Sequential Manifestation of Different Forms of Early-Onset Periodontitis. 
A Case Report


PATHOGENIC BACTERIA CONSTITUTE THE PRIMARY EXTRINSIC AGENT in the etiology of early onset periodontitis. However, the risk of developing periodontal disease is not equal for all individuals, suggesting host factors are involved in determining an individual’s disease susceptibility. In this report, a case of an otherwise healthy female, who exhibited prepubertal periodontitis (PPP) at age 10, juvenile periodontitis (JP) at age 13, and rapidly progressive periodontitis (RPP) at age 29 years, is presented. Microbial, immunological, and genetic features of the case are presented. PPP, JP, and RPP are considered distinct disease entities, albeit with similar pathology and pathogenesis, yet all were manifest sequentially in the same individual. This report presents the idea that certain individuals are predisposed to early-onset periodontal diseases and the early identification of risk factors is important in the management of these individuals. J Periodontol 1994;65:631–635.

Key Words: Host factors; periodontitis, early-onset, etiology; periodontitis, prepubertal/ etiology; periodontitis, juvenile/etiology; periodontitis, rapidly progressive/etiology.

Although periodontal diseases are infectious in nature with a specific pathogenic flora, 1 recent evidence has indicated that disease susceptibility and individual variability in the host-response plays a major role in the disease process. 2 3 Alveolar bone loss may already be evident in children 4 5 and may be indicative of an inherent susceptibility to further periodontal breakdown in the permanent dentition. 6 Therefore, the early diagnosis and treatment of individuals at risk for periodontal diseases in childhood should be considered a goal in clinical dentistry. The establishment of risk factors and risk indicators will help to achieve this goal. In this paper, we present a longitudinal clinical report of a medically healthy female, with sequential periodontal diagnoses of pre-pubertal periodontitis (PPP) at age 10, juvenile periodontitis (JP) as a young adult, and rapidly progressive periodontitis (RPP) at age 29 years. This case emphasizes the need for early detection of individuals at risk for periodontal breakdown.

CASE REPORT

A 29-year-old female was referred to the Department of Periodontics of the Hadassah Faculty of Dental Medicine of Jerusalem for treatment of severe periodontitis. The patient had no history of systemic disease and since she previously attended the Hadassah Faculty of Dental Medicine, past dental records were available. Comprehensive dental treatment plans were done at ages 10, 13, and 22 years. However, due to compliance difficulties, the treatments were never completed. At age 10 years, enamel hypoplasia of the permanent first molars and central incisors, gingival inflammation and alveolar bone loss (Fig. 1) characteristic of idiopathic PPP were recorded. Differential diagnosis of other systemic diseases were excluded by laboratory tests. At age 13 years, shedding of the primary teeth and eruption of the premolars apparently resulted in an improvement of the alveolar bone status (Fig. 2). In contrast, incipient signs of alveolar bone loss on the mesial surfaces of the first permanent molars could be seen, typical of localized juvenile periodontitis (LJP), but the presence of stainless steel crowns could be the possible reason for this process. However, at age 22 years, alveolar bone loss was evident around all the first permanent molars and the mandibular and max-

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Figure 1. Bite-wing radiographs at age 10 years. Note the alveolar bone loss, characteristic of prepubertal periodontitis, affecting the primary dentition. Enamel hypoplasia on the first permanent molars is also evident.

Figure 2. Radiographs at age 13 years. Incipient alveolar bone loss is evident at the alveolar bone located mesial to the first permanent molars.

Figure 3. Radiographs at age 22 years. Alveolar bone loss, characteristic of generalized juvenile periodontitis/rapidly progressive periodontitis, affecting the first permanent molars, mandibular and maxillary incisors, lower canine, and second molars and second premolars is evident.
illar incisor areas, including teeth with no restorations (Fig. 3). In addition, some bone loss also occurred around lower canines, second molars and second premolars. At age 29 years further deterioration of the periodontium was evident with the radiographic image of RPP (Fig. 4).

Microbial Examination
At the latest examination carried out at age 29, four sites with probing depths of >6 mm were chosen for sampling (maxillary first premolars and lateral incisors). Briefly, supragingival plaque was removed and 3 sterile paper points were inserted into the periodontal pocket. The samples were diluted in reduced transport media,7 plated in duplicate with an automated spiral platter8 on enriched trypticase soy agar (ETSA) and onto selective media for Actinobacillus actinomycetemcomitans.9 The plates were incubated in an anaerobic chamber for 8 days.10 Following incubation, the total number of colony forming units, black-pigmented bacteroides (BPB), and Aa were counted and identified by means of colony morphology and biochemistry.9,11 The findings of the microbiologic examination are presented in Table 1. All four sites were positive to BPB, while only one site was positive for A. actinomycetemcomitans.

Table 1. Percentage of Colony Forming Units of Black-Pigmented Bacteroides (BPB) and Actinobacillus actinomycetemcomitans (Aa)

<table>
<thead>
<tr>
<th>Tooth</th>
<th>%BPB</th>
<th>%Aa</th>
</tr>
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<tbody>
<tr>
<td>Maxillary right lateral incisor</td>
<td>1.18</td>
<td>0.0</td>
</tr>
<tr>
<td>Maxillary right first bicuspid</td>
<td>1.33</td>
<td>0.0</td>
</tr>
<tr>
<td>Maxillary left lateral incisor</td>
<td>1.91</td>
<td>0.0</td>
</tr>
<tr>
<td>Maxillary left first bicuspid</td>
<td>0.49</td>
<td>0.12</td>
</tr>
</tbody>
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HLA Typing
Several studies have found an association between HLA phenotypes and periodontal disease (for review see reference 12). Our aim was to find if the present case had any HLA markers which might serve as a risk indicator for disease susceptibility. Peripheral blood lymphocytes of the patient, drawn at age 29, were used for HLA class I (ABC) and class II (DR, DQ) typing by the microlymphocytotoxicity method.13 The HLA phenotype of the patient was A2, A23 (9), B7, B44 (12), Cw5, DR4, DQ8 (3), DRw53.

Monocyte Functions
Monocytes can respond to bacterial stimuli by secretion of inflammatory mediators. Some of these mediators, such as tumor necrosis factor alpha (TNFα), interleukin-1β (IL-1β), interleukin-6 (IL-6), and prostaglandin E2 (PG-E2) are known to have bone resorptive potential.2,14 Due to the fact that the monocyte response to bacterial components is genetically determined,15 we examined the patient monocyte response to lipopolysaccharide (LPS).

At the same time of HLA typing, adherence-purified monocytes of the patient were cultured in serum-free RPMI 1640 for 24 hours in the presence of 30 μg/ml Escherichia coli LPS.** The media was analyzed for TNFα by ELISA, IL-1β, IL-6, and PG-E2 by radioimmunoassay. DNA content of the cultures was determined according to Shapira et al.16 Fourteen healthy age-matched controls were also studied for comparison.17 Secretion of TNFα by the patient monocytes was higher than mean control level + 2 standard deviations. In contrast IL-1β secretion was lower than the

**Sigma Chemical Co., St. Louis, MO.
controls. IL-6 and PG-E₂ secretion between the patient and the control group did not differ (Table 2).

DISCUSSION

The observation that children with periodontal diseases involving the primary dentition may develop advanced periodontal diseases involving their permanent dentition corresponds with the observation that there are inherent host factors which make certain individuals more susceptible to periodontal breakdown. Sjödin et al.⁶ reported 17 cases of LJP, in which all but one showed some evidence of bone loss in radiographs of their primary dentition examined retrospectively. Therefore, periodontal diseases in a child should be considered a sign of susceptibility to further periodontal breakdown. Furthermore, a connection between periodontal diseases in the primary and permanent dentitions is feasible since, in the mixed dentition, the pathogenic flora associated with the primary teeth may facilitate the establishment of periodontal diseases in the adjacent permanent teeth. The fact that, in the present case, at age 10 years, the alveolar bone located between the second primary and first permanent molars was affected, suggests the possibility that the pathogenic bacteria from the primary teeth accelerated the disease process associated with the first molars.

The predominant microorganisms found in the affected pockets at age 29 years were BPB species. No attempt was made to differentiate between the BPB species. On the other hand, only one site was found to be positive for low number of A. actinomycetemcomitans colonies. Although many reports have implicated A. actinomycetemcomitans as the principal pathogen at least in LJP,¹⁸ other studies have shown that A. actinomycetemcomitans is not always detected.¹⁹,²⁰ The flora at an earlier age of this patient could have been much different, contributing to the evidence that disease susceptibility is the major factor in early onset periodontitis.

Today, subclassification of EOP diseases is not complete. LJP and PPP are relatively well defined according to the clinical manifestations of the periodontal lesions.²¹ However, the borderline between LJP and generalized juvenile periodontitis (GJP) is not clear. Furthermore, RPP and GJP are frequently used for similar cases. The distinction between GJP and RPP²¹ may be arbitrary, and may be confusing the laboratory data involved in studies looking for disease markers or disease pathogenesis. In the present case, the patient showed signs of LJP at age 13, which developed to GJP or RPP at age 22. Better definition of EOP diseases are needed for the understanding the pathogenesis of these conditions and for the development of treatment strategies.

The association between HLA and antigens and periodontal susceptibility have been recently reviewed by Wilton²² and Page.²² Katz et al.¹³ found in a study of 10 patients with rapidly progressive periodontitis (RPP), that 8 patients exhibited HLA-DR4 antigen, compared to 38% in the control group. Other studies found increased frequency of HLA-A9 in RPP patients.²³-²⁵ In the present case, the patient had both antigens HLA-A9 and DR4, raising the possibility that these associations may be used as a risk markers. More studies are needed to verify those HLA associations with EOP, and to try to explore the nature of this process. However, one working hypothesis can be suggested from this patient monocyte function data (Table 2). The in culture monocyte studies revealed that the patient cells are “high producers” of TNFα as compared to the control group. Molvig et al.¹⁵ showed that monocytes from DR4 positive individuals are “high producers” of TNFα in response to bacterial lipopolysaccharide. The TNFα gene is located on chromosome 6, in close proximity to the HLA cluster. There is also evidence today that overproduction of TNFα in periodontal breakdown is important.²⁶,²⁷ The relationship between periodontal diseases, hyper-secretion of TNFα and HLA phenotype are interesting and need further investigation.

The case reported here clearly represents a person who is at high risk for periodontal disease. However, had we been able to address the primary causative agent, plaque, when the disease was initially detected we probably would have been able to prevent or, at least diminish, the advanced pathology seen at age 29 years. Future use of markers for disease susceptibility can be an effective tool for preventive regimens.

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