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Review Article

Immunosenescence in Autoimmune Related to Periodontal Disease : A Review Article

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Abstract

Introduction: Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder characterized by the development of autoantibodies and immune complexes associated with a variety of clinical manifestations and tissue damage. SLE is the production of reactive antibodies against the body's own cells. SLE is multifactorial and most likely involves complex interactions between genetic, environmental, and hormonal factors. There is an aging process in immune cells due to changes in the innate and adaptive immune system compartments. This phenomenon is known as Immunosenescence, also occurs on autoimmune. One of the characteristics of elderly people is their inability to respond to vaccines and infections properly.

Discussion This situation also occurs in patients with systemic lupus erythematosus (SLE). In SLES patients, the aging of the immune system is the concept of inflammation; a state where there is a chronic pro-inflammatory status, characterized by increased levels of pro-inflammatory cytokines such as TNF, or IL-6, thereby stimulating a decrease in IL-2 and IFNγ and an increase in IL-10. Clotting factor and acute phase reactants under constant conditions. These biomarkers correlate with the incidence of various age-related diseases, such as heart disease, cognitive decline, cancer, and other physical disabilities. Immunosenescence and inflammation are the result of disruption in the cellular immunity properties of the innate and adaptive immune.

Conclusion: Defect production of T cells and B cells in autoimmune disease could results immune aging. This phenomenon causes neutrophil activation, forming antibody DNA consisting of immune complexes resulting in severe inflammation and tissue damage, as periodontal disease in oral cavity.

Introduction

As we age, there is an aging process in immune cells due to changes in the innate and adaptive immune system compartments. This phenomenon is known as Immunosenescence. One of the characteristics of elderly people is their inability to respond to vaccines and infections properly. This condition can be the result of low immune system efficiency and a thymus involution in which the thymus loses the ability to produce and replace naïve T cells in the periphery. As a result, thymus dysfunction results in decreased cell-mediated responses to foreign antigens, self-tolerance, and naive T cell populations. These changes lead not only to modifications in the lymphocyte subsets but also to functional changes in the cell population subsets [1]. This situation also occurs in patients with systemic lupus erythematosus (SLE). In SLES patients, the aging of the immune system is the concept of inflammaging; a state where there is a chronic pro-inflammatory status, characterized by increased levels of pro-inflammatory cytokines such as TNF, or IL-6, thereby stimulating a decrease in IL-2 and IFNγ and an increase in IL-10. Clotting factor and acute phase reactants under constant conditions. These biomarkers correlate with the incidence of various age-related diseases, such as heart disease, cognitive decline, cancer, and other physical disabilities. Immunosenescence and inflammaging are the result of disruption in the cellular immunity properties of the innate and adaptive immune [2]. Proinflammatory cytokines in systemic inflammation cause an inflammatory process, which is a loss of balance between the inflammatory response and the efficiency of anti-inflammatory control in the elderly. Furthermore, in the natural aging process,

this control fails to neutralize the inflammatory process so that the elderly will experience a higher risk of being more susceptible to infection, malignancy and the process of atherosclerosis, as periodontal disease. This article aims to review immunosenescence in Autoimmune related to periodontal Disease [1].

Immunosenescence in autoimmune disease

Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder characterized by the development of autoantibodies and immune complexes associated with a variety of clinical manifestations and tissue damage. SLE is the production of reactive antibodies against the body's own cells. SLE is multifactorial and most likely involves complex interactions between genetic, environmental, and hormonal factors. The clinical manifestation of SLE patients is inflammation of various organ systems, including skin and mucous membranes, joints, kidneys, brain, serous membranes, lungs, heart, and sometimes the gastrointestinal tract. Organ systems can be affected either alone or in combination. The main features of SLE are the overproduction of autoantibodies and a rash of induration (Figure 1). The SLE classification requires that patients meet four of the 11 criteria established by the American College of Rheumatology (ACR). Clinical manifestations that appear are identified by clinical examination, laboratory tests, and patient records [3]. The prevalence of SLE is nine times more common in women, but the main cause of the sex differences remains unclear. The prevalence of SLE is 31 per 100,000 women in a population of European descent, which is 50-75% lower than in other populations. SLE predominantly affects women in a 9: 1 ratio. The prevalence of women is 90% in African Americans, compared with men [4]. The decreased expression of IL-2 and IFNγ can prolong chronic inflammation so that it can aggravate both SLE and periodontitis (Marques et al, 2016; Fu et al, 2013). IL-10 causes an increase in autoantibodies due to failure of immunoregulation so that when the amount increases, there will be a persistent inflammatory response. (Marques et al, 2016). Immunohistochemical staining studies with specific antibodies to IL-2, IL-10 and monospecific anti-IFN-γ antigens have also shown increased severity of chronic inflammation [5,6].

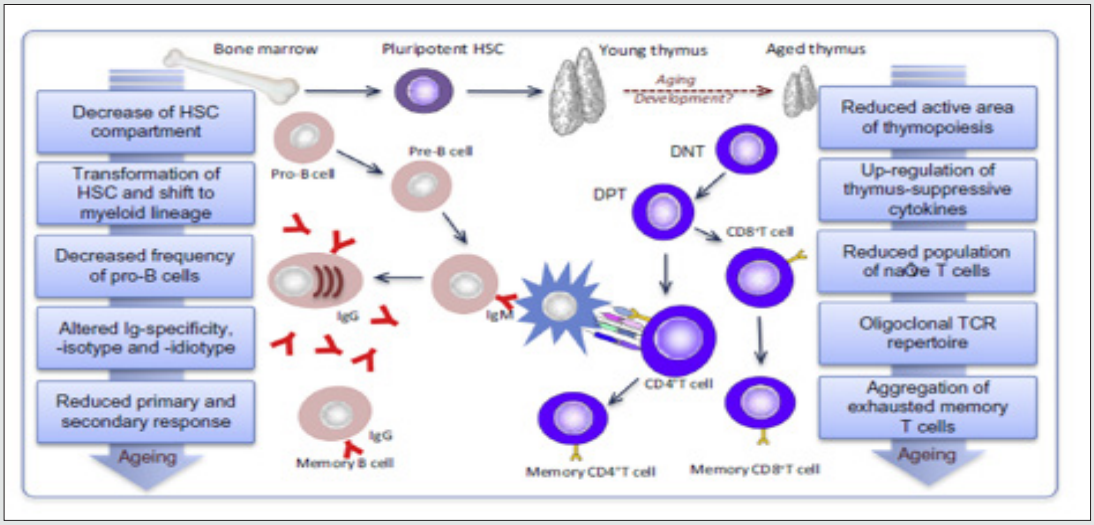

Figure 1: After 1 year of implantation and prosthesis installation.

Discussion

Impact of Immunoscenesens on Humoral Immunity

B cells also undergo age-related changes which further exacerbate functional defects of the adaptive immune response. Similar to the aging T cell system, the number of naïve B cells decreases, and effector B cells accumulate in old age. This leads to a reduction in the diversity of antibody responses. There is a defect in isotype switching and somatic mutation which is an important process in the production of IgG antibodies, thus triggering a weak antibody response with low affinity in the elderly. During the aging process, the total number of B cells decreases, with some increase in total memory B cells (CD27+), while other subsets have decreased. IgD-CD27 + B-cells, and B cell precursors were consistently reduced. There was an accumulation of A CD11c + CD21- B cells identified associated with aging [2]. Humoral immunity in the elderly has decreased as a result of two main mechanisms, namely:

a) A decrease in the number of B lymphocytes that produce long-term immunoglobulins due to intrinsic defects and microenvironment defects, and

b) Loss of diversity and affinity of immunoglobulins as an effect of disruption of germinal center formation.

The effects of aging on peripheral B cells vary, the number of B cells from the bone marrow has decreased, exacerbating peripheral

defects. Despite a four- to fivefold decrease in B cell production in old mice, the number of peripheral B cells remained relatively constant. In addition, oligoclonal expansion of B cells is associated with CD5 expression, independent immunoglobulin production and production of low affinity auto-antibodies known to occur in the elderly, as a result of which other B cell populations cannot occupy their positions [2,7]. This condition in humoral immunity causes the aging of the immune system, which is marked by expansion of memory T cells, clonal exhausting occurs so that it produces dominant cytokines, namely IL-2, IL-10 and IFNγ. The production of inflammatory cytokines in the LES also plays a role in the periodontitis mechanism, IL-2, IL-10 and IFNγ can stimulate chronic inflammation so as to stimulate osteoclasts and resorption of alveolar bone, and periodontitis occurs [8]. The disruption of T cell proliferation causes an imbalance in the number of naive T cells and memory. The number of naïve T production in the periphery decreases, and there is a decrease in function leading to decreased IL-2, IFNγ and increased IL-10 (Table 1). There is a decrease in IL-2 and IFNγ production due to T lymphocytes, both in their latent and active form in SLE patients [9].

Table 1: Effects of immunoscenes on humoral immunity [1].

Humoral Response
Cell B
↓ Pre-B lymphocytes with fixed peripheral B cell count
↑ CD5 + B cells (CD19 + CD5 +) that produce low affinity antibodies independent of T cells
↓ Naive B cells
Accumulation of memory B cells with ↓ diversity and affinity for T cell dependent antibodies (primary humoral response)
Secondary humoral response is maintained
Immunoglobulin
↑ serum IgA and IgG (IgG1, IgG2, and IgG4) levels.
Production of monoclonal immunoglobulin by CD19 + CD5 + clones.
Secretion of organ non-specific self-antobidy (rheumatoid factor, antinuclear
antibodies, antiphospholipid antithyroglobulines, and parietal cells).
Interleukins
↓ IL-2 production due to:
↓ T cell co-operation with B cells
↑ IL-10 production,
↓ IFN-γ production.

Immunosenescence related periodontal disease in autoimmune.

Studies show, IL-2 decreases with the severity of periodontitis. This reduction was associated with advanced periodontitis, with a greater clinical severity. These results show the same results as previous studies, IL-2 has decreased. Interleukin-2 is a cytokine that has many functions, being the main regulator of the body's resistance mechanism against various pathogens and plays an active role in the pathogenesis of periodontal disease [10]. Decreased IL-2 can inhibit the proliferation and signaling of T cells. This failure causes robus of calcium inlux, hyperphosphorylation and an increase in Fc receptors. This condition reduces immune dysregulation, the mechanism of CREM and CREB resulting in severe inflammation. IL-2 is also able to cause T cells to experience anergy and induce autoantibodies in B cells. This situation also affects the fimbria protein of Porphyromonas gingivalis at the protein level, namely by suppressing the transcription factor activator protein 1 (AP-1) and mediating bacteria through leupeptin so that bacteria can damage the wider periodontal tissue [7,8]. The higher the amount of IL-10 indicates the worse periodontal condition. This condition is in accordance with previous studies that a positive correlation with the cytokine IL-10 was found in periodontal disease which was exacerbated by smoking. In vivo studies showed an increase in IL-10 in severe gingival inflammation and an increase in IL-10 in gingival crevicular fluid in patients with periodontitis [11].

Interleukin-10 functions as both proinflammatory and anti-inflammatory to control the production of several cytokines and other mediators. IL10 has the main target, namely myeloid cells that can inhibit cytokine production and regulate inflammation. The regulation of T cells in alveolar bone inflammation is impaired due to increased IL-10 (Goncalves et al, 2010). IL-10 is important in regulating balance and is a modulator of infection response to JAK-STAT signaling. IL-10 was found to have strong anti-inflammatory activity and a broad spectrum, which has been proven in various models of infection, chronic inflammation, autoimmune and even cancer [12]. IL10 can induce T cell proliferation and cytotoxic

activity. have a function since higher levels of these mediators are associated with a decreased likelihood of experiencing periodontitis. IL-10 is able to increase metalloproteinase production. In addition, IL-10 through the GM-CSF pathway can mediate pro-inflammatory cytokines and increase the differentiation and chemotaxic of cytotoxic T cells so that inflammation becomes severe [13]. IL-10 was found to trigger RANKL production, thereby triggering osteoclasts. IL-10 can trigger periodontitis and regulate other pro-inflammatory cytokines, including those involved in alveolar bone resorption. Individuals with high levels of IL-10 were found to have severe chronic periodontitis by examining the mouse HPA. The role of IL-10 can increase inflammation leading to bone resorption, and in this study, it was shown that higher levels of IL-10 were found in patients with more severe periodontitis status [14].

Research shows that examination of the gingival crevicular fluid a decrease in the amount of IFN-γ indicates a manifestation of periodontal disease. IFN-γ is a cytokine that plays a role in increasing the expression of toll-like receptors (TLRs), increasing antigen presentation by MHC class I and II, triggering chemokine secretion, phagocytosis, activation of CD8 + T cells and radically fighting pathogenic microorganisms and tumor cells [15,16]. The effect of interferon in the gingival crevicular fluid and saliva of periodontitis patients suggests that IFNγ, an immunoregulatory cytokine, plays an important role in periodontal disease. Stem cells in the periodontal ligament and stem cells from other tissues, have an immunomodulatory capacity that is IFNγ regulated. IFNγ plays a role in systemic disease through its receptors consisting of two polypeptide chains and is called IFNGR1 and IFNGR2. IFN-γ can regulate the production of T cells and B cells to produce autoantibodies through the NETs pathway. (Extracellular Neutrophil Traps). Decreased IFN-γ causes neutrophil activation, forming antibody DNA consisting of immune complexes resulting in severe inflammation and tissue damage [17]. Both in vitro and in vivo studies on lupus mice have shown that the IFN-γ cytokine has a low rate of periodontal disease and contributes to the onset and progression of periodontitis. IFN-γ can activate the ubiquitine-proteasome pathway in osteoclasts, resulting in TRAF6 degradation and inhibiting RANKL signaling, so its main function is to control bone resorption in the T cell response. The mechanism that occurs is when the IFN-γ state is low, the RANKL barrier function is reduced so that the induction of osteoclast genesis is high and bone resorption occurs [18].

Conclusion

Defect production of T cells and B cells in autoimmune disease could results immune aging. This phenomenon causes neutrophil activation, forming antibody DNA consisting of immune complexes resulting in severe inflammation and tissue damage, as periodontal disease in oral cavity. The mechanism that occurs is when the IFN-γ induce the RANKL barrier function is reduced so that the induction of osteoclast genesis is high and bone resorption occurs.

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