European Journal of Musculoskeletal Diseases
ISSN 2038-4106 print - ISSN 2975-044X online

GINGIVA INFECTION AND INFLAMMATION CAN LEAD TO PERIODONTAL DISEASE AND AUTOIMMUNITY

A. Coppola[1], R. Padula[2], A. Annicchiarico[3] and C. Annicchiarico[3*]

[1] Private practice, Studio Armando Coppola, Corso Garibaldi 246, 80141 Naples, Italy;
[2] Clinical and experimental biology, University of Foggia, Foggia, Italy;
[3] Independent Researcher, University of Bari, 70100 Bari, Italy.

Correspondence to:
Ciro Annicchiarico,
Independent Researcher,
University of Bari,
70100 Bari, Italy.
e-mail: annichiarico.ciro63@gmail.com

KEYWORDS: *Autoimmunity, immune system, periodontal disease, porphyromonas gingivalis, inflammation*

INTRODUCTION

In autoimmunity, the immune system mistakenly targets the body's tissues and causes damage (1). Autoimmunity is a group of very common diseases which occur in response to the body's production of antibody-producing B lymphocytes and T lymphocytes against self-antigens or auto-antigens. With autoimmunity, the immune system does not recognize the body's self-antigens, such as proteins and nucleic acids, which develop autoantibodies. B cells participate in the disease by producing autoantibodies, while T cells intervene as autoreactive lymphocytes. Autoreactive T cells and autoantibodies can be present in individuals with no clinical disease state.

DISCUSSION

Autoimmunity and gum infection can occur in periodontal disease. In gingival infection and periodontitis, autoimmunity can play an exacerbating role in tissue destruction (2). In addition, dental implants can become infected with bacteria and infection can open the way for autoimmune diseases (3,4).

Porphyromonas gingivalis belongs to the phylum Bacteroidota and is a non-motile, rod-shaped, Gram-negative, anaerobic pathogenic bacterium. It is found in the oral cavity, as well as the upper gastrointestinal tract, respiratory tract, and colon, where it is implicated in periodontal disease. *P. gingivalis* participates in collagen degradation in periodontal disease, can infect gingival epithelial cells, and is resistant to antibiotics (5).

P. gingivalis invades gingival epithelial cells in large numbers, in which case both bacteria and epithelial cells survive for long periods. High levels of specific antibodies can be detected in patients harboring *P. gingivalis*. The bacterium produces antigens similar to those produced by host tissues, leading the immune system to attack both microbial and autologous antigens (6). Some bacterial proteins such as bacterial heat shock proteins (HSPs) can mimic human HSPs, triggering autoimmunity.

Microbial infection induces inflammation that exposes autologous proteins to immune cells, triggering an autoimmune reaction with activation of T and B lymphocytes that attack periodontal tissues. Autoantibodies can attack gingival collagen of connective tissue, causing inflammation and tissue dysfunction. The activation of CD4+ T-helper lymphocytes, Th1 and Th17, leads to a high secretion of inflammatory cytokines such as interleukin (IL)-1, TNF, IL-6 and IL-17, resulting in tissue destruction. The intervention of regulatory T cells (Tregs) cannot adequately suppress the

Received: 12 September, 2024
Accepted: 11 November, 2024

ISSN 2038-4106 print
ISSN 2975-044X online

immune response or inflammation. Activated B cells also participate in the autoimmune reaction by producing autoantibodies, such as anti-citrullinated protein antibodies (ACPAs) that target the gingival connective tissue.

Gum infections are usually triggered by a biofilm of bacteria on teeth and gums. The infection causes a strong immune and inflammatory response with tissue damage. Certain bacteria, including *P. gingivalis*, release enzymes such as collagenases that damage connective tissue.

Lipopolysaccharides (LPS) from Gram-negative bacterial cell walls stimulate an innate immune response via Toll-like receptors (TLRs). Prolonged activation of the immune system by a persistent infection leads to overproduction of cytokines, such as IL-1β, IL-6, and TNF, which degrade bone and periodontal tissues. Neutrophils also participate in inflammation by being recruited to the site of infection and releasing reactive oxygen species (ROS) and proteolytic enzymes. TLRs on immune cells recognize bacterial LPS, activating the NF-κB pathway to produce pro-inflammatory cytokines. CD4+ cells, particularly Th17, secrete IL-17, which recruits neutrophils and increases inflammation. Activation of osteoclasts via receptor activator of nuclear factor κ B (RANK) receptor signaling with RANK-L ligand, leads to alveolar bone resorption.

Bacteria produce enzymes such as citrulline that can act on proteins to generate new antigens that trigger autoimmunity. Protein citrullination can be increased by peptidylarginine produced by *P. gingivalis*, with increased levels of new antibodies. Immune tolerance can be impaired by chronic microbial infections, an effect that causes susceptibility to autoimmune reactions. During the infection process of the gingiva, ROS can be released that can damage both proteins and DNA of the host, with the formation of new antigens that can trigger autoimmunity. Bacterial infection causes inflammation with production of pro-inflammatory cytokines such as IL-1, TNF, IL-6, and IL-17, which can be followed by the generation of anti-inflammatory cytokines such as IL-10 and TGF-β (7). Bacterial products are recognized by TLR2 and TLR4 that activate the inflammatory process, and tissue damage is mediated by enzymes that degrade the extracellular matrix. Bone resorption is regulated by the RANK-RANK-L- osteoprotegerin (OPG) pathway, an effect that favors the activity of osteoclasts. Individuals with cleidocranial dysplasia (CCD) might develop secondary complications (e.g., chronic infections or inflammatory responses) that could mimic or contribute to autoimmune-like conditions, though these are not inherently part of CCD (8).

CONCLUSIONS

Inhibition of inflammatory cytokines can reduce inflammation, even that which occurs in autoimmunity. Reducing infection with antibiotics, with the restoration of the balance of immunity, can also be helpful. Experimental therapeutic effects involving stimulation of Tregs and suppression of inflammatory cytokines are still under investigation. The multifactorial reactions involving autoimmunity and infections of gingival tissue are very complex and require further studies.

Conflict of interest

The authors declare that they have no conflict of interest.

REFERENCES

1. Massironi S, Chiara Viganò, Palermo A, et al. Inflammation and malnutrition in inflammatory bowel disease. *The lancet Gastroenterology & hepatology*. 2023;8(6):579-590. doi:https://doi.org/10.1016/s2468-1253(23)00011-0
2. Kebschull M, Demmer RT, Papapanou PN. "Gum Bug, Leave My Heart Alone!"—Epidemiologic and Mechanistic Evidence Linking Periodontal Infections and Atherosclerosis. *Journal of Dental Research*. 2010;89(9):879-902. doi:https://doi.org/10.1177/0022034510375281
3. Mastrangelo F, Gastaldi G, Vinci R, et al. Immediate Postextractive Implants With and Without Bone Graft. *Implant Dentistry*. 2018;27(6):638-645. doi:https://doi.org/10.1097/id.0000000000000816
4. Tetè S, Mastrangelo F, Traini T, et al. A Macro- and Nanostructure Evaluation of a Novel Dental Implant. *Implant Dentistry*. 2008;17(3):309-320. doi:https://doi.org/10.1097/id.0b013e318182d494
5. Li Y, Guo R, Oduro PK, et al. The Relationship Between Porphyromonas Gingivalis and Rheumatoid Arthritis: A Meta-Analysis. *Frontiers in Cellular and Infection Microbiology*. 2022;12. doi:https://doi.org/10.3389/fcimb.2022.956417

6. Lin J, Huang D, Xu H, Zhan F, Tan X. Macrophages: A communication network linking Porphyromonas gingivalis infection and associated systemic diseases. *Frontiers in Immunology*. 2022;13. doi:https://doi.org/10.3389/fimmu.2022.952040
7. Sammartino G, Marenzi G, Tammaro L, et al. Anti-inflammatory drug incorporation into polymeric nano-hybrids for local controlled release. *International Journal of Immunopathology and Pharmacology*. 2006;18(3 Suppl):55-62.
8. Muzio LL, Stefano Tetè, Mastrangelo F, et al. A novel mutation of gene CBFA1/RUNX2 in cleidocranial dysplasia. *Annals of clinical and laboratory science*. 2007;37(2):115-120.