Periodontal Disease and the Antigen-Presenting Cells: A review

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Abstract

The underlying cause of periodontal disease is a complex interplay of genetic, environmental, and immunological variables, making its diagnosis and treatment difficult. Mucosal barrier dysfunction, immune system dysregulation, and persistent mucosal inflammation all contribute to this ongoing pathology. Plaque formed by germs and left on the teeth is the primary cause of periodontitis. Periodontal disease is an immunoinflammatory condition brought on by a complicated interaction between host and microbiome. The ability of the immune system to differentiate self from nonself is a defining characteristic. When an organism develops acquired immunity, it does so by producing a particular antibody response. Antigen presentation cells (APCs) serve as a connecting link between the two stages. In order to elicit a certain kind of lymphocyte response, these cells express a variety of antigenic epitopes. To further modulate the immune response, APCs may also express a variety of costimulatory molecules. The APC are the primary subject of this study because of their connection to periodontal disease.

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Introduction

Most periodontal illnesses result from an immune-inflammatory response triggered by bacteria in the microbial plaque. The immune system is a complex network of cells and chemicals that cooperate in a well-orchestrated fashion to protect the body against outside invaders. Self-and no self-discrimination is the primary role of the immune system. The immune system's job is to protect the body against pathogens by using both innate and adaptive defenses. By secreting inflammatory cytokines and chemokines, phagocytic cells serve as the initial line of defense in the body's immune system, also known as the innate immune response. The adaptive immune response provides a secondary line of protection but takes time to mount an effective attack. The latter is limited in its responsiveness to just those microorganisms capable of eliciting an antigen-specific response from T cells and B cells.

There are two main ways in which periodontal disease manifests clinically: as a stable lesion or

as a progressing one. T helper cell type 1 (Th1) mediates the stable response, which is dominated by T cells, while T helper cell type 2 (Th2) mediates the predominant B cell response in the progressive lesion. Neither T cells nor B cells are directly stimulated to destroy microbes or neutralize poisons by viral or bacterial antigens. Specialized cells, known as antigen-presenting cells, are responsible for stimulating lymphocytes by displaying antigens on their surface (APC). After the first antigen presentation procedures have established a lymphocyte response, antigen will be presented to the activated cells by a diverse array of cell types. Dendritic cells (DC), macrophages, and B-lymphocytes are the three main kinds of APCs found in the immune system. Professional APC are cells with a particular role in initiating or promoting lymphocyte activation. For efficient antigen absorption, these cells express major histocompatibility complex (MHC) molecules and other processes, and they also express costimulatory molecules, which facilitate cellular contact.[1]

Antigen Presentation

Antigen-presenting cells (APCs) are responsible for acquiring antigen, processing it, and presenting an immunogenic fragment to a T cell or B cell in order to trigger an immune response. Also, APCs may release costimulatory molecules that play a role in activation.[2]

"Antigens presented to CD4+ helper T cells are displayed on the surface of the macrophage or other antigen-presenting cell in conjunction with MHC class II molecules, whereas antigens presented to CD8+ cytotoxic T cells are displayed on the surface of the antigen-presenting cell in conjunction with MHC class I molecules. When peptides are delivered to the immune system, they must firmly attach to MHC class II molecules. Those peptides are not delivered that are not bound to MHC class II molecules or are just weakly bound." CD4+ helper T cell receptors engage with certain antigens and MHC class II molecules to activate CD4+ lymphocytes, which subsequently release IL-2 and express IL-2 receptors on their cell surfaces. The microbicidal activity of phagocytes is increased as a result of the production of interleukin-2 (IL-2) by activated cells. This IL-2 activates receptors on both the activated cells and the phagocytes. Additionally, IL-2 stimulates B cell production of antibodies. When given in the context of major histocompatibility complex molecules, T cells only detect the peptides that result from antigen processing, in contrast to B cells, which may recognize an unprocessed protein antigen.[3]

Antigen-Presenting Cells

To increase the likelihood that they will be recognized by particular T cell receptors, antigen-presenting cells (APCs) break protein antigens into smaller bits termed peptides before presenting them on the cell surface in association with class II major histocompatibility complex components. The term "professional antigen-presenting cells" is often used to describe cells that have differentiated to initiate or promote lymphocyte activation. [4]"Typical APCs include dendritic cells, macrophages, and B cells. Dendritic cells, macrophages, and B cells all serve as antigen-presenting cells (APCs) for T cells, but follicular dendritic cells play a far larger role in B-cell immunity. Antigen is first provided by dendritic cells, macrophages, and B cells before it is encountered by immunoreactive lymphocytes such CD4+ helper/inducer T cells." The term "nonprofessional antigen-presenting cells" is used to describe the larger population of tissue cells that may be stimulated to acquire antigen presentation skills that foster the development of secondary or effector functions. Antigen-presenting cells (APCs) such as thymic epithelial

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cells and vascular endothelial cells have a temporary function in the immune system.[3]
The contact between APCs and antigen is the initial stage in the activation of an immune response, which is why they are so important.[5,6]

Immunologic Aspects of Periodontal Disease

Multiple variables, including genetics, the environment, and the immune system, contribute to periodontal disease's complicated pathophysiology. This ongoing pathology may be traced back to a combination of factors, including a compromised mucosal barrier, immune system dysregulation, and mucosal inflammation. Plaque, a film of germs constantly forming on a tooth's surface, is the primary cause of periodontitis. Damage to periodontal tissue occurs when the delicate equilibrium between bacterial antigens and the host immune system is upset from inside a healthy dental cavity. An increase in endothelial permeability and a widening of capillaries are both effects of periopathogenic microorganism invasion. Addressins, adhesive molecules found on the surface of endothelial cells, attach to surface receptors produced by leukocytes to encourage their movement. Following this, an inflitration develops underneath the junctional epithelium of the gingival sulcus. When the gingival crevice is irritated, the plasmocytes, neutrophils, and macrophages in the bloodstream migrate to the area. Inflammatory cells, upon being stimulated by bacterial antigens and toxins, generate inflammatory mediators such as cytokines and prostaglandins, which eventually activate immune cells. Moreover, these cells release proteolytic enzymes. In conjunction with phagocytosis, this process causes the progressive degeneration of periodontal tissue. When it comes to adult periodontal disease, chronic periodontitis is by far the most common kind. Gram-negative bacteria set off an inflammatory response in the immune system that destroys periodontal tissue. The oral cavity's local immune response is triggered when pathogenic bacteria contact with periodontal tissue. Secretion of particular antibodies and the development of adaptive immunity are two important components of this response that ultimately contribute to the clearance of antigen.

Safe cells move into the mucosa of the mouth. Certain of these cells participate in cell-safe responses; these include polymorphonuclear lymphocytes, monocytes, B cells, and T cells. The dynamic component of the humoral reaction is found in the immunoglobulins IgG, IgA, and IgM. Salivary immunoglobulins An and G, in addition to mucins, PRP3, histatines, and defensins, all play intermediary roles in the humoral response. When an antigen-specific immune response is triggered, there is a noticeable shift in the chemical composition of the fluid discovered in the gingival crevice. Several researchers have hypothesized that the presence of an immunizer in the liquid that fills the gingival crevices may serve as an early humoral response indication in the development of periodontitis. Patients with persistent periodontitis have been shown to have higher levels of peripheral IgG against some PorphyromonasgingivalisRgpA-Kgp edifices in their sera, in comparison to those with a healthy clinical status. Ebersole et colleagues. discovered an increase in IgG levels in the fiery penetrate of the periodontal pocket as a result of bacterial infections. However, both aggressive and chronic forms of periodontitis have been linked to significantly elevated levels of circulating IgG compared to a healthy control group. “Increased levels of IgA and IgG in both saliva and peripheral blood serum were also associated with periodontitis. Has to mount a coordinated, safe response to periopathogens if it wants to be really protected. The major cell types that are

genetically predisposed to identify and fight off the invincible bacteria are antigen-presenting cells, B cells, and regulatory T cells (cytotoxic Tc cells, aide Th cells, silencer Ts cells, and contra suppressor Tcs cells).” Antigen is first presented to B cells as part of the highly adaptable and risk-free response process.[7]

APC and Periodontium

When bacteria form a biofilm around teeth, it may lead to periodontal disease, which causes inflammation. Cells such as neutrophils, monocytes/macrophages, and T and B lymphocytes play a significant role in mediating this host inflammatory response (T and B cells). A thick inflammatory infiltration in the connective tissue is a hallmark of the disease's progression; these immune cells, such as polymorphonuclear leukocytes and macrophages, are among the first to react to the bacterial assault. When inflammation is not controlled, bacterial products stimulate antigen-presenting cells (APCs), which then engage with naïve T helper cells (Th0), causing the Th0 cells to differentiate into numerous subsets. 8 Teeth and gums contain a wide variety of immune cells. Their contact with antigen is the initial step in inducing an immune response, hence antigen-presenting cells are thought to be crucial to the initiation and development of an immune response. Lymphoid tissue MHC class II antigen expression is a defining feature. Critical to the launch of immune responses is their ability to take in and digest complicated antigens before presenting them to T cells. [5]

There have been a number of previous studies that have linked APCs to both the preservation of oral health and the development of periodontal disorders. An APC's primary function is to induce and maintain mucosal immunological homeostasis in response to both innocuous commensal bacteria and self-antigens. During their development, they go to different lymphoid organs where they play a role in creating a state of immunity known as tolerance to certain antigens. Changes in the levels of pro- and anti-inflammatory cytokines occur in APCs during the change from health to illness, causing the immune system to react strongly. Recent research has linked the invasion of antigen-presenting cell (APC) and the APC's reaction to the oral microbiota to the development of periodontal disease. Interactions between immune cells in peripheral tissues, such as the oral mucosa and lymph nodes, are complicated yet systematic, allowing the immune system to work in a well-orchestrated fashion. 1 An increase in endothelial permeability and a widening of capillaries are both effects of periopathogenic microorganism invasion. Addressins, adhesive molecules found on the surface of endothelial cells, attach to surface receptors produced by leukocytes to encourage their movement. Following this, an inflitration develops underneath the junctional epithelium of the gingival sulcus. When the gingival crevice is irritated, the plasmocytes, neutrophils, and macrophages in the bloodstream migrate to the area. Inflammatory cells, upon being stimulated by bacterial antigens and toxins, generate inflammatory mediators such as cytokines and prostaglandins, which eventually activate immune cells. Moreover, these cells release proteolytic enzymes. In conjunction with phagocytosis, this process causes the progressive degeneration of periodontal tissue.

When it comes to adult periodontal disease, chronic periodontitis is by far the most common kind. Gram-negative bacteria set off an inflammatory response in the immune system, which ultimately destroys periodontal tissue. “Some of the most well-known periopathogenic microorganisms include Porphyromonasgingivalis, Tannerella forsythia

(Bacteroides forsythia), Treponemadenticola, Prevotellaintermedia, Fusobacteriumnucleatum, Eikenellacorrodens, Campylobacter rectus, Aggregatibacter"gloeosporioides, and Campylobacter rect (Actinobacillus) To prevent further infection, the body reacts quickly when pathogenic germs come into touch with periodontal tissue. Antigen's leeway is bolstered in part by this reaction's ability to release particular antibodies and to foster the development of flexible resistance. 7

Inflamed tissues shift their composition as periodontitis develops, with T cells becoming more prevalent in the inflamed gingival tissues and an increase in the number of B cells and plasma cells in the periodontal ulcers. Lymphocytes maintain equilibrium between the aggressive and protective immunizer responses in response to bacterial antigens by responding to incoming cytokines. In order for T cells to recognize and respond to a particular antigen, antigen presentation is necessary. Some researchers have hypothesized that antigen-presenting cells (APCs) may steer T cells along either the Th1 or Th2 route by delivering antigenic epitopes that activate distinct second signals, so inducing T cells to secrete one of two distinct sets of cytokines. Dendritic cells have an exceptional ability to kick off both primary and secondary T-cell responses, making them expert APCs. Dendritic cells, namely immature ones, may be found in the bone marrow but are later seen processing antigen in peripheral nonlymphoid organs. However, contrary to what one would expect, macrophage numbers do not rise and macrophage activation is hardly detectable in advanced periodontitis compared to moderately inflamed tissues. This is supported by evidence suggesting that when gingivitis develops into periodontitis, the ratio of macrophages to B cells decreases and the B cells exhibit a more activated phenotype.[9]

"Dendritic Cells in Linking Innate and Acquired Immunity

In 1992, Polly Matzinger hypothesized that the normal safe system was compromised due to the recognition of dangers and the transfer of ambiguous information on to order express T and B cells, motivating them to undergo clonal growth and division into effector lymphocytes and immunizer generating cells." As time went on, people stopped believing the very bizarre theory that self-awareness develops automatically in the brain's protective system. The more recent theory posits that competent APCs, in response to typical indications, convey an antigenic message to responder cells, which in turn instructs them to mount an immune response of either hostility or beneficial safety. 10 Consolidating dendritic cells, macrophages, and B cells is a function of competent APCs, whereas integration of thymic epithelial cells and vascular endothelial cells is a function of non-capable APCs. 3 Dendritic cells stand out as the most unusual of these cells. 10

Ralph Steinman, working in the 1970s, initially displayed a selection of cells in the spleen that had a certain dendritic architecture and were likely to activate a basic safe response. From what I can tell, the only bodily areas they do not check are the brain and the scrotum. As early as the 1970s, it was widely accepted among immunologists that macrophages served as the body's primary APC. Macrophages are ubiquitous and located all throughout the body, but they are not specialized like DCs; instead, their antigen-presenting abilities are strictly controlled. In light of the unusual nature of the situation, early evaluations revealed the need for more testing, and it was not until far into the 1980s that the idea that DCs were "competent" APCs became widely accepted. 10 Dendritic cells may be divided into two distinct groups. The medulla is home to the majority of

the main set. Langerhans cells, also found in the skin, are the first to be seen in the T zones of lymph nodes and the spleen. They are a typical precursor of macrophages and they are quite effective at their duty as antigen-presenting cells. The second type of dendritic cells are follicular dendritic cells. Their personal history must be kept secret. Location: germinal sites of lymphoid tissue (LTC). Potential antigen-immunizer structures on the surface of these cells may be accessible for a considerable amount of time. In addition, in situ, in vitro, and in vivo studies have indicated that dendritic cells in the mouths of persons with chronic periodontitis have a sophisticated limit plan. "The oral mucosa contains mature dendritic cells in the lamina propria and CD1a+ cells (adolescent Langerhans cells) in the epithelium. It has been discovered that the epithelium of healthy gingiva is teeming with Langerhans cells. [3]

"It has been shown that dentritic cells (DCs) play an important role in the prevention and treatment of oral health problems, as well as their ongoing monitoring. This study focused only on CD1a+ Langerhan cells (LCs) and not other types of DCs to better understand how to recognize them. The epithelium of patients with gum disease, early gum disease, and periodontitis has increased LC levels. In a similar vein, most research on the potential role of DCs in severe periodontitis has been conducted in vitro (AP). To blame for localized aggressive periodontitis (LAP), Aggregatibacteractinomycetemcomitans (Aa) is suspected since it seems to organize/mature DCs and generate a Th1-reaction. It has been speculated that DCs are to blame for the widespread IgG2 responses seen in LAP patients.

Because of bacterial-related small atomic RNAs (PAMPs) in the oral biofilm, LCs or their progenitors migrate to the epithelium in periodontitis, and it is hypothesized that these DCs contribute to the development of so-called "oral lymphoid follicles" or lymphoid foci that form interproximally around the teeth. The epithelium/keratinocytes may also be responsible for the establishment of LCs by sending out cytokine signals for lymphoid/myeloid management. Adolescent DCs migrate from the gingival/pocket epithelium to lymph nodes during chronic gum disease, where they strengthen the T cell response. This theory proposes that OLF forms when mature DCs are "dialed back" in the gingival lamina propria, triggering a more limited T cell response. Inferring from this, subgingival verdure organisms and commensals like P. gingivalis (Pg) and F. nucleatum provide a needed antigenic test for OLFs to develop. Overall, the presence of mature DCs in the interdental papilla is indicative of the existence of OLF.

"To a lesser degree, DCs are thought to play a roving role in B cell feeling by commanding T cells to up-oversee CD40L and release B cell helper factors. Of fact, it is possible that interdigitating DCs in the paracortical areas of the lymph center obviously connect with CD40-ordered nave B cells to promote extension via an inexplicable cycle. DCs also aid IL-12-dependent B cell differentiation into IgM-secreting plasma cells.

There is evidence to show that DC-B cell interaction in the T cell area is facilitated by Ebstein-Barr virus-induced iota 1 ligand chemokine (ELC) release. This, in turn, recruits active B cells and naive T cells to the DCs' microenvironment."

DCs lose the ability to release polarizing cytokines like IL-12 and enter senescence as they age, reducing the window of opportunity during which they may activate immunity. To sum up, DCs connect innate and adaptive immunity by their ability to mature and induce

productive immunity rather than tolerance in response to threat signals.

The fact that DCs generate IL-2 also helps to understand the connection between innate and adaptive immunity. Natural killer cells, which are part of the innate immune response, were not considered to have been exposed to IL-2 before the adaptive immune response was triggered since it was previously believed that only T cells were responsible for manufacturing IL-2. IL-2 produced by DCs in response to bacterial activation has an impact on natural killer cells before IL-2 produced by T cells does. Hence, the role of DCs as intermediaries between the innate and adaptive immune responses is made more clear.[10]

Conclusion

Sentinel cells in the immune system are antigen presenting cells (APCs), which are responsible for antigen presentation. It has been hypothesized that APCs release costimulatory chemicals, which play a critical role in the activation process. Understanding that antigen presentation is a two-way street is particularly crucial, since cytokines released by T cells and other inflammatory cells may dramatically enhance the antigen presenting potential of certain cells. Treatment for periodontitis focuses on antimicrobial, mechanical, and surgical/regenerative methods. Despite their efficacy, these remedies are often administered too late to prevent more "harm." There is a clear need for the development of pharmacotherapeutic drugs that may intervene "upstream" of the processes that lead to the destruction of the dentition's supporting tissues. Inhibiting antigen presentation by DC, the limiting step in the development of the safe/fiery response, or the mechanisms that pave the road to it, may be a valid approach for upstream regulation of periodontitis.

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