Aggressive and acute periodontal diseases

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In 1999 the International Workshop for a Classification of Periodontal Diseases and Conditions classified disorders that affect the supporting tissues of teeth into eight main categories (4). This volume of Periodontology 2000 addresses the aggressive and acute forms of periodontal diseases, which include a number of the categories and subcategories described in the aforementioned workshop. Compared with other forms of periodontal diseases, the aggressive and acute forms have a relatively low prevalence in populations. However, the importance of these diseases stems from their significant clinical impact on patients’ quality of life because they usually have a relatively rapid course of disease development and also typically cause a profound destruction of the tissues supporting the teeth.

Aggressive periodontitis is a destructive periodontal disease that develops early in life. This disease is unlike chronic periodontitis in that its progression rate is higher, it presents distinctive clinical features and its etiology may be different. There are indications that systemic factors may play a greater role in the etiology of aggressive periodontitis than in that of chronic periodontitis. Other aggressive forms of periodontal diseases are usually found in patients who are affected with certain systemic diseases. The category of acute gingival and periodontal lesions includes an assortment of disorders that range from nondestructive to destructive forms, and as all such lesions are usually associated with pain, patients may seek urgent dental help. In addition, some of these lesions may cause a rapid and severe destruction of the periodontal tissues and therefore prompt diagnosis and treatment is paramount.

Aggressive periodontitis

Case definition

Although there is ample evidence showing that aggressive periodontitis is a distinct disease category which is different from chronic periodontitis, unequivocal case definitions of these two diseases are still lacking. An ideal case definition of aggressive periodontitis should be based on its distinctive clinical signs, in combination with the presence of key causal factors of the disease. However, because the etiologic factors of this disease have not yet been fully established, at present the recommended case definition relies mainly on the disease case history and the diagnosis of characteristic clinical and radiographic criteria.

The first comprehensive case definition of aggressive periodontitis was proposed more than four decades ago by Baer (5), who characterized the disease using seven clinical criteria. Although several of these criteria are still valid as distinctive clinical features of this disease, there is now sufficient evidence showing that some of the clinical features recommended by Baer are not valid. Other case definitions were described during professional workshops in 1989 and 1999, but these had issues that limited their validity, and hence, their utilization (1).

A contemporary case definition of aggressive periodontitis is presented by Albandar in this volume of Periodontology 2000 (1). Key diagnostic criteria of this disease include an early age of onset, involvement of multiple teeth with a distinctive pattern of clinical attachment loss and radiographic bone loss, a relatively high rate of disease progression and the absence of systemic diseases that compromise the
host’s response to infection. Although in some patients the disease may start before puberty, in most patients the age of onset is during, or somewhat after, the circumpubertal period. A typical patient shows disease onset at an early age (i.e. before 25 years of age), although identification of the affected patient usually occurs after disease commencement. Aggressive periodontitis is characterized by a relatively high rate of disease progression; consequently, when the patient is diagnosed, there is usually a significant loss of periodontal attachment at multiple permanent teeth. Initially, the periodontal lesions show a distinctive pattern, depicted radiographically as vertical bone loss at the proximal surfaces of posterior teeth, and the bone loss usually occurs bilaterally. In advanced cases of aggressive periodontitis the periodontal lesions may be depicted radiographically as a horizontal loss of bone. The primary teeth may also be affected, although early exfoliation of these teeth is not common.

Aggressive periodontitis may be localized or generalized. In localized aggressive periodontitis, tissue loss usually starts at the permanent first molars and incisors, and with increasing patient age the disease may progress to involve the adjacent teeth. The generalized form of aggressive periodontitis involves most or all of the permanent teeth. Although generally these are regarded as different forms of the same disease, some research findings suggest that in certain cases the two forms may represent two distinct diseases. Clinically, however, there is little evidence that the localized and generalized aggressive periodontitis are mutually exclusive clinical entities, and the clinical distinction between the two forms can be challenging, particularly at the advanced stage of the disease as more teeth are involved with periodontal destruction. This often results in misclassifications of cases into localized or generalized categories, and this may profoundly influence the validity of studies that use these disease subclassifications. The presence, and the type and amount, of etiologic factors may determine the clinical features and severity of the disease, and future diagnostic methods that make the identification of key etiologic factors possible may enable the early detection of subjects with aggressive periodontitis, thereby improving disease prevention and control, and may also increase the validity of disease classification into distinct disease entities.

**Epidemiology**

A systematic review of epidemiologic studies of aggressive periodontitis found high variability in the estimates of the prevalence of this disease in different populations (24). However, it is also noted that the methodologies used in several of these studies were often inconsistent, as different study designs, examination methods and case definitions were applied. Furthermore, surveys of aggressive periodontitis that use only clinical examinations and low thresholds of attachment loss as case definitions, without radiographic examination to confirm the presence of a distinctive pattern of tissue loss, may overestimate the prevalence of this disease. As these inconsistencies may greatly confound the findings of epidemiologic studies, the use of suitable methodologies, particularly an unequivocal case definition of aggressive periodontitis, is recommended.

The prevalence of localized aggressive periodontitis varies considerably between continents, and differences in race/ethnicity seem to be a major contributing factor. Most studies show a comparable prevalence of aggressive periodontitis in male subjects and female subjects. Among children and young adults the disease is detected more frequently in the older age groups than in younger subjects. Epidemiologic studies show that localized aggressive periodontitis is most prevalent among Africans, and is least prevalent among Caucasians in Europe and North America. Estimates of the disease prevalence are 1–5% in the African population and in groups of African descent, 2.6% in African-Americans and 0.5–1.0% in Hispanics in North America, 0.3–2.0% in South America, and 0.2–1.0% in Asia. Among Caucasians, the disease prevalence is 0.1% in northern and in central Europe, 0.5% in southern Europe, and 0.1–0.2% in North America (24). These findings show that localized aggressive periodontitis is a significant health problem in certain populations. Still, there is a lack of information on the epidemiology and demographics of this disease in many parts of the world, particularly Asia and Africa.

**Microbiologic etiologic factors**

Aggressive periodontitis is an infectious disease and its pathogenesis is somewhat similar to that of chronic periodontitis (23). The search for the microbial causal agent(s) has endured for decades, and it remains inconclusive. Recent advances in microbiologic detection methods and genome mapping have considerably increased our knowledge of the composition of subgingival biofilms in health and in various forms of periodontal diseases. Previous findings that *Aggregatibacter actinomycetemcomitans* plays a primary role in the pathogenesis of all types
of aggressive periodontitis may not be supported by more recent findings from studies using more sensitive molecular microbiologic methodologies. The current understanding is that aggressive periodontitis contains a mixed microbial flora, with a wide heterogeneity in the types and proportions of microorganisms recovered from patients with the disease, and there are significant differences between different geographic regions and ethnicities (15). There is evidence that the A. actinomycetemcomitans-JP2 clone may play an important role in the development of aggressive periodontitis in certain populations (6, 9). The role of novel and not-yet-culturable bacteria in the pathogenesis of aggressive periodontitis is not known. It has also been hypothesized that herpesviruses, including Epstein–Barr virus and cytomegalovirus, may impair the local host defenses, and hence may increase the aggressiveness of periodontopathic bacteria and thereby contribute to the etiology of aggressive periodontitis (21, 22).

Host response

The host response to microbial infection plays an important role in the susceptibility to aggressive periodontitis. To that extent, a prevailing view has been that chemotactic defects in neutrophils are a major etiologic factor in the etiopathogenesis of this disease. However, a critical review of the significance of host responses in aggressive periodontitis suggests that neutrophil dysfunction is not a major cause of this disease in nonsyndromic individuals (16). In a competent host, the innate and inflammatory immune systems provide early responses and contribute to protect the host from potentially pathogenic microorganisms. In contrast, the adaptive immune system includes the humoral and cellular immune responses, and it plays a role during the later stages of infection. The type of immune response mounted by the host to infection will depend on the type of microorganisms, and because the microbial infection in aggressive periodontitis is a mixed infection, the immune response may be complex and involve multiple mechanisms. These mechanisms are described in detail by Kulkarni & Kinane in this volume of Periodontology 2000 (16). Diagnostic methods of this disease, based on a specific microbiologic or immunologic profile, currently do not exist.

Genetic risk factors

Cases of aggressive periodontitis tend to show a familial pattern, and this suggests a role for genetic factors in the pathogenesis of this disease (27). Syndromic periodontal diseases are associated with monogenic diseases, and the genetic bases for these diseases have been identified. However, nonsyndromic periodontal diseases seem to have different, more complex, genetic mechanisms. Insofar, available data suggest that aggressive periodontitis is caused either by mutations in a few major genes or by multiple small-effect genes, and there is also evidence of gene–gene and gene–environment interaction effects. The genetic association study approach is useful for the identification of genetic variants that could affect susceptibility to complex diseases, such as aggressive periodontitis. Most association studies have focused on the abnormal effects of various gene polymorphisms on host responses, including the chemotaxis and functions of neutrophils, cytokines and inflammatory mediators, and on other genes, such as the vitamin D receptor gene. Many of these studies have yielded inconsistent findings. This may be attributed to multiple reasons, including relatively small study samples, inadequate phenotypic characterization of cases and controls, and variability of the genetic profiles among different populations. In addition, as most studies focused on only one or a few genes, the study design may not have been adequately powered to detect potentially small effects. Most recent genetic studies have documented father-to-son transmissions of aggressive periodontitis, which is not consistent with the X-linked mode of transmission that was previously the accepted mode of inheritance of the disease. Rather, an autosomal mode of inheritance is now considered more valid. Genetic markers have the potential to be implemented as screening tools to identify subjects at risk for developing aggressive periodontitis. This approach may significantly enhance treatment outcome through the early detection and treatment of patients, as well as using future approaches based on gene therapy.

Treatment of aggressive periodontitis

As aggressive periodontitis is primarily an infectious disease, its treatment is somewhat similar to the treatment of chronic periodontitis (25). Nonetheless, controlling and treating aggressive periodontitis is more challenging than controlling and treating chronic periodontitis. The initial treatment is directed toward eliminating the bacterial load in the periodontal pockets and other local risk factors. Studies show that scaling and root planing in combination with adequate home care is effective in improving the clinical periodontal parameters in
aggressive periodontitis patients. However, the adjunctive use of appropriate systemic antibiotic regimens may further improve the clinical outcome and contribute to a longer suppression of microbial infectious agents. To achieve this, the bacterial biofilm should be mechanically disrupted before antibiotics are administered (11). The recommended antibiotic regimen is azithromycin, or amoxicillin combined with metronidazole. A limited number of studies have investigated the effect of surgical treatment of aggressive periodontitis, and the results show good outcome for both surgical access methods or regenerative techniques, and comparable efficacy with that of chronic periodontitis, provided that the treated patient is followed up in a thorough maintenance program to ensure an adequate level of oral hygiene and the control of risk factors (25).

Aggressive forms of periodontal disease secondary to systemic disorders

Certain systemic disorders increase the patient’s susceptibility to periodontal disease, either by compromising the immune response (particularly neutrophil count and function) or by influencing the mineralization of bone and dental tissues (14). As a result, patients who are affected with these diseases may develop severe periodontitis and usually lose their teeth at an early age.

Systemic disorders with a periodontal component include rare genetic syndromes where the patients develop aggressive periodontitis as a secondary manifestation. The leukocyte adhesion deficiency syndrome is caused by defects in adhesion receptors of the leukocytes. The Papillon–Lefèvre syndrome is caused by a loss-of-function mutation affecting the cathepsin-C gene, which affects a key enzyme in the activation of granule serine peptidases, thus leading to a disruption of inflammatory cell functions. In the Chediak–Higashi syndrome there is impaired function of multiple body cells and systems, such as a decrease in phagocytosis. In these syndromes the affected patients show severe gingival inflammation and severe, rapidly progressive periodontitis, which leads to early loss of the primary and permanent teeth.

Down syndrome is characterized by the presence of an extra copy of chromosome 21, and the disease is more common than other genetic disorders, with a prevalence rate of about 1 per 800–1,000 births (20). Periodontal disease is a common manifestation among subjects with Down syndrome, with an estimated prevalence of 58–96% in those under 35 years of age, and periodontitis is more severe in these subjects than in non-Down syndrome subjects. A combination of factors, including altered immune response, early microbial colonization and increased gingival inflammation, may contribute to the increased susceptibility to periodontitis in individuals with Down syndrome.

Early exfoliation of the primary and permanent teeth is also a secondary manifestation of certain metabolic disorders, such as hypophosphatasia, a genetic disease characterized by a deficiency of tissue-nonspecific alkaline phosphatase activity leading to an inhibition of skeletal and/or dental mineralization. Notably, in this disease the early loss of teeth is not caused by severe inflammatory periodontal disease. Rather, the premature loss of teeth is attributed to a severely compromised periodontal attachment apparatus (26).

Management of the periodontal component of these diseases is very challenging. Proper diagnosis is a prerequisite for a proper management; hence, a differential diagnosis should be established and the associated genetic disorder identified if possible. A detailed review of the medical and dental history, family history and pertinent laboratory findings should be undertaken. Consultation with other medical specialists is important. In certain cases molecular genetic testing may be indicated and may help to validate a clinical diagnosis. Future advances in research, including gene targeting and the resolution of enzyme deficiencies, may bring about adequate remedies of the underlying genetic defects and may significantly improve the outcome of periodontal treatment in these patients. In the meantime, current treatment methods include control of the supragingival dental plaque, conventional periodontal therapy and systemic antimicrobial therapy.

Acute gingival and periodontal lesions

Acute lesions in the periodontium and oral mucosa are clinically important and often require urgent attention from dental-care providers because they are usually associated with pain and could lead to a rapid destruction of the periodontal tissues (12). Some of these lesions also cause systemic symptoms, such as fever, malaise and lymph adenopathy.

Abscesses in the periodontium are a common dental emergency that if not treated promptly may compromise the prognosis of the affected tooth, and the
infection may spread to other body sites. Gingival abscesses affect the marginal and interdental gingiva, whereas periodontal abscesses affect deeper periodontal tissues. Symptoms of acute periodontal abscess include swelling of tissues, pain and tenderness to palpation, whereas a chronic abscess is asymptomatic or elicits mild symptoms only because the pus usually drains through a fistula or the periodontal pocket. Treatment of an acute abscess consists of drainage, and systemic antimicrobial therapy should be considered. The treatment of a chronic periodontal abscess is similar to the treatment of chronic periodontitis.

Necrotizing periodontal diseases are a group of infectious diseases that include necrotizing gingivitis, necrotizing periodontitis and necrotizing stomatitis, depending on the type of tissues involved. The diseases are caused by microbial infectious agents and a compromised host immune response. The typical clinical features are necrosis of the interdental papilla, gingival bleeding and pain. A severe inflammation develops promptly and it may progress rapidly, leading to a profound loss of soft tissues and alveolar bone. Predisposing factors play a key role in the pathogenesis of necrotizing periodontal diseases. These factors include poor oral hygiene, severe stress, inadequate sleep, malnutrition, alcohol abuse, tobacco smoking and systemic diseases, such as HIV infection. Prompt diagnosis and treatment of necrotizing periodontal diseases is important. The treatment of necrotizing periodontal diseases should be performed in stages, where the acute phase is addressed first, followed by a subsequent phase to treat any pre-existing periodontal condition and the disease sequelae. The patients are then scheduled for a maintenance phase.

Other acute lesions may affect the periodontal tissues and may present a clinical appearance similar to that of soft-tissue erosions or ulcerations. They have an acute onset, are painful and may impede chewing and oral-hygiene practices. These lesions are a common reason for emergency dental consultations. Several etiological factors may give rise to these lesions. They may be primary lesions, or manifestations of certain systemic diseases or conditions, including infectious diseases, mucocutaneous diseases and traumatic or allergic lesions.

Acute focal infections of dental origin

A recent newspaper report described an incident involving a 12-year-old American child who report-
edly died because of an infection from a dental abscess, associated with a molar tooth, that spread to the child’s brain (19). Although the focal infection theory was proposed in the 19th century (17) and there have since been several case reports in the literature corroborating this hypothesis (2, 3, 7, 8, 10, 13, 18), this incident drew vast attention and prompted a deluge of interest in the importance of dental health to general health. It also motivated a nationwide debate in the USA about access to regular dental care, particularly for children. This re-emphasized the importance of a healthy mouth to a healthy body.

In this volume of Periodontology 2000, Olsen & van Winkelhoff focus on important acute oral infections that can spread to extra-oral sites and describe the mechanisms of the dissemination of oral infections, anatomical pathways of the dissemination and the proper management of these oral focal infections (18). Insofar, the early diagnosis and treatment of dental infections are imperative, and potential infectious foci should be identified and eliminated in order to prevent serious medical complications that may result from the spread of dental infections.

References