Aggressive periodontitis

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The diagnosis "aggressive periodontitis", defined by the International Workshop for a Classification of Periodontal Diseases and Conditions in 1999, refers to the multifactorial, severe, and rapidly progressive form of periodontitis, which primarily – but not exclusively – affects younger patients. Direct and indirect bacterial effects influencing the host immune response play a significant part in the etiology of aggressive periodontitis comparable to chronic periodontitis. In addition to various virulence factors of specific periodontal pathogens, a genetic predisposition influences the outbreak and progression of the disease. After diagnosis, which should be made as early as possible by clinical and microbiological diagnostics, the usual treatment methods include: mechanical debridement as well as the supportive use of antibiotics, in some cases guided tissue regeneration methods. In addition, the dentition has to be reconstructed functionally and esthetically restorations or implants. A long-term success of therapy demands an appropriate periodontal maintenance.

Key words: Aggressive periodontitis, classification, diagnostics, therapy

INTRODUCTION

At the "International Workshop for a Classification of Periodontal Diseases and Conditions" in 1999, the classification of periodontal diseases was revised (Armitage 1999). The various types of periodontitis were divided into three main categories (chronic, aggressive, and necrotizing periodontitis) as well as into a periodontal a manifestation of systemic diseases. This article provides a synopsis of the current classification, epidemiology, etiology, diagnostics and therapy of the aggressive types of periodontitis. The term "aggressive periodontitis" (AgP) does not refer to a new disease, but is used to describe the rare, but extremely progressive forms of periodontitis, which in most cases manifest themselves clinically during youth. This now replaces the terms "juvenile", or "early onset" periodontitis (EOP). The presence of systemic diseases, resulting in an impaired immune system of the host and thereby causing severe periodontal diseases and premature tooth loss, must be excluded.

CLASSIFICATION

With regard to its clinical and paraclinical aspects, AgP can be distinguished from chronic periodontitis. It is defined by the following characteristics (Land et al, 1999):

- Except for the presence of periodontitis, patients are otherwise clinically healthy,
- Rapid attachment loss and bone destruction
- Familial aggregation.

Non-constant characteristics of the disease:
- Amounts of microbial deposits are inconsistent with the severity of periodontal tissue destruction,
- Elavated propotion of *Actinobacillus actinomycetemcomitans*, and in some populations *Porphyromonas gingivalis* may be elaveted,
- Phagocyte abnormalities,
- Hyper-responsive macrophage phenotype including elevated levels of PGE_2 and IL-1β,
- Progression of attachment loss and bone loss may be self-arresting.

Figs. 1a to g Localized, aggressive periodontitis: a 30-year-old patient, smoker, typical infection of the first molars and incisors, identification of *Porphyromonas gingivalis*, *Tannerella forsythensis* and *Treponema denticola* (PadoTest®, Institute for applied Immunology, Zuchwil, Switzerland).

Furthermore, the Consensus Report of the Workshop for the Classification of Periodontal Diseases (Lang et al, 1999) identified certain clinical and paraclinical features, which allow a subclassification of AgP into a localized (figs. 1 and 2) and a generalized form (figs. 3 and 4). Localized AgP begins during puberty. The first molars and/or the incisors and at no more than to additional teeth are affected (fig. 1). Generalized AgP, however, occurs mostly in young adults (although older patients can also be affected), generally affecting the approximal areas and entailing attachment loss of at least three permanent teeth other than first molars and incisors.

Figs. 2a to b Early onset of localized aggressive periodontitis: 14-year-old patient with attachment loss at teeth 12 to 22, hardly any signs of marginal inflammation, *Actinobacillus actinomycetemcomitans* diagnosed (PadoTest®).

Figs. 3a and b Generalized aggressive periodontitis: a 23-year-old female patient, non-smoker, diagnosed with *Actinobacillus actinomycetemcomitans* and *Porphyromonas gingivalis* (PadoTest®).
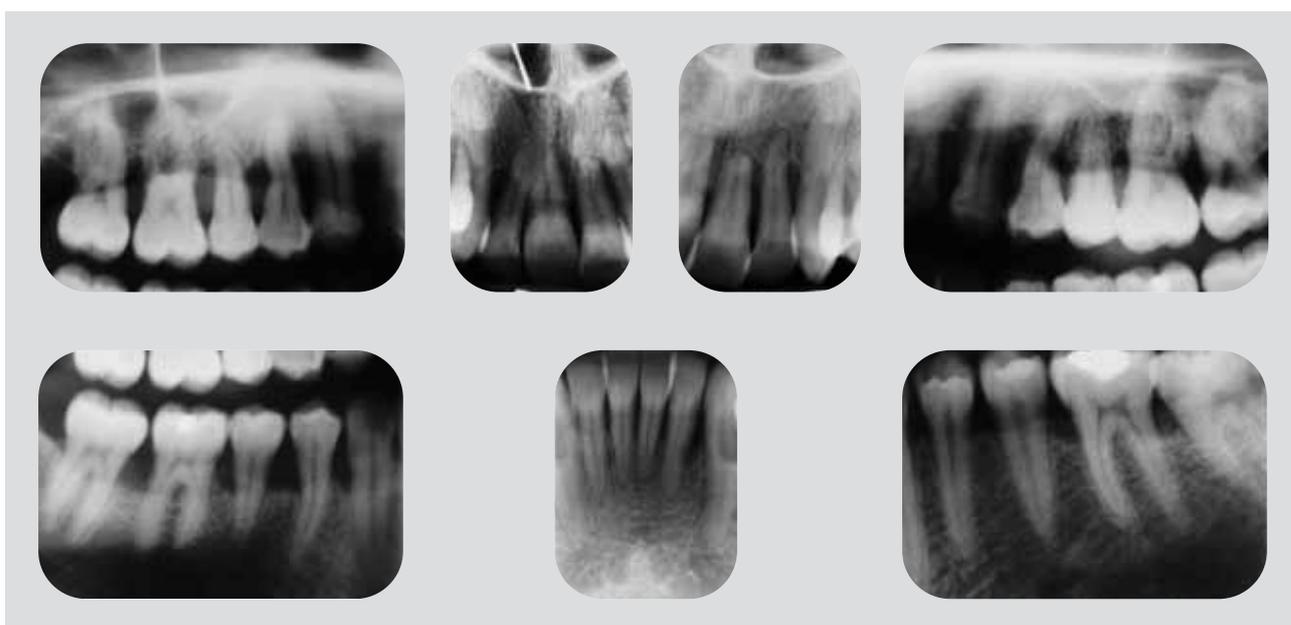
Figs. 4a to f The progression of generalized aggressive periodontitis. Initial situation: a 39-year-old female patient diagnosed with *Porphyromonas gingivalis* (PadoTest®), no further systemic diseases, detailed blood analysis revealed no pathological results. Therapy: subgingival scaling followed by open surgical debridement in combination with the systematic dosage of 3 x 400 mg/d of metronidazol over a period of 7 days. Maintenance therapy included: In the first 4 years therapy was performed at 3–4 months intervalls, in the third year due to increased probing pocket depths (up to 6 mm) and bleeding on probing subgingival scaling was repeated on the molars. After the 4 years period of time maintenance therapy was performed in a 6 months intervall due to stabilized periodontal conditions.

Figs. 4a and b Baseline findings.

Generalized AgP is the most severe form of all periodontal diseases. It is extremely heterogeneous in its clinical progression and response to treatment. Uncertainties with regard to causal mechanisms and individually variable and genetically determined susceptibility to illness, however, prevent a clearer classification at present. Some case reports describe the presence of AgP also in deciduous dentition (formerly termed prepubertal periodontitis). In the case of these patients, however, there is often an increased susceptibility to periodontitis on due to the presented of systemic diseases. Thus, this category was omitted in the current classification (Armitage, 2002).

Fig. 4c   clinical situation after subgingival scaling.

Fig. 4d   clinical situation 4 weeks after completion of treatment.

Fig. 4e   clinical situation 4 years after completion of treatment.

Fig. 4f   clinical situation 6 years after completion of treatment. Tooth 27 had to be extracted due to a combined periodontic-endodontic lesion.

The known risk indicators/factors for chronic periodontitis (e.g., smoking, stress), are also of significance for the aggressive forms of periodontitis.

EPIDEMIOLOGY

Considerably less epidemiological data are available on AgP than on chronic periodontitis. These data are mostly related to the previously valid definition of juvenile periodontitis or EOP. Wide variation in prevalence of early onset (aggressive) periodontitis has been reported of the last 20 years period time (Jenkins and Papapanou, 2001), that can possibly be due to differences in examination methods and disease definitions (Lopez and

Baelum, 2003). Topographical, possibly also racial factors should be considered. For Europe, low rates of 0.1% to 0.2% have been reported (Hansen et al, 1984; Kronauer et al, 1986; Saxby, 1984). The values for the US fluctuate between less than 1% and 10% depending on race (Albandar, Löe). Relatively high prevalence rates have been observed for some South American (Albandar 1991), African (Albandar 2002), and Asian (Timmerman) countries.

On the basis of these data, it can generally be concluded that only a small number of children and young adults are affected by any form of periodontitis, and that most of these, however, have AgP.

ETIOLOGY AND PATHOGENESIS

The aggressive periodontal diseases are characterized by relatively severe and rapid destruction of periodontal tissue. This is attributed on one hand to the particular virulence of the pathogens, and on the other hand to an increased, and possibly genetically determined susceptibility of the patients. There is no doubt regarding the particular significance of specific periodontal pathogens in the etiology of periodontitis, although the amount of microbial deposits are often inconsistent with the severity of periodontal tissue destruction.

The following species are principally associated with advanced periodontal lesions: *Actinobacillus actinomycetemcomitans* (A. a.), *Porphyromonas gingivalis* (P. g.), *Tannerella forsythensis* (T. f.), and *Treponema denticola* (T. d.) (Zambon, 1983). Many studies identified A. a. as the key factor in the genesis of localized AgP (e.g., Mandell et al., Socransky and Haffajee, and Zambon et al.). Various specific virulence factors pertaining to A. a. and immunological reactions to this microorganism were defected. Clinical studies showed a correlation between the result of treatment and the persistence of A. a. after therapy. Generalized aggressive periodontal diseases are mainly associated with the occurrence of P. g. and T. f., A. a. was also found. Similar to A. a., the obligate anaerobes P. g. and T. f. can – by means of various virulence factors such as bacterial enzymes, endotoxins and fimbria – contribute to the pathogenesis of AgP (Amano, 2003; Travis et al, 1997). A certain and differentially diagnostic distinction of AgP from chronic periodontitis, however, cannot be made solely on the basis of microbiological findings (Mombelli et al, 2002).

In the case of both chronic periodontitis and AgP, direct and indirect bacteriological effects influencing the body's immune system play a role in the destruction of periodontal structures. A local, bacterially induced inflammatory response plays a significant part in the etiology and pathogenesis of AgP, particularly in its localized form. Localized AgP characterized by a concentrated accumulation of polymorphonuclear leukocytes (PMNL) in the periodontal lesion. Not only both inactivity or defective function of the PMNL is of importance for the pathogenesis of AgP (Clark et al, 1977; van Dyke et al, 1980, 19985). Hoewever, like recent research results suggest a chronic hyperactivation of these immune cells is importance to a continuous release of toxic substances, and is hence at least partly responsible for the periodontal tissue destruction (Kantarci et al, 2003).

Altered antibody reactions to periodontitis-related microorganisms seem to be of significance for the generalized form of AgP (Lu et al, 1994; Quinn et al, 1996; Takahashi et al, 2001), Cytokines and other inflammatory mediators also play a particular role in the pathogenesis of both AgP and chronic periodontitis (Salvi et al, 1998). However, host response in AgP patients is found to be heterogeneous. Numerous studies carried out in the course of the last 10 years support the theory that the host immune reactions, i.e., the quality and quantity of the local inflammatory response, are at least partially genetically determined. Thus, the occurrence within a family of 20% to 50% was reported for early onset periodontitis (EOP) supports (Beaty et al, 1987; Hart, 1996). That corroborates the theory of a genetically determined predisposition for this form of periodontitis. Furthermore, associations of polymorphisms with varying degrees of prominence have been described in the inflammatory and immune response of involved genes with regard to the occurrence of aggressive forms of periodontitis (described systematically by Hart, 1996).

According to this, AgP, like chronic periodontitis, is to be seen as a multifactorial disease which results from complex interactions between the microbial attack and specific host responses. Exogenous factors (e.g., smoking) and a genetic predisposition for the disease are of particular significance.

DIAGNOSTICS

Every form of periodontitis is diagnosed mainly of the clinical parameters probing depth and attachment loss as well as on the basis of radiological and possibly microbiological data. In order to recognize an AgP case as early as possible, probing of the entire periodontal region of children and young adults, if possible at six different locations, is indispensable; the Periodontal Screening Index (PSI) is an efficient diagnostic tool for this purpose. The differential diagnosis of AgP is made on the basis of its distinction from other forms of periodontitis by further parameters. Necrotizing periodontitis is relatively simple to identify on account

of its characteristic clinical appearance. A comprehensive medical history is necessary for identifying the presence of systematic conditions that impair host defense, and are thus acompanied by periodontitis. Finally, after excluding these forms of periodontitis, a differential diagnostic distinction from chronic periodontitis is necessary. The criteria of the international workshop for the classification of periodontal diseases are decisive (see section on classification). The main characteristic of AgP is, according to this, an extremely progressive form of tissue destruction. Although the current classification system is no longer principally based on the age of the patient, the evaluation of the loss of periodontal support tissue which has already occurred in relation to age can be helpful in the evaluation of the progression of the disease (fig. 3). The specific distribution of the periodontal lesions (molars/incisors or generalized occurrence) permits the identification of localized or generalized AgP, as described in detail above.

The further diagnostic criteria for AgP include the presence of specific microorganisms, mainly of A. a.; microbiological diagnostics also provide insights relevant for differential therapy (see below). Nowadays, the periodontal pathogens are normally identified using the methods of modern molecular biology (PCR, DNA probes).

TREATMENT STRATEGIES

The successful treatment of AgP depends mainly on an early diagnosis. As in the case of all other forms of periodontitis, the main focus of therapy is reducing the pathogens to, in combating infection in order to overcome the local pocket infection and to establish a subgingival flora that is compatible with healthy oral conditions. The main objective is the substantial reduction, or better, the eradication of A. a. The motivation and capability of the patient with regard to effective oral hygiene is the prerequisite for a successful periodontal treatment. On the other hand, the clinician or qualified assistants must create conditions which facilitate oral hygiene. This means that teeth with a hopeless prognosis must be extracted, andmust be replaced with hygienic provisional restorations that facilitateeffective home care. Thorough, professional tooth cleaning serves to remove all calculus and plaque as well as to rectify potential plaque retention surfaces (defective margins of fillings and crowns, caries).

In the second stage of the initial therapy, infection is further mechanically combated with subgingival scaling. This could take place in one single treatment session (or within 24 hours) involving the entire periodontium and further intraoral niches ("full-mouth disinfection") (Mongardini et al, 1999; Quirynen et al, 1996). After re-evaluation, this may be followed by surgical pocket therapy where persisting, active lesions exist. The application of regenerative techniques brings similar results as in the case of chronic periodontitis (Mengel et al, 2003; Zucchelli et al, 2002).

The treatment success of AgP therapy is depends on the successful elimination of the respective periodontal pathogens involved, particularly to that of A. a. It was, however, demonstrated in several studies that by mechanical debridement, whether using the traditional method of subgingival scaling, or surgically by means of creating an access flap (Christerson et al, 1985; Gunsolley et al, 1994; Komman and Robertson, 1985; Mombelli et al, 1994; Slots and Rosling, 1983). A. a. cannot be eradicated enirely because it has the ability to penetrate tissue (Christersson et al, 1987). P. g., which is often associated with generalized AgP, can be more reliably eliminated by mechanical means, but here too, inadequate results and progressive attachment loss due to insufficient reduction of the quantity of bacteria were reported. Combining mechanical therapy with an additional systemic dosage of suitable antibiotics can, however, achieve a lasting suppression of the pathogens. The medication is generally selected according to the results of microbiological diagnostics (Kamma and Baehni, 2003; Mombelli et al, 2000), i.e., depending on the predominant pathogens (Mombelli and van Winkelhoff, 1997). Guidelines for use according to the recommendations of the German Society of Dentistry and Oral Medicine (DGZMK) and the German Society for Periodontology (DGP) are summarized in table 1; combinations of active ingredients are possible. Hence, for example, the combination of metronidazol and amoxicillin has proven to be beneficial (van Winkelhoff et al, 1989). By means of the development of specific vehicle systems with a controlled release of the active ingredients, local antibiotic treatments are increasing in significance. Two to 3 months after completion of the therapy, including additional adjunctive

Table 1 General dosage recommendation for therapy-relevant antibiotics according to recommendations in the joint scientific statement of the DGZMK and the DGP: "Adjuvante Antibiotika in der Parodontitistherapie" (Adjuvant Antibiotics in Periodontitis Therapy) 2003.
* = according to Mombelli and von Winkelhoff

Antibiotics	Dosage/duration (d)		Use*
Doxycyline	2 x 100 mg/d	1 d	Recurrent A. a.-determined periodontitis activity
	1 x 100 mg/d	18 d	(collagenase inhibition)
Amoxicillin (+ clavulan acid)	3 x 500 mg/d	14 d	Against most periodontal pathogens, usually as combination against mixed infection (do not combine with tetracycline)
Metronidazole	3 x 400 mg/d	7 d	Against obligate anaerobes
Ciprofloxacin	2 x 250 mg/d	10 d	Instead of amoxicillin in the case of allergy to penicillin
Metronidazole plus	3 x 400 mg/d and		Localized/generalized aggressive periodontitis Mixed infection from A. a. + gram negative
Amoxicillin	3 x 500 mg/d	7 d	anaerobes
Metronidazole plus	2 x 500 mg/d und		
Ciprofloxacin	2 x 250 mg/d	7 d	Instead of amoxicillin in the case of allergy to penicillin
Climdamycin	4 x 300 mg/d	7 d	Against obligate anaerobes

antibiotic treatment, the success of the therapy is clinically re-evaluated and the sufficient reduction of the pathogens can be confirmed by means of microbiological diagnostics. Gaps in the dentition can be closed functionally and esthetically restorations and/or implants.

In order to avoid or significantly reduce the risk of a relapse or progression of the periodontitis, an effective maintenance therapy is essential for patients with AgP. Depending on the number of remaining pockets, the inflammatory activity and the number of further risk factors for progressive attachment loss (smoking, genetic factors, systemic diseases), an individualized, periodontal maintenance program is devised (Lang and Tonetti, 1996). As in the case of all other forms of periodontitis, periodontal maintenance here includes diagnostic measures, professional tooth cleaning, an oral hygiene check-up with the instruction of the patient, oral hygiene training, and the treatment of any relapses of the periodontitis in indicated regions (Hoffmann, 2002).

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