physical agents such as irradiation, chemical agents such as drugs, infectious agents include bacteria and viruses. Such altered self antigens elicit autoimmune response⁴.
- Genetic factors: Major histocompatibility (MHC) complex plays a genetic role. Autoimmunity could result from failure of MHC antigens to delete certain auto reactive T- cells, molecular mimicry between microbial antigen and MHC antigen and abnormal expression of MHC antigens on tissues⁵.
- Abnormal T- cell function: Enhanced helper T- cell and depressed suppressor T- cell functions are causes of autoimmunity.
- 7. Polyclonal B-cell activation- antigen generally activates only its corresponding Bcell. Certain stimuli may activate the multiple B- cell clones. Such stimuli includechemicals like mercaptoethanol; bacterial products like purified protein derivative of tuberculin and lipopolysaccharide; enzymes like trypsin; antibiotics like nystatin; bacteria like mycoplasma; viruses like Epstein- bar virus; parasites like malaria⁶.
- Abnormal immunoregulation: suppressor T- cells may block the self-antigens from triggering a signal that activate the helper T-

cells and there by inhibit the competent Bcells from producing autoantibodies. Failure of this results in autoimmunity⁷.

- 9. Idiotype and anti idiotype network: The antigen binding site of both heavy and light chains of immunoglobulin molecule is called Sets of antigenic as variable region. variable determinants of region of immunoglobulin molecule are called as idiotypes. These idiotypes induces anti-The anti-idiotypic idiotypic antibodies. antibodies are bind to the antigen binding site of the immunoglobulin that is idiotypic region. Defects in this network results in autoimmunity⁸.
- ^{10.} Molecular mimicry: A phenomenon in which similar structures are shared by molecular products from dissimilar genes. Viral or bacterial structure mimics similar structure in normal host resulting in autoimmune reaction².

Autoimmune Oral diseases

Autoimmune disease is a condition in which host immune response acts against self components, which contributes to the pathogenesis. Type II or cytotoxic and Type III or immune complex hypersensitivity reactions are the causes of tissue injury. Certain autoimmune skin disorders exhibit predominant oral manifestations before skin manifestations^{9,10}.

Pemphigus is an autoimmune mucocutaneous disease characterized by action of autoantibodies against specific desmosomal proteins that is desmogleins 1 & 3 of squamous epithelium results in intraepithelial blister formation. Diagnosis based on clinical presentation can be confirmed by histologic and direct immunofluorescence studies. In Bullous pemphigoid and Benign mucous membrane pemphigoid autoantibodies are directed against basement membrane zone antigens socalled bullous pemphigoid antigens 230 & 180 results in subepithelial blister formation. Similarly in Linear Ig A disease and Dermatitis herpetiformis autoantibodies are directed against basement membrane zone antigens results in subepithelial blister formation¹¹.

CONCLUSION

The review of this article states that there has been a constant study over the multiple pathogenic mechanisms of autoimmunity, thus elucidating break down of tolerance to self- antigens is the main factor for induction of autoimmunity. The same mechanisms are involved in certain oral diseases leading to the fact that autoimmunity has a critical role in pathogenesis.

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