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Etiology and Pathogenesis of Aggressive Periodontitis: A Mini Review

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ABSTRACT

Periodontitis is a common gum disease affecting many individuals worldwide. It may be associated with systemic diseases, auto immune disorders, hormonal changes, syndromes or may not be associated with no such factors. Plaque is considered to be a monster to initiate mostly or a majority all the diseases affecting the gingival, periodontia or the tooth. It sometimes may not initiate but may play a significant role in the progression and severity of the disease. There is a certain balance between the bacteria and the immune response from the host individual. The imbalance causes the prevalence of pathogenic bacteria to multiply and also the addition of the pro inflammatory mediators to cause periodontal destruction and eventually tooth loss. Aggressive Periodontitis is a unique disease affecting the periodontium causing irreparable damage. Early diagnosis and the specific treatment is the key to the success of therapy.

Key words: Periodontitis, periodontia.

INTRODUCTION AND BACKGROUND

Periodontitis is an opportunistic disease caused due to the imbalance between the bacteria and the host response.

Why is it so unique? Following are the primary features.

- Medical history is non contributory.
- Rapid attachment loss and bone destruction is seen.
- Familial aggregation of cases. [1]

Secondary features:

- The microbial amount is scanty which doesn't correspond to the severe periodontal breakdown.
- Elevated proportions of periodonto pathogens namely Aggregatibacter actinomycetemcomitans and Porphyromonas gingivalis.
- Abnormal phagocytic functions.
- Elevated production of prostaglandin E2 (PGE2) and interleukin-1β (IL-1β) which are pro inflammatory mediators in response to bacterial endotoxins.
- The disease is self limiting.

The following is the history of the terms coined by several authors.

Gotileb (1923)	diffuse atrophy of the alveolar bone
Gotileb (1928)	deep cementopathia
Wannenmacher (1938)	parodontitis marginalis progressiva.
World Workshop in Periodontics (1966)	Periodontosis
Chaput (1967) & Butler (1969)	juvenile periodontitis
World Workshop in ClinicalPeriodontics (1989)	Early Onset Periodontitis
World Workshop in Periodontics	Aggressive Periodontitis

[2]

Classification:

1. According to the location:

- Localized Aggressive Periodontitis
- Generalized Aggressive Periodontitis

Localised aggressive Periodontitis (LAP):

Localised Aggressive Periodontitis is localized in nature and doesn't involve all teeth in the dentition.

A] Clinical characteristics of LAP:

- It is confined to the incisors and first molars or atleast two permanent teeth one of which is a molar and not more than two teeth other than molars and incisors.

- Lack of local factors such as plaque and calculus. Clinically there is lack of inflammation. But it presents with deep periodontal pockets.
- Distolabial migration of the maxillary incisors with diastema formation.
- Increased mobility of the maxillary and mandibular incisors and first molars.
- Hypersensitivity of denuded root surfaces is observed to thermal and tactile stimuli.
- Deep, dull, radiating pain during mastication probably caused by irritation of the supporting structures by mobile teeth and impacted food.
- Periodontal abscesses formation.
- Regional lymph node enlargement.
- Rate is 3 to 4 times more and severe than in Chronic Periodontitis.
- Prevalence: Blacks are more prone to suffer from LAP. Among whites, females are more prone and among blacks, men are prone more to have LAP. [3]
- Incidence: Puberty to 30 years of age.

B] Radiographic findings:

- Vertical bone loss around the first molars and incisors which begins around puberty in otherwise healthy teenagers is a classical diagnostic sign of Localised Aggressive Periodontitis.
- "Arc-shaped loss of alveolar bone extending from the distal surface of the second premolar to the mesial surface of the second molar" which is a mirror image seen on both sides.
- Bone defects are usually wider than usually seen in chronic Periodontitis.

Burn out phenomena or why does LAP affect only specific areas?

- As molars and incisors are the first to erupt in the oral cavity, Aa colonizes the teeth and evades host defense causing periodontal destruction. The host body produces opsonic anti bodies to attack against invading bacteria preventing colonization of other sites.
- Bacteria antagonistic to Aa colonise the teeth inhibiting it from further colonization.
- Aa loses its leucotoxin producing ability.
- Cementum defect formation. [4]

Etiology and Pathogenesis:

A] Bacteria:

As plaque is the main culprit for Periodontitis, we shall discuss about the bacteria being an etiological factor in Aggressive Periodontitis (Ag). Gram-negative organisms comprised approximately two-thirds of the isolates from deep periodontal pockets of the individuals suffering from AG. But these organisms averaged only about one-third of the isolates in control sites with normal gingiva.

The bacteria of interest were A. actinomycetemcomitans, Capnocytophaga spp., Eikenella corrodens, saccharolytic Bacteroides-like organisms now classified as Prevotella spp., and motile anaerobic rods today labelled Campylobacter *rectus*. Gram-positive isolates such as streptococci, actinomycetes, and peptostreptococci. *A. actinomycetemcomitans*, *Capnocytophaga* spp., and *Prevotella* spp. were also seen. to be the most prominent members of the subgingival microbiota of Periodontitis lesions in the primary dentition. The microbial patterns observed in periodontal lesions of the primary dentition were more complex than the ones found in LAP patients.

A. actinomycetemcomitans (Aa) gained more importance because of

1. Aa was seen to be less frequent in periodontally healthy individuals. [5]
2. Aa produced leukotoxin, that was capable of translocating across epithelial membranes, and could induce disease in experimental animals and non-oral sites. [6]
3. Elevated levels of serum antibodies to *A*a was seen in such individuals. Also they produce antibodies locally against this organism at diseased sites. [7]

4. The subgingival load of Aa could not be reduced after treatment. [8]

Hence avoidance of exposure to this organism becomes a relevant issue in prevention and the elimination of *A. actinomycetemcomitans* may be a valid treatment goal. However it can be also transmitted from one to another like mother to child or between spouses. [9]

There have been studies showing not all humans are equally susceptible and/or that there is variation in virulence and pathogenic potential. The virulence of *A. actinomycetemcomitans* is variable, and proving the existence of at least one particularly virulent subpopulation of *A. actinomycetemcomitans.* There are five serotypes of Aa namely a, b, c, d, e. Each serotype was found to be present in different populations worldwide.

All Gram-negative bacteria are enveloped by two membranes and the outer is rich in endotoxin. This has a lipid and a polysaccharide part and is therefore frequently termed lipopolysaccharide (LPS). LPS is set free when bacterial cells die or multiply. *A. actinomycetemcomitans* secretes membrane vesicles that can serve as transport vehicles to spread endotoxin and pathogenic substances produced by the bacteria. LPS activate host cells, macrophages thereby secreting inflammatory mediators such as prostaglandins, IL-1β, and tumor necrosis factor-alpha (TNF-α). Also Aa is immunosuppressive, collagenolytic and inhibits neutrophil chemotaxis.

The leucotoxin destroys PMNs and macrophages. Leucotoxin was seen to be produces highly by serotype b (now known as JP2 clone) which was seen in the African descent. *A. actinomycetemcomitans* is considered an opportunistic pathogen or commensal bacterial species as a whole. However, at least one distinct subpopulation, the JP2 clone, truely displays the properties of a pathogen in at least one group of humans of North and West African descent. [10]

The organisms associated with LAP and GAP are *P. gingivalis*, *Tannerella forsythia*, and *A. actinomycetemcomitans. P. gingivalis* produces collagenases and proteases, endotoxin and fatty acids. [11] High local and systemic immune response against P Gingivalis has been demonstrated in patients with GAP. [12]

B] Bacterial damage to Periodontium:

Periodontal breakdown occurs via two related mechanisms: (1) the direct action of the microbes or their products on the host tissues (2) due to the inflammatory responses. [13]

Investigations in humans have confirmed that *Aa* is able to translocate across the junctional epithelium and invade the connective tissue. [14] Apical spread of bacteria is controlled by the first line of defense consisting of mechanisms such as the high turnover of junctional epithelium keratinocytes, the outward flow of crevicular fluid, and the directed migration of PMNs through the junctional epithelium; the efficiency is highly enhanced by the presence of specific antibodies and complement fragments in the gingival crevicular fluid. [15]

C] Host response to bacteria:

Local inflammatory responses are shown by an intense recruitment of PMNs both within the tissues and into the periodontal pocket. B cells and antibody-producing plasma cells represent a significant component. IgG-producing cells, with a lower proportion of IgA-producing cells. [16] Local IgG4-producing cells seem to be elevated. It has been noticed that there is a depressed T-helper-to-T-suppressor ratio as compared to both healthy gingiva and peripheral blood due to altered local immune regulation. [17,18]

Local inflammatory responses are characterized by high levels of PGE2, IL-1α, and IL-1β in both gingival crevicular fluid and tissue. [19] PGE2 production is highly elevated in AgP subjects in

comparison to healthy and chronic Periodontitis patients. Also specific antibodies against AgP-associated microorganisms; [20] have also been detected in crevicular fluid from AgP lesions. Substantial titers of antibodies against *A. a* and *P. g* have been detected in the serum of AgP
patients.

Anti-*A. actinomycetemcomitans* serotype polysaccharide IgG2, is considered to be protective against AgP. [21] Patients suffering from GAP, frequently show both low levels of serum antibodies against *P. gingivalis* and low levels of antibody avidity, indicating a specific inability of some GAP patients to cope effectively with the mentioned bacteria. Importantly, however, both titers and avidity of antibodies reacting with *P. gingivalis* can be improved as a result of a successful periodontal therapy.

PMNs of some LAP and GAP patients show decreased migration and antibacterial functions which is a minor abnormality, clusters in families like AP. [22] Other reports indicate that PMN abnormalities in LAP patients may be, the result of a hyper inflammatory state resulting in the presence of pro-inflammatory cytokines in the serum of some AgP patients. [23]

D] Environmental aspects of host susceptibility:

Cigarette smoking is a risk factor for patients with generalized forms of AgP. [24] Smokers with GAP had more teeth affected and greater attachment loss than patients with GAP who did not smoke. The mechanisms indicate that IgG2 serum levels as well as antibody levels against *Aa* are significantly depressed in subjects with GAP who smoke. Since it is a protective response against *A. actinomycetemcomitans*; it leads ti the increase in disease extent and severity in these individuals.

CONCLUSIONS

Aggressive Periodontitis both generalized and localised are severe in the rate of progression and extent. Early diagnosis is very essential for the successful treatment and good prognosis. It has been noted that antibiotic therapy with mechanical debridement can give a positive outcome. It could be prevented in families with history of Aggressive Periodontitis with periodontal screening, maintaining good oral hygiene, eliminating the risk factors and the causative micro organisms.

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