Neutrophil Chemotaxis and Periodontal Status in Down’s Syndrome Patients

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Abstract

Along with clinical parameters, chemotaxis and random migration of neutrophils were evaluated in 15 patients with Down’s syndrome (DS) and 15 healthy subjects. Signs of more severe gingival inflammation were present in the DS group. The random migration and chemotaxis of neutrophils were significantly decreased in comparison with the control group. In DS, the pathological status was attributed to these impaired host defense factors besides the existing bacterial plaque.

Introduction

Down’s syndrome (DS), which was first defined by Langdon Down, is characterized by physical and mental abnormalities due to underlying chromosomal aberrations[1,2]. In DS, susceptibility to infection is increased as a result of both specific and non-specific abnormalities of the immune system[3–8]. It has also been demonstrated that in DS patients, the prevalence and severity of advanced periodontal disease are increased[9–12]. The periodontal disease associated with DS is attributed to both endogenous and exogenous factors[13].

In the different stages of periodontal disease, accumulation of neutrophils in the connective tissue, junctional epithelium and gingival sulcus is a characteristic morphological finding[14]. A decreased number of neutrophils and impairment of their function both damage periodontal health[14]. As shown in patients with juvenile periodontitis (JP), it has been demonstrated that patients with DS have impaired neutrophil chemotaxis[3,8,10]. A similar pattern and severity of periodontal destruction exists in patients with DS and JP, the lower and upper incisors, mandibular and maxillary first molars and deciduous molars and premolars being primarily affected[13,15–17].

These findings suggest that a similarity exists between DS and JP in defective neutrophil chemotaxis and the localization and pattern of tissue breakdown. Therefore, patients with DS are considered to be a good model for evaluating the tissue destruction mechanisms related to neutrophil functions. The purpose of the present study was to examine periodontal status and neutrophil chemotaxis in patients with DS.

Materials and Methods

Ten male and five female DS patients with a mean age of 19±0.5 yr were evaluated. Care was taken to ensure that none of the patients had signs of infection and/or history of immunomodulatory drug administration. Cytogenetic analysis was performed at the Departments of Pediatrics and Genetics, Faculty of Medicine, Hacettepe University.

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The control group consisted of 15 patients, 8 female and 7 male, with a mean age of 23.67 yr. The subjects in this group were both systemically and periodontally healthy.

**Clinical studies:**

Pocket depths were recorded using a periodontal probe. The amount of plaque accumulation was determined according to the method of O'Leary et al.\[18\] In order to determine the overall periodontal status of the subjects, Russell's\[19\] periodontal index was employed.

**Laboratory studies:**

Zymosan-A at a concentration of 1 mg/ml was used in the activation of pooled AB serum. The activation procedure was performed at 37°C for 45 min, and the zymosan-activated serum (ZAS) was divided into small aliquots of 0.2 ml. The samples were stored at −20°C until the time of assay. The same ZAS sample was used during the study period.

**Chemotaxis assays:**

Heparinized (20U/ml) peripheral blood samples were obtained from a peripheral vein. Polymorphonuclear leukocyte-rich cells were obtained by the two-step technique described by Boyum\[20\]. After washing three times in medium 199, PMNs were suspended in the same medium at a final concentration of 5 × 10⁶/ml for the Boyden Chamber method\[21\]. Briefly, 0.5 ml PMN cell suspension (2.5 × 10⁶) was added to the upper chamber. The lower compartment was filled with 0.5 ml of 10% ZAS. Three-micrometer pore size Millipore filters were used, and the incubation time was 1 h. After incubation for 37°C in a 5% CO₂ atmosphere, chemotaxis was evaluated by the leading front method described by Zigmont and Hirsch\[22\]. The distance between the upper surface of the filter and the three most advanced cells in five different fields on each filter was measured, and the mean values were expressed in micrometers.

**Statistical studies:**

The differences between the means for the two populations were evaluated statistically\[23\].

**Results**

The clinical findings are presented in Table 1 and laboratory findings in Table 2. In patients with DS, the mean plaque index and periodontal index scores were 68.0 ± 10.7 and 1.56 ± 0.04, respectively. The mean probing depth was 2.68 ± 0.03 mm.

In the patient group the mean neutrophil chemotaxis value was 45.56 ± 13.58 μm, and the mean random migration and chemotactic index values were 18.86 ± 5.31 μm, and 2.61 ± 1.13, respectively.

Statistical evaluation of the results demonstrated a significant reduction in the chemotaxis and random migration values in the DS group compared with the control group (p < 0.05). The difference in mean chemotactic index values between the two groups was not significant (p > 0.05).

**Discussion**

It has been suggested that patients with DS (Trisomy 21), in comparison with non-trisomic subjects, show a tendency for periodontal disease\[10,24\]. In a study by Saxen et al.\[25\], a higher prevalence of periodontal disease was detected in patients with DS compared with age-matched children with mental retardation. They also suggested that various systemic factors were responsible for this difference. Reuland-Basma and Van Dijk\[13\] suggested that local factors such as macroglossia, malocclusion, tooth morphology, bruxism and masticatory function, as well as systemic factors related to the immune system, were responsible for such periodontal breakdown. Previous studies have shown abnormalities of the humoral and cellular immune systems in addition to non-specific abnormalities of immunity. Decreased neutrophil phagocytosis\[4,8\], NBT reduction\[25,27\] and functional defects of B and T cells and monocytes\[5,29,29\] have been demonstrated.

It is apparent that in all forms of periodontal disease, continuous neutrophil accumulation
occurs in connective tissue, the junctional epithelium and gingival sulcus\cite{14,17}. Therefore, functional defects of these cells and also a decrease in their number are hazardous for the maintenance of periodontal health. Furthermore, it has been suggested that neutrophil functions are related to the progression of gingivitis to advanced periodontitis. In the early phases of inflammation, an impaired neutrophil chemotactic response may lead to the establishment of destructive periodontal disease\cite{14,30}. It has also been suggested that in diseases where neutrophil function is impaired, such as neutropenia, lazy leukocyte syndrome, Chediak-Higashi syndrome, Papillion-Le Fevre syndrome, Job's syndrome, diabetes mellitus and DS, severe periodontal breakdown is usually present\cite{14,16,17}.

In the present study, random migration and chemotaxis of neutrophils were found to be significantly decreased in patients with DS, when compared with the healthy subjects (Table 2). Periodontal examination also revealed clinical signs of significant gingival inflammation (Table 1). REULAND-BASMA et al.\cite{31} in a previous study of 2 siblings, one with DS and the other without demonstrated significantly decreased phagocytosis, killing and chemotaxis in peripheral blood and crevicular PMNs from the former. Furthermore, severe gingivitis was noticed in the patient with DS when oral hygiene attempts were discontinued, indicating an anomaly of specific and non-specific immune responses. These findings, together with the clinical signs of gingivitis, are consistent with the findings of the present study.

<table>
<thead>
<tr>
<th>Table 1 Clinical findings in DS patients and healthy volunteers</th>
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<td>Patient Group</td>
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<tr>
<td>Down's syndrome (n=15)</td>
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<td>Healthy volunteers (n=15)</td>
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<tr>
<th>Table 2 Neutrophil chemotaxis, random migration and chemotactic index values in DS patients and healthy volunteers</th>
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<tr>
<td>Patient Group</td>
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<tr>
<td>----------------</td>
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<tr>
<td>Down's syndrome n=15 (10 M, 5 F)</td>
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<tr>
<td>Healthy volunteers n=15 (7 M, 8 F)</td>
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<td>Significance (p-value)</td>
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IZUMI et al.\cite{16} have suggested that the severity of periodontal breakdown in patients with DS is related to both poor oral hygiene and impaired neutrophil chemotaxis.

In different forms of periodontal disease (prepubertal periodontitis, juvenile periodontitis, rapidly progressive periodontitis), impaired neutrophil chemotaxis has been well demonstrated previously\cite{29,32,33}. Severe periodontal destruction at an early age together with comparable alveolar bone loss and various degrees of impairment of the host response, are prominent features of both DS and juvenile periodontitis. SHAW AND SAXBY\cite{34} have recently pointed out similarities of periodontal breakdown and diminished host response in DS and juvenile periodontitis patients. VAN DYKE\cite{35} in a previous study concerning the mechanism of chemotaxis dysfunction in localized juvenile periodontitis (LJP) suggested that the reduction of
chemotaxis in neutrophils of these patients was due at least partly to a reduction in the number of cell surface receptor sites for chemotactic factor. Direct association has also been demonstrated between neutrophil chemotaxis and the density of chemotactic binding sites.

Few data are available on the pathological mechanism of impaired neutrophil chemotaxis in DS. Khan et al.\[3\] have attributed this to secondary defects in the leukocytes. Although the nature of this defect is still not clear, it may be related to the relatively shorter half-life of these cells in DS patients (3.7 h, compared with 6.6 h in normal individuals).

Since chemotaxis is an active energy-dependent function, decreased chemotaxis may also be related to a known enzymatic defect of leukocytes in patients with DS. Björksten et al.\[36\] have demonstrated a decreased serum zinc level associated with impaired neutrophil chemotaxis in DS patients, and found that 2 months of zinc treatment improved the serum zinc levels and chemotaxis values.

It appears likely that the increased susceptibility to infection in patients with DS reflects several abnormalities of immunologic function including defective leukocyte chemotaxis. Further studies will be necessary in order to clarify the exact nature of the defects in these patients and their role in the pathogenesis of periodontal disease and infections.

**Conclusions**

1. In patients with DS, compared with age-matched healthy subjects, signs of more severe gingival inflammation were noticed.
2. Neutrophil chemotaxis in patients with DS was significantly reduced.
3. Random neutrophil migration was significantly reduced in patients with DS, compared with the control group.
4. The severe gingival inflammation noticed in DS patients was attributed to impaired host defense factors, besides the existing local factors.

**References**

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