Juvenile periodontitis: A review of pathogenesis, diagnosis and treatment

Kevin James Donly / Malka Ashkenazi

Abstract

Juvenile periodontitis (JP) and its treatment has become a critical concern to the practicing dentist. *Actinobacillus actinomycetemcomitans* has been diagnosed as the prime etiological agent associated with this disease. Decreased chemotaxis and phagocytosis of polymorphonuclear leukocytes have also been described in these patients. The precise treatment regimen must be individualized for each patient. In addition to aggressive antibiotic therapy, root planing, curettage or a surgical approach, with mandatory follow-up care, should be considered. This review discusses the etiology and pathogenesis of JP and recommends treatment regimens, according to patient diagnosis.

Introduction

Juvenile periodontitis (JP) often referred to as periodontosis is a destructive periodontal disease that affects children and adolescents. As dentists, we should be aware of the devastating and rapid effects that this disease can have. To have an understanding of the disease, this paper will review the literature to note the clinical signs and symptoms, presumed etiology, and suggested treatment.

Description of the disease

The Nomenclature Committee of the American Academy of Periodontology defines periodontosis as a degenerative non-inflammatory destruction of the periodontium originating in one or more of the periodontal structures, characterized by a migration and loosening of the teeth in the presence or absence of secondary epithelial proliferation and pocket formation or a secondary gingival disease.[1] Baer[2] defined periodontosis as a disease of the periodontium, which is characterized by a rapid loss of the alveolar bone in one or more teeth in the permanent dentition, with minimal accumulation of plaque, and little or no clinical inflammation that occurs in an otherwise healthy adolescent. Baer described two forms of the disease: a localized form, in which only permanent first molars and incisors are affected, and a more generalized form. Other criteria were: onset at an age of 11 to 13 years and up to 20 years; bilateral symmetrical patterns of vertical bone loss in the molar regions with horizontal bone loss in the incisors; rapid progression of the disease; and tendency to occur in families. Therefore, there is a lack of involvement of the primary dentition.

Typical findings upon radiographic examination reveal arc-shaped bone loss in the molar region, starting from the mesial surface of the second molar region and extending to the distal surface of the second premolar. Bone loss is also noted in the incisor areas with the mandibular premolar area showing the least involvement by this disease.

Clinically, the initial localized juvenile periodontitis (LJP) lesion is characterized by deep periodontal pockets and vertical bone defects.[2-5] Bone loss progression is reported to be three times faster in JP than in adult periodontitis. Gjermo[6] reported a bone loss rate of 2 mm/year, and Mandell et al.,[7] defined active destruction as a loss of connective tissue attachment of at least 2mm within a 37 day period. Although the disease attacks the molar and incisor teeth in the early stages, as the disease progresses abscesses and loosening of teeth may be experienced.[6] The disease gives negligible subjective symptoms, and unlike adult periodontitis, JP does not involve gingival inflammation as an early feature.[8] Inflammation is usually not overt, which often results in the lesion being rather advanced before the disease is diagnosed and properly treated. Subgingival plaque, which is loosely attached to the tooth surface, is found in LJP lesions.[9]

The prevalence of JP is difficult to estimate from the wide variation in its reported incidence, differences in examination procedures and differences in diagnostic criteria. LJP is relatively rare and appears to affect 0.9-2.4% of North American populations. The localized pattern is more prevalent in teenagers, while the generalized pattern is predominant in the 26 to 32 year age group.[10]

Pathogenesis and etiology

Microbiological studies have shown that the subgingival plaque consists predominantly of gram-negative anaerobic bacteria.[11] Haffajee et al.,[12] obtained subgingival plaque and found that the proportion of *Actinobaciilus actinomycetemcomitans* (A.a.) and

Selenomonas sputigena (S.s.) were elevated in active sites. Other bacteria that were associated with active disease sites is Capnocytophaga.[13,14] Zambon et al.,[15,16] reported that 90% of the patients with LJP harbor A.a at high numbers in sub-gingival lesions. Mandell et al.[7] showed that A a. occurred in active sites at levels 100 fold greater than those found in inactive sites, while proportions of *Bacteroides intermedius* were elevated in control sites.

Five months after successful treatment the number of pathogenic bacteria decreased in the inactivated sites, while the number of non-pathogenic bacteria increased.[15,16] Humoral antibody response to A.a. and S.s. significantly increased in a period when affected sites were breaking down during treatment. Increased concentrations of serum immunoglobulins have been reported as a response to the accumulation of gram negative bacteria.[17] Elevated antibody against A.a. were also found in gingival fluid and in the saliva.[18-20] A.a. possess numerous virulence factors, which may be relevant to the disease. They include: leukotoxin, collagenase, endotoxin, epitheliotoxin and a fibroblast-inhibiting factor.[21-24] In addition, A.a. is known to produce a soluble, heat labile factor that inhibits the growth and proliferation of *A. viscosus* and *Streptococcus sanguis,* the bacteria most closely associated with heavy plaque formation.[25] An endotoxin of A.a. has been isolated; it has a major bone resorbing activity, is able to activate complement and induce lysosomal release from polymorphonuclear leukocytes (PMNs).[26] This serves as the vehicle by which pharmacologically active toxins of bacterial origin gain access to the periodontal tissue. The rapid progression of JP lesions is not only reported to be associated with elevated antibody titer against A.a., but is also related to a defect in the PMNs' function.[27]

Genco el al.,[28] compared the PMNs function in JP patients with their first-dégree relatives and with healthy control subjects. A marked reduction in PMNs chemotaxis was noted in JP patients, their affected siblings, and siblings with no signs of periodontal disease. About 70% of the patients have depressed chemotaxis, with poor response to FMLP (N-formyl-Lmethionyl -L-leucyl-L-phenylalanine), to complement fragment (C5a),[29-32] and glycoprotein 110 (a neutrophil membrane matrix component).[28,33-34] In other studies, normal surface glycoprotein structure, with normal or enhanced chemotaxis response, was found.[35-38]

The reports on the phagocytic and bacteriocidic capacity of PMNs in patients with LJP also showed conflicting results. Several investigators have found that phagocytic activity of blood and gingival PMNs appears to be abnormal in LJP patients,[39-43] while others have found normal phagocytic function.[44-48] Depressed bactericidal activity of PMNs in patients with LJP have been noted,[40,44] although others have found a normal oxidative capacity.[43,47-49] Moreover, Ashmen and Shapira[45,50] found that PMNs from JP patients have the potential to produce higher quantities of oxyradicals than healthy controls, following stimulation with opsonized bacteria. The reduced ability of the PMNs to respond to chemoatractant agents, and maybe to phagocytosis, may consequently impair the host defense and potentiate the rapid progression of the disease.

The low prevalence of JP in the population and the high frequency of the disease among additional members of the family suggests a hereditary predisposition to this immunodeficiency.[51] Data implies that PMNs defect may be inherited with this immunodeficiency, predisposing patients to early and severe bone loss. Although familial studies have not formulated precise inheritance patterns, two Mendelian inheritance modes have been proposed: autosomal recessive and X-linked dominant. The autosomal recessive trait would be expected to occur in one-fourth of the offspring of two carrier parents, both sexes being equally affected.

Studies by Jorgenson and Saxen[52,53] supported the autosomal recessive inheritance hypothesis. X-linked dominant inheritance hypothesis refers to carrying the trait on the X chromosome, in which only one gene is necessary for expression. Therefore, an affected male would transmit the trait to one-half the daughters and one-half the sons. Melnick and Vandesteen[54,55] supported the X-linked dominant inheritance hypothesis as their research suggested JP to be genetic; the disease being inherited as an X-linked trait with relatively consistent expressivity, but variable penetrants.

Diagnosis

Since gingival inflammation is not one of the early features, JP may first be detected in a routine radiographic examination. A general loss of alveolar bone may be seen, often occurring in a vertical direction in molar areas, a horizontal direction in molar areas, a horizontal direction in incisor areas and often involving isolated teeth. A suspected case should be thoroughly evaluated to dismiss the possibility of other diseases. Goepferd[56] reviewed the differential diagnosis of diseases that may initially appear as JP. The differential is cited as follows: (1) hypophosphatasia; (2) Papillon-Lefevre syndrome; (3) histiocytosis X; (4) neutropenia; (5) cyclic neutropenia; (6) leukemia; (7) diabetes mellitus; (9) fibrous dysplasia; (10) acrodynia and (11) prepubertal periodontitis.

Before final diagnosis, patients should be referred for complete physical and hematological examination, including complete blood count, chemistry profile and urinalysis to exclude the presence of any contributing systemic medical disorders.

Prepubertal periodontitis

Prepubertal periodontitis (PP) has been introduced in the past as another type of JP, although, today it is accepted as a separate disease. The disease affects the periodontium of primary teeth, in both a localized and generalized form.[57] The onset appears at approximately

four years of age and seems to be more prevaent in females than males.[57,58] PP involves minimal microbial plaque with the gingival tissue presenting minor inflammation. Alveolar bone destruction proceeds more rapidly in PP than in adult periodontitis or JP. Page[57] presents the features of PP; onset during or immediately after eruption of the primary teeth; prevalence unknown, but probably rare and possibility of a genetic basis for some types.

The generalized form of PP is identified as the oral manifestation of a systemic disease called leukocyte adhesion deficiency (mac-1 deficiency, CD18 deficiency).[55]

The lack of the adhesion ability in PMNs leads to a defect in chemotaxis and absence of PMNs in the gingival tisues, although, the peripheral blood white-cell count is markedly elevated. This disease is characterized by acute inflammation, including the marginal and attached gingiva around all the teeth. Gingival proliferation and recession, and alveolar bone destruction (sometimes accompanied by destruction of the tooth roots) are often present.[57] The onset occurs at the time of tooth eruption. In some cases, otitis media, epidermal and upper respiratory infections are also present. PP may be refractory to antibiotic therapy. All primary teeth are affected and the permanent dentition may or may not be affected.

The localized form of PP (L-PP) is a disease defined by clinical criteria and the pathogenesis is unknown. Only some teeth are affected and gingival tissue may exhibit little or no inflammation. The destruction of bone is not as rapid as the generalized form. Functional defects are present in either neutrophils or monocytes, but not both. Recurrent otitis media is not a frequent finding and usually there is no history of frequent infections. The disease is amenable to treatment by curettage and antibiotic therapy. L-PP may lead to LJP or generalized JP.[59]

Treatment

Several methods of treatment for JP have been proposed. First, and most importantly, treatment should not be delayed, as it has already been mentioned that the disease takes a rapid and destructive course of action. Patients and parents must be educated on the nature of the disease and have a thorough understanding of their role in successful treatment. *In vitro* tests demonstrated that several antibiotics can be effective: tetracycline, penicillin, erythromycin and metronidazole.[13] The major antibiotics that are used for this disease are described below:

Tetracycline — There are several different tetracyclines (tetracycline, chlortetracycline, oxytetracycline, doxycycline, minocycline) which are closely related chemically.

Several studies have shown the effectiveness of tetracycline and minocycline against A.a. and Capnocytophaga *in vitro*.[60,61] Recommended dosage of tetracycline hydrochloride is 250 mg four times per day for a duration of two to four weeks, since this was shown to supress subgingival population of A.a. and Capnocytophaga to very low or undetectable levels.[4,10,61,62] Gordon et al.[63] demonstrated this dosage to produce tetracycline concentrations in gingival crevicular fluid two to four times greater than in serum. The effect of tetracycline on tooth discoloration is not a significant problem in these patients. Parents should be advised that posterior crowns may be discolored, placing emphasis on the prognosis if treatment is avoided.

Minocycline is a semi-synthetic tetracycline effective against a similarly broad spectrum of organisms. It has a longer serum half life, lower urinary excretion rate and greater lipid solubility than most of the other tetracyclines. A further advantage of minocycline, which is common with tetracycline, is that when given in doses of 200 mg per day for eight days, the gingival fluid concentration reaches five times the serum level after 48 hours. This concentration is higher than the concentration which has been proven to inhibit bacterial growth *in vitro*.[64] The higher concentration of these antibiotics in the gingival fluid is partially caused by binding to calcium-containing substances.[65] Golub et al.[66] demonstrated that minocycline can inhibit tissue collagenolytic activity, that is not related to its antimicrobial activity. This may provide a new therapeutic approach for suppressing excessive collagen resorption that occurs with adult periodontitis. It is possible that other tetracyclines may also exert this effect.

Metronidazole — Metronidazole (flagyl) appears to be bactericidal for many gram negative anaerobes, most notably bacteroides species, and less effective against facultative and capnophilic anaerobes as A.a.[67]

Administration of metronidazole, 200 mg three times daily for seven days, has demonstrated a significant reduction in the level of bacteroides and spirochetes in periodontal pockets. An improvement in clinical parameters, such as decreased probing depths and increased attachment levels were also apparent.

A study, in which the effect of metronidazole was compared with tetracycline in nine patients with "refractory" sites, found both drugs to be equally effectve when combined with scaling and meticulous plaque control.[68] Since metronidazole has been shown to be effective against many organisms associated with destructive periodontitis, but to have little activity against A.a. and Capnocytophaga *in vitro*, resistance development remains a concern, therefore short term use should be reserved for well selected subjects.

Penicillin — Clinical and laboratory trials have shown penicillin ineffective as an adjunct to treatment of localized JP.[69,70] Daily use of penicillin is not recommended. due to the potential development of resistant bacterial strains and possible hypersensitivity reactions. The combination of metronidazole and amoxycillin has been shown to be a valuable adjunct to mechanical therapy in the elimination of A.a. from the subgingival pocket in WP patients.[67]

Clinical trials[62,71] indicate that systemic antibiotic therapy, when used as an adjunct to meticulous scaling and

root planing, can provide additional clinical benefits. A study by Wennstrom et al.,[72] subjected JP patients to split mouth treatment. Half the mouth was exposed to scaling and root planing treatment and half was exposed to the same treatment including modified Widman flap surgery. The treatment included scaling every four weeks during the first six months, and every three months thereafter. Final examination was performed five years after the initial examination. Results revealed that excision of the granulation tissue in conjunction with flap elevation did not enhance the degree of probing pocket depth reduction, improving attachment gain and bone regeneration that occurred following meticulous scaling root surface instrumentation.

Another study followed seven JP patients, post-treatment, for at least 22 months.[73] The patients received meticulous scaling and root planing of all teeth with concomitant irrigation to probing depth. The patients were recalled at approximately two to three month intervals for maintenance care. Six out of the seven patients received at least two courses of systemic tetracycline (1g/d for 14 days) during the study. Patient home maintenance included: daily application of sodium bicarbonate and 3% hydrogen peroxide, as well as inorganic salt irrigation. Improvement was noted in bleeding, pocket depths and clinical attachment levels. This approach is also recommended in the treatment of children when surgery is contra-indicated, as in the transitional dentition of the adolescent or during orthodontic therapy.

Surgical treatment

Treatment by removal of subgingival plaque and inflamed periodontal tissues, using a modified Widman flap technique, resulted in resolution of gingival inflammation, gain of gingival attachment, and bone replacement in angular bony defects.[12,74] Soft tissue over bony defects is excised to relieve the inflammatory cell infiltrate, predominantly plasma cells and blast cells, which might interfere with bone regeneration and healing.[5]

Baer and Socransky[75] reported successful treatment of a LJP patient following full thickness flap surgery and tetracycline (1g/d for 30 days).

A recommended approach for surgical treatment is published by Lindhe and Lijenberg.[71] Patients were placed on tetracycline therapy for two weeks. Surgery was performed one to two days after tetracycline therapy began. Buccal and lingual modified Widman flaps were raised, the bony defects and root surfaces being carefully curetted. The flaps were repositioned and sutured with interrupted proximal sutures. In this particular technique, no surgical dressing was used, but patients did rinse with 0.2% chlorhexidine twice a day for two minutes, over a two week post-surgical duration. The first six months following surgery, patients were recalled monthly for a professional prophylaxis. Subsequently, they were placed on three month recalls. We believe that this strategy of treatment is a good example of a clinical approach for the treatment of JP.

Implantation of autologous bone grafts may be helpful in the treatment of JP when conventional treatment methods have failed.[70] Surgical approach includes the laying of buccal and lingual flaps, exposing the periodontium, at root and furcation region, followed by thorough root planing and cleaning. Bone grafts are placed into the boney defects of the periodontium, then the flaps are sutured. The surgical pack is changed after one week and the sutures removed at 15 days.

Therefore, in light of current information, tetracycline and minocycline appear to be the antibiotics of choice in the treatment of LJP. Antibiotic therapy is recommended as an adjuct to periodontal scaling and root planing. Following initial treatment, patients should be on strict follow-up every two to three months, the evaluation including: plaque control, gingival bleeding, probing pocket depth with application of chemical antimicrobial agents, bone loss, and microbiological evaluation. Anaerobic culture to determine the percentage ot A.a. from total black pigmented Bacteroides and *Bacteroides gingivalis (Bacteroides intermedius),* may be achieved by placing a sterile paper point in the socket for 10 seconds and culturing anaerobically.[72] Samples from active sites and from healthy sites should be taken for a control.

Patients that show deterioration secondary to the disease, namely bleeding, high percentage of A.a. in the gingival sulcus or rapid bone loss, should be considered for additional courses of antibiotic treatment, which can be administered at six months to year intervals, and for surgical treatment. The possibility of reinfection or incomplete elimination of the organisms remains. Careful long term follow-up, including clinical and microbiological monitoring, is highly recommended in these patients.

Liljenberg[7] treated patients that were placed on tetracycline therapy tor two weeks. Surgery was performed one to two days after tetracycline therapy began. Buccal and lingual modified Widman flaps were raised. The bony defects and root surfaces being carefully curetted. The flaps were repositioned and sutured with interrupted proximal sutures. In this particular technique, no surgical dressing was used, but patients did rinse with 0.2% chlorhexidine twice a day for two minutes, over a two week post-surgical duration. The first six months following surgery, patients were recalled monthly for a professional prophylaxis. Subsequently, they were placed on three month recalls. We believe that this strategy of treatment is a good example of a clinical approach for the treatment of JP.

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after one week. Patients are given tetracycline, 1 g/d for 10 days, post-surgically. Strict follow-up, as indicated, is continued following this treatment.

Therefore, in light of current information, tetracycline and minocycline appear to be the antibiotics of choice in the treatment of LJP. Antibiotic therapy is recommended as an adjunct to periodontal scaling and root planing. Following initial treatment, patients should be on strict follow-up every two to three months,

Conclusion

Recent data implicate A.a. as the prime etiologic agent of JP. In addition, decreased chemotaxis of PMNs, and in some cases decreased phagocytosis and/or bacteriocidal activity, has been described in these patients. Whether this disease is a specific bacterial infection or immunodeficiency of white blood cells, possibly genetic in nature, or both, remains unknown. Reported studies demonstrate that the precise therapeutic regimen depends on the status of the disease and should be individualized. In addition to antibiotic therapy, root planing, curettage or a surgical approach should be considered. Careful follow-up is mandatory for successful treatment.

All correspondence should be sent to Dr. Donly, who is associate professor, department of pediatric dentistry, Dental Branch, University of Texas Science Center at Houston, 6516 John Freeman Avenue, Houston, TX 77030.

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