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Review Article

ROLE OF INNATE IMMUNITY IN PERIODONTAL DISEASE: A BRIEF UPDATE

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ABSTRACT

Periodontitis disease is the most condition caused by the inflammatory response in the periodontal tissue. It is well known and established that alone the presence of pathogenic bacteria is insufficient in causing periodontitis disease. Immune response and pathways play a key role in the development of lesions and hence it is necessary to understand the same to assess on how the disease is progressing. Further, it is observed that a comprehensive immune response is initiated in cases with periodontal disease. It is essential to summarize the mechanisms of the immune system involved in periodontal disease. Hence, to understand the immune mechanism and pathways that are also contributory factors for the progression of the disease, a database search is conducted with the keywords and two research articles are shortlisted and reviewed in this review article.

Keywords: NLRP3, Inflammasome, Innate immunity

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INTRODUCTION

Periodontitis is an inflammatory disease and its diagnosis is most common. The primary cause of the disease can be genetic, traumatic, developmental or metabolic origin. The two primary forms of periodontitis which are reported according to the literature are Chronic periodontitis and Aggressive periodontitis. The chronic periodontitis is a condition which is caused due to the inflammatory response in the tissue and also due to the presence of microorganisms in dental plaque.

In aggressive case a progressive form of periodontal disease is observed, which results in rapid destruction or damage of complex tissue support of the dentition. This aggressive periodontitis occurs relatively at a very early age, and the leading cause of the disease can be hereditary issues. The severity of periodontitis depends on three key factors: pathogenic bacteria, genetic factors, and environmental factors.

Though the main etiological factor of the periodontal disease is the bacteria that is present in the plaque, the fundamental element for the development of illness is the host's immune response toward the bacteria in order to damage or destroy both hard and soft tissues in either aggressive or chronic periodontitis [1]. It is well known and established that the presence of pathogenic bacteria is insufficient in causing periodontitis disease. The development of the disease happens because of a combination of factors. This includes other than the presence of periodontopathic bacteria, such as the presence of very high levels of pro-inflammatory cytokines and MMPs (matrix metalloproteinase), PGE2 (prostaglandin E2) combined with low levels of anti-inflammatory cytokines including IL-10 (interleukin-10) (IL-10) and TIMP's (Tissue inhibitors of MMPs). Further, the immune response initiated in the cases of periodontal disease is comprehensive. It is essential to summarize the mechanisms of the immune system involved in periodontal disease.

Rationale of the review

In order to understand complex diseases like periodontitis and its pathogenesis, it is critical to understand the inflammatory responses and the immune mechanisms are regulated. The innate immunity is invaded by the bacteria that are colonized in the subgingival plaque biofilm. Studies found that the immune response of the host against the pathogens is the key part in the disease. Hence it is important to study the interaction between the immune system of the host and the periodontophatic bacteria.

Furthermore, it is critical to comprehend the influence of oral bacteria on host immunological responses. and the response of the immune system as the disease progresses into chronic and aggressive periodontitis. The primary aim of this article is to review the role of immunity as periodontal disease progresses and to study the problems due to immune responses that may lead to periodontal disease.

The systematic review approach is adopted for this research and the same is done by compiling and evaluating the discussions of appropriate studies in order to conclude the role of immunity in the development of the disease [2]. There are various databases are available for review of medical literature. A database search is conducted on PubMed, CINHAL Plus, EMBASE databases and the Health Technology Assessment Database and Cochrane Reviews. Also, relevant articles available online from Emerald and Springer were also searched for research objectives.

The database search is conducted with several keywords, and the results which are not relevant to the research questions and the research older than the year 2010 are excluded from the study. After the same two research articles are shortlisted for review. The keywords used in the database search are Immunity, Periodontal Disease, inflammation, and Immune Pathways. One of the shortlisted pieces of literature is a brief review of the immune system's role in developing the condition of periodontal disease. The rest of the research focuses on the role of inflammatory and immunological pathways in the disease's pathogenesis.

Current knowledge on the disease

Rather than pathology, Initially, the periodontal tissues experience inflammation and is observed as a physiologic defence mechanism to fight the microbes. Furthermore, at this early stage of the disease, clinical findings include plaque formation in supragingival and subgingival tissues, which is accompanied by inflammation and calculus formation. When this plaque is eliminated, there is a resolution with a return to homeostasis and still when the lesion persists, then it is to be considered a pathology [3].

There are different lesions, such as initial, early, established, and advanced lesions. As gingivitis progresses to periodontitis, the advanced lesion is referred to as the destructive phase. The overlapping of immunologic processes at various stages of the illness might be perplexing. As a result, the division of immune response into subsystems such as innate and adaptive immunity should be emphasised.

Though the differentiation and description of inflammation in compartments is comparatively easy but the healing and inflammation mechanisms often include the total immune system

components and collaborate with each other to protect the periodontium. Hence it is critical to understand the preceding immune pathways which also continue to operate as the lesion progresses [4].

Though there are very few observations of the clinical inflammation during the initial lesion, histologically, The tissues have undergone modifications that may be seen. It is the response of endothelial cells and resident leukocytes to the bacterial biofilm. Further, the metabolic products of several bacteria also signal the junctional epithelium cells for the production of cytokines and stimulation of neurons in order to produce neuropeptides.

Innate immunity and its response in the case of periodontal disease

The NLRP3 inflammasome is a dynamic innate immune system module that prevents caspase-1 from initiating and releasing proinflammatory cytokines. Specifically, interleukins (IL-18/IL-1), through cleavage by caspase1 in riposte to periodontal pathogens. Histological examination of the lesions in the cases of periodontitis reveals that the PMN (Polymorphonuclear leukocyte) plays a significant role in periodontal health, and they are present in the junctional epithelium in large numbers. The PMN Molecular defects and several functional consequences also result in accelerated periodontitis. The failure of these PMNs to transmigrate to the endothelium can produce an increased inflammatory response and reduce the required response on the periodontal pathogens.

In innate response, epithelial tissues are the key as they will be in contact constantly with several bacterial products. Hence this Periodontal junctional epithelium will act as a physical barrier to infection and is critical for innate host defence. It has recently been shown that these epithelial cells produce a variety of antimicrobial peptides, and that their production is also enhanced in response to periodontal bacteria.

The host's innate recognition of bacteria involves an array of receptors that provide specific pathogen detection. The TLRs (Toll-like Receptors) belong to this class of receptors. In periodontal disease, TLR 2 and TLR 4, which belong to the above category of receptors, have a crucial role in antigen sensing [5]. Neutrophils are the first kind of innate immune cells that move to an infection site and can use TLRs, which are relevant in responding to various kinds of microbial challenges. Similarly, the monocytes and also macrophages are crucial in the defence of the host as they can recognize and engulf in order to kill the microorganisms.

During the innate immune response, neurons generate electric impulses, and due to the same neuropeptides will be secreted into the extracellular fluid. They act locally on other immune cells through receptors. It suggests a specific modulation in the immune response due to the above communication between neurological systems and immune cells. Hence the nervous system is considered a key regulator of inflammation in the case of periodontal disease.

Further, the link between inflammation and the nervous system is limited not only to immune cell recruitment. Cytokines are other components of the product cells that can affect the function and survival of nerve cells. When these Cytokines engage a neuron receptor, neuropeptides are released and play a significant role in the cases of chronic inflammation.

In the above cases of the disease, an adaptive immune response is activated whenever a breach in the epithelial barrier is detected which is due to the antimicrobial peptides and several components of innate systems. Cytokines which represent the intercellular messages, are also integral to the above immune response.

Several studies pointed out that the fundamental mechanism responsible for the host defense is diapedesis, which involves the scenario of leukocyte emigration. In the context of periodontal disease, studies also suggested that the balance between bone resorption and deposition by osteoclasts and osteoblasts, respectively, depends on the integrity of the bone tissues. Hence this central mechanism of regulation of activity by osteoclasts is performed by certain members such as the receptors family of TNF, Receptor activator of nuclear factor (β) and OPG (osteoprotegerin) [6].

Regulatory T cells and their role in periodontal disease

There has been an intense focus and research on a distinct set of regulatory T cells called CD4+T Cells from the past decade. It is mainly due to their role in the regulatory network, which controls the immune systems' response. There are three different types of regulatory T cells. A certain subset of regulatory T cells (Th3) is observed to have a critical role in immune regulation mainly due to the secretion of TGF-β and IL-1 inhibitors, as both of these inhibitors play a crucial role in regulating the immune system. Recently, studies concluded that regulatory T cells are related to the immune response, which is also responsible for the development of periodontal disease.

As discussed earlier in innate immunity, the inflammation in the periodontitis lesions is caused by a particular group of bacteria. It is characterized by vast numbers of plasma and B cells combined with a significant number of T cells with the concentration of cytokines (Th1 and Th2). Several studies on the regulatory T cells subset's contribution to periodontitis disease. These studies provided evidence that the inflammatory infiltrates of the tissues in the patients suffering from the above condition is attributed to the increased Treg cells (T cells). This strengthens the discussion on the role of T cells in the pathogenesis of the above disease. However, more studies need to be conducted on the accurate position of the population cells as this impacts the current understanding of the disease and also can change the treatment procedures followed currently for the disease [7].

CONCLUSION

The reviews noted that specific individuals are more susceptible to this pathology present with periodontal disease. Also, innate and adaptive systems, which are complex immune mechanisms, interfere and aid the development of this disease. However, there was no consensus on the immune response pattern that controls this illness. The response generated seems to be having a role in maintaining the clinical situation observed in the patients affected with periodontitis. Though many studies have been conducted till date to understand this immune process, there are still many gaps that need to be clarified to utilize the knowledge on the immune response in understanding the development of periodontal disease and for the betterment of the current treatment procedures adopted for the disease.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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