

THE IMPORTANCE OF AGGREGATIBACTER ACTINOMYCETEMCOMITANS IN ETIOLOGY OF PERIODONTAL DISEASE - MINI REVIEW

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Periodontal disease is a chronic, degenerative disease of parodontium which is made of gingiva, periodontal ligament, cementum and alveolar bone. The main etiological factor for development of periodontal disease is dental plaque or oral biofilm in association with anaerobic bacteria. *Aggregatibacter actinomycetemcomitans* is one of the most powerful periodontopathogens. This microorganism produces many virulent factors: leucotoxin as the most important, then bacteriocin, chemotaxis inhibiting factor, cytotoxic factors, Fc binding proteins, immunosuppressive factors, lipopolysaccharide collagenase, fibroblast inhibiting factor, antibiotic resistance determinants, adhesives, invasives and function inhibiting factor of polymorphonuclear leukocytes. The ability of *Aggregatibacter actinomycetemcomitans* lipopolysaccharides to stimulate macrophages to release interleukins IL-1, IL-1 β , and tumor necrosis factor (TNF) is of main importance. These cytokines are able to stimulate the bone resorption. *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis* represent exogenous microorganisms, based on its minor presence in healthy individuals. It has been recommended that periodontal diseases associated with periodontal pathogens represent "true infections". *Acta Medica Medianae* 2009;48(3): 35-37.

Key words: *Aggregatibacter actinomycetemcomitans*, periodontal disease

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Introduction

Periodontal diseases, besides caries, represent the most common diseases of adults as well as one third of the children's population. They are the cause of dental loss after the age of forty-five (1).

Periodontal disease is a chronic, degenerative disease of parodontium which is made of gingiva, periodontal ligament, cementum and alveolar bone. Periodontal disease develops from a pre-existing gingivitis. The main etiological factor for development of periodontal disease is dental plaque or oral biofilm in association with anaerobic bacteria. Pathogenic activity of dental plaque bacteria, organism resistance, systemic and local risk factors contribute to the genesis and development of periodontal tissue disease (5). Oral biofilm is made of microbes and host proteins. They adhere to dental enamel a few minutes after oral hygiene procedure. Healthy gingival sulcus has a flora dominated by equal proportions of Gram positive cocci, especially *Streptococcus* spp, and *Actinomyces* spp. Later, dental plaque "matures", resulting in the flora which consists of facultative anaerobic microorganisms, spirochaetes and motile rods. The proportion of strict anaerobic, Gram-negative and motile microorganisms increases in keeping with growing of disease severity. Periodontal disease activity can range from slow, chronic, progressive destruction to brief and acute episodic bursts with varying intensity and duration variation in the severity and episode duration.

The composition of the subgingival microbiotic flora and the level of pathogenicity differ from person to person as well as from site to site. The research into pathogens of periodontal disease has been underway for more than one hundred years. The most important microorganisms are Gram negative as *Aggregatibacter actinomycetemcomitans* (Aa), *Porphyromonas Gingivalis* (Pg),

Prevotella intermedia (Pi), *Bacteroides forsythus* (Bf), *Fusobacterium nucleatum* (Fn), *Capnocytophaga* species (C.sp), *Campylobacter rectus* (Cr) (6-10). Also, the following bacteria could be isolated: *Eubacterium* spp, *Pepto-streptococcus micros*, *Selenomonas noxia*, *Spirochaetes*. The range of pathogens has been extended to include not only cultivated bacteria but also non-cultivated bacteria and viruses (11-15). Each species possesses a large number of virulence factors (components of cell structure, aggressive enzymes, exotoxin and endotoxin), relevant to the periodontal disease process. During disturbances of tissue homeostasis, these species show their pathogenic potential by causing the disease. Bacteria and their products stimulate the inflammation, which leads to increased release of proinflammatory mediators such as cytokines and prostaglandins, which impair the periodontal tissue (16, 17). This etiological concept of periodontal disease encompasses three groups of factors which determine whether the periodontal disease will occur: a sensitive host, the presence of pathogenic species and absence of the so-called "beneficial bacteria" (18, 19). Dental plaque bacteria *Aggregatibacter actinomycetemcomitans* stands out as one of the most powerful periodontopathogens.

Aggregatibacter actinomycetemcomitans

Aggregatibacter actinomycetemcomitans (*A. actinomycetemcomitans*), previously *Actinobacillus actinomycetemcomitans*, is of spherical, oval or rod shape. Bacilar form is the most frequent; also, they could appear in coccid form, which looks like the Morse code. This microorganism is associated with different human infections, including endocarditis infectious, brain abscess and hard form of periodontal disease. *A. actinomycetemcomitans* is gram negative facultative immobile coccobacillus, which has fimbria. It grows on blood and chocolate agar; there it forms the colonies after incubation of 48 to 72 hours. This immobile anaerobe bacillus grows at the temperature of 37 $^{\circ}$, but also at temperatures of 20 to 42 $^{\circ}$ C. It

produces colonies on special plates which are in the primary isolation small and sticky, and it is difficult to take them off from the surface of agar plate. A marked culture forms after 5-7 days of growth. Since carbohydrate breaks down glucose and fructose to acid without gas, methyl-red and indol test give the positive results. Nitrate reduces to nitrite. Most of the urease strains are positive. The colonies were anhemoliticus, smooth, partially transparent to light, with irregular edges. It belongs to the biochemical active bacteria (it produces catalase and ferments carbohydrates).



Picture 1. *Aggregatibacter actinomycetemcomitans* (from Samaranyake LP. *Essential Microbiology for Dentistry*. Philadelphia: Elsevier Ltd.; 2002.)

Discussion

A. actinomycetemcomitans is normally found in dental plaque, periodontal pockets and gingival sulcus. His presence in periodontal pockets is associated with preadolescents (20), localized juvenile (21, 22) and advanced aggressive periodontal disease (23, 24). The microorganism produces many virulent factors: leukotoxin as the most important, then bacteriocin, chemotaxis inhibiting factor, cytotoxic factors, Fc binding proteins, immunosuppressive factors, lipopolysaccharide collagenase, fibroblast inhibiting factor, antibiotic resistance determinants, adhesives, invasives and function inhibiting factor of polymorphonuclear leukocytes. Leukotoxin is an RTX (repeat in toxin) bacterial cytotoxin family (25) and it shares sequence similarity with the α -hemolysin from *Escherichia coli*, the cytotoxin from *Pasteurella haemolytica* and the leukotoxin from *Actinobacillus pleuropneumoniae* (26). Leukotoxin from *A. actinomycetemcomitans* could kill the human and non-human primate and polymorphonuclear leukocytes, macrophages and peripheral blood monocytes (27, 28), while other types of cells (epithelial and endothelial cells,

erythrocytes and platelets) are resistant to lysis. Lysis cell can be induced by rapid formation of large viability of ions, which leads to membrane depolarization, loss intracellular K⁺ ions, osmotic pressure and finally can cause the death of cell. With this role, leukotoxin provides a unique system for studying events on molecular level, such as searching for the target cells, insertions and translocations of soluble proteins through the cell membrane. Leukotoxin has destructive effect on neutrophils, monocytes and T-lymphocytes, and in that way leads to the local immunosuppression in supragingival area which has a central role in development of periodontal lesions in the juvenile periodontitis. That is why the leukotoxin from *A. Actinomycetemcomitans* is an essential virulent factor, and this microorganism is important periodontopathogenic.

A. actinomycetemcomitans endotoxin has the potential to modulate the host responses and contribute to tissue destruction. The ability of *A. actinomycetemcomitans* lipopolysaccharides to stimulate macrophages to release interleukins IL-1, IL-1 β , and tumor necrosis factor (TNF) is of main importance. These cytokines are able to stimulate the bone resorption. *A. actinomycetemcomitans* and *P. gingivalis* represent exogenous microorganisms, based on its minor presence in healthy individuals. It is recommended that periodontal diseases associated with periodontal pathogens represent "true infections". Bacteriological diagnosis of these diseases is based on the cultivation of microorganisms on appropriate substrates. The identification of culture is done by biochemical activity (fermentation of sugar, positive catalase test and nitrate reduction) (33).

Conclusion

Aggregatibacter actinomycetemcomitans is a very important periodontopathogen which has one of the main roles in the etiology of different forms of periodontal diseases. Considering that it is found in dental plaque and periodontal pockets, its occurrence should be prevented. This is achieved by educating patients and motivating them to maintain proper oral hygiene, and if the disease occurs, excellent results could be achieved with classic treatment and the application of antibiotics such as tetracycline. They are indicated in periodontal disease of the young population, while in adults, besides tetracycline, metronidazole (Orvagil R) and Clindamycin R can be prescribed.

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ZNAČAJ AGGREGATIBACTER ACTINOMYCETEMCOMITANS-A U ETIOLOGIJI PARODONTALNIH OBOLJENJA - MINI REVIEW

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Parodontopatija predstavlja hronično, destruktivno oboljenje potpornog aparata zuba, koga čine: gingiva, alveolarna kost, cement i periodoncijum. Glavni etiološki faktor u razvoju parodontalnih oboljenja je dentalni plak ili oralni biofilm sa anaerobnim bakterijama. *Aggregatibacter actinomycetemcomitans* je jedan od najmoćnijih periodontopatogena. Ovaj mikroorganizam stvara mnoge virulentne faktore: leukotoksin kao najvažniji, bakteriocin, inhibišući faktor hemotakse, citotoksični faktori, Fc vezujući proteini, imunosupresivni faktori, lipopolisaharidne kolagenaze, fibroblast inhibični faktor, antibiotik rezistentne determinante, adhezive, invazive i faktor inhibicione funkcije polimorfonuklearnih leukocita. Sposobnost *Aggregatibacter actinomycetemcomitans* lipopolisaharida da stimuliše makrofage za oslobađanje interleukina IL-1, IL-1β i tumor nekrosis factora (TNF) od velike je važnosti. Ovi citokini su sposobni da stimulišu resorpciju kostiju. *Aggregatibacter actinomycetemcomitans* zajedno sa *Porphyromonas gingivalis*-om predstavljaju egzogene mikroorganizme, na osnovu njihovog malog prisustva kod zdravih osoba. Predloženo je da parodontalna oboljenja udružena sa ovim patogenima predstavljaju "prave infekcije". *Acta Medica Medianae* 2009;48(3):35-37.

Ključne reči: *Aggregatibacter actinomycetemcomitans*, parodontalna oboljenja