Case Report

Periodontal Manifestation of Leukocyte Adhesion Deficiency Type I

Lida Toomarian DDS MSD•[1], Nazanin Hashemi DDS MS[2]

Abstract:

Progressive periodontal disease in leukocyte adhesion deficiency children may lead to severe systemic infections and even death. A five-year-old Iranian male child with leukocyte adhesion deficiency I was first seen in December 2005 at the Pediatric Dentistry Department of Shahid Beheshti Medical University and diagnosed with periodontitis as a manifestation of systemic disease. The treatment approach was based on assessing plaque index, oral prophylaxis, periodic supra and subgingival scaling, in addition to strict oral hygiene instruction with a chlorhexidine prescription and restoration of decayed teeth. The patient attended two dental visits at a one month interval. At the second session, an improvement was seen in the plaque index. Gingival inflammation and bleeding were decreased. Unfortunately he did not regularly attend treatment sessions and at the following examination, progression of periodontitis and bone destruction occurred. The present case emphasizes the need for cooperation between medical and dental professionals, parents and the pediatric patient in order to achieve treatment goals in controlling oral infection in these patients.

Keywords: Leukocyte adhesion deficiency, periodontitis

Introduction

Immune deficiencies are a heterogeneous group of rare disorders characterized by the decreased ability of the immune system to fight infections, abnormal leukocyte function, the inability of neutrophils and monocytes to leave blood vessels and go to the sites of injury and bacterial challenge, and decreased cellular adhesion. Aggressive gingival and periodontal diseases, with rapid and extensive alveolar bone loss that leads to early exfoliation of primary teeth, are significant and dramatic finding in children with immune deficiencies.[1]

Crowley et al.[2] (1980) described a patient with severe disseminated infection who lacked expression of gp110, a neutrophil surface protein. This condition, leukocyte adhesion deficiency (LAD) is a rare immunodeficiency disorder infrequently reported in the literature.[1,2,3] In type I of this disease there are defects in leukocyte function due to the lack of the integrin β2 subunit (CD18) which causes impaired migration and phagocytosis. In type II, neutrophils fail to express the ligand (CD15) for P and E-selectins, resulting in impaired transendothelial migration in response to inflammation.[4] To reach the periodontal tissues, blood-borne phagocytes must adhere to and then traverse the blood vessel wall. Surface molecules present on both the phagocyte and endothelium mediate this adhesion. Three adhesion molecules expressed on leukocytes are composed of a unique α subunit (CD11a, b, or c) and a common β subunit (CD18).[4,5] When too few of these molecules are present, cells cannot adhere to the endothelium and an important component of the cellular immune response is compromised.[4] In LAD-I, which has an autosomal recessive mode of inheritance, mutations in the ITGB2 gene on chromosome 21 (21q22.3) lead to a genetic defect of the β chain[6–8] with a defect in all three adhesion molecules. CR3 (complement receptor 3) is composed of two polypeptide chains: one α chain (CD11b) and one β chain (CD18). A defect in this receptor in the phagocyte membrane that binds to C3bi on opsonized microorganisms affects phagocytosis. Two other integrin proteins share the same β chain, namely LFA-1 and P 150-95; these proteins are also deficient in LAD. Because of the defect in LFA-

Authors' affiliations: [1]Department of Pediatric Dentistry, Dental School, Shahid Beheshti University of Medical Sciences, Tehran, Iran, [2]Pediatric Dentist, Private Practitioner, Dubai, UAE

•Corresponding author and reprints: Lida Toomarian DDS MSD, Department of Pediatric Dentistry, Dental school, Shahid Beheshti Medical University, Tehran, Iran. Tel: +98+212-990-2304, E-mail: ltoomarian@yahoo.com

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1, phagocytes from these patients cannot adhere to the vascular epithelium and thus cannot migrate out of blood vessels into areas of infection.[6] In other words, a defect in expression of CD18 leads to a defect in leukocyte adhesion, migration from blood vessels, chemotaxis, and phagocytosis.[3,4]

Clinical features of patients with LAD-I include recurrent necrotic infection of the skin and mucous membranes, particularly the mouth and gastrointestinal tract.[3,6] These patients also have frequent respiratory tract infections and occasionally otitis media.[4] Additionally, patients with LAD cannot form pus efficiently[6,8] and show delayed wound healing despite extreme neutrophilia.[7] The severity of clinical manifestations correlates with the degree of glycoprotein deficiency. Patients whose leukocytes do not express any level of CD11/CD18 have the worse prognosis, and 75% will die in infancy. An expression of 1% to 10% of normal amounts of CD11/CD18 results in a moderate phenotype, and more than 33% survive to 40 years of age or more. An expression of greater than 10% is mild and may not be diagnosed until the teen years or early adulthood.[9] Prognosis depends largely on the amount of expression of CD18.[3,8]

Periodontal manifestations in individuals who are homozygous for the defective gene are aggressive periodontitis at an early age which affects primary and/or permanent dentition. The disease begins during or immediately after eruption of the primary teeth. Extreme acute inflammation and proliferation of the gingival tissues with rapid bone destruction is noted. Although all primary teeth are affected, however, permanent dentition may not be. Histologically, almost no extravascular neutrophils are evident in the periodontal lesions.[4] Other research indicates focal epithelial hyperplasia[10] and areas of hypoplasia in the root cementum[11] as occurring in LAD patients.

LAD-II is also an autosomal recessive disorder secondary to a mutation in the FUCT1 gene.[12] The exact defect in the system is due to absence of the sialyl Lewis-x (Sle X) structure antigens or CD 15 on leukocytes. These antigens are important ligands for the selectin molecules on endothelial cells.[7] The ligands with which the selectins interact are glycoproteins that contain fucosylated sugars such as the blood group sialyl Lewis. A genetic defect in the conversion of mannose to fructose results in the failure of normal synthesis in these ligands.[6,8] Consequently, the leukocytes of such patients cannot roll on the endothelium which causes a marked decrease in chemotaxis, accompanied by pronounced neutrophilia.[6,7] Apart from the leukocyte defect, these patients suffer from severe growth and mental retardation and exhibit the rare Bombay blood group type.[7]

Periodontal manifestations are aggressive periodontitis at a young age[4] or chronic severe periodontitis.[7]

LAD is a rare disorder which affects nearly one out of every million individuals.[13] Moreover, the associated dental therapeutic challenges have seldom been suggested. It should be kept in mind that oral environment is a very important source of infection in these patients. The purpose of this manuscript is to describe a case of LAD-I and to discuss considerations of the treatment of associated generalized prepubertal periodontitis.

Case report

A five year-old Iranian male child was first seen in December 2005 at the Pediatric Dentistry Department, College of Dentistry of Shahid Beheshti Medical University. The chief complaint of the parents was gum bleeding and loosening of the teeth. The mother reported that the swelling and bleeding had worsened during the past six months. The medical history indicated that the child was diagnosed at the 26th day of birth with LAD-I due to recurrent infections and had been under medical care since then. He was under chronic antibiotic therapy for recurrent systemic infections facilitated by the immune deficiency (cotrimoxazole suspension 200mg/5mL, 1 tbsp per night). The dental history revealed that the child received a dental check up nine months previously with slight gingival bleeding and no treatment. He was the only child of a middle socioeconomic class family and the parents had a history of consanguity.

On admission to the Department of Pediatrics the child was in a good physical condition with a weight of 16 kg and height of 104 cm. A complete hematological work up indicated leukocytosis (529000/mm^4; neutrophil differential 70%, band cells 2%, lymphocytes 12%, and monocytes 4%). Red blood cell count was normal; however, both hemoglobin (77g/dL) and hematocrit were less than the lower limit of normal. Flow cytometry revealed low, but detectable expression of CD18 on neutrophils (5.65%), low lymphocytes (3.65%) and CD11a and CD11b expression (5.1% and 6.5%, respectively). Therefore the patient

was classified as moderate LAD-I.

Extraoral examination revealed pale appearance with bilateral lymphadenopathy. A thorough oral examination revealed gross plaque accumulation, generalized and severe gingival inflammation, recession, hyperplasia, and localized loss of periodontal attachment in some areas (Figure 1).

Primary central and lateral incisors in the mandible had grade I mobility that elicited pain during examination. Some discoloration was evident in the marginal areas of the lower right primary molars (Figures 2 and 3).

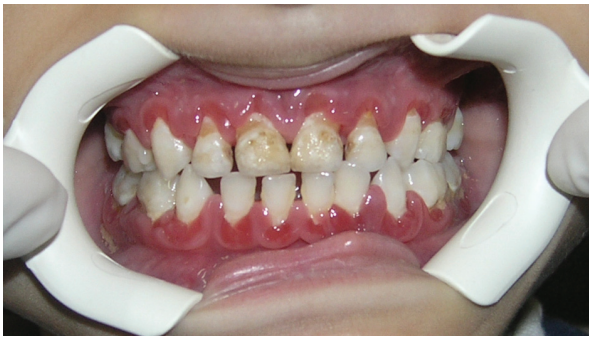

Figure 1. Frontal intraoral view

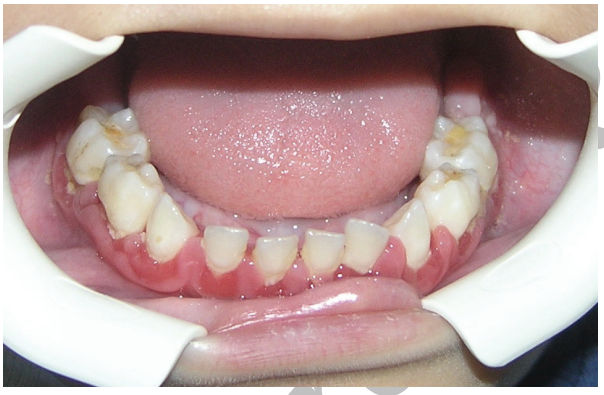

Figure 2. Mandibular view

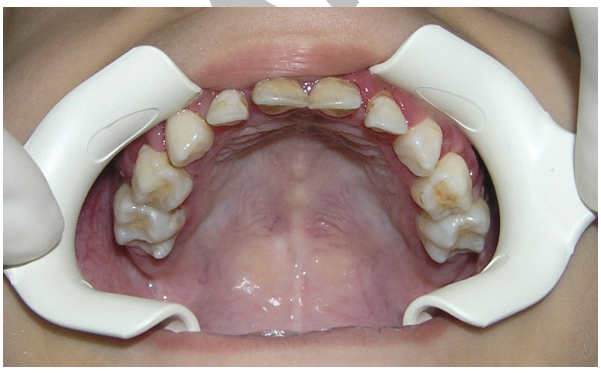

Figure 3. Maxillary view

A panoramic film revealed bone destruction in the posterior regions and also confirmed interproximal caries. The dental development was normal in primary and permanent dentition and no missing teeth were evident (Figure 4).

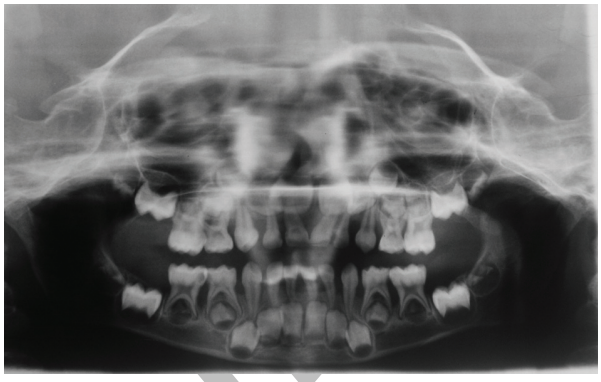

Figure 4. Radiographic view

After consultation with the Periodontics Department, the diagnosis was confirmed to be generalized prepubertal periodontitis. The treatment approach was based on taking a plaque index, professional dental prophylaxis, and both supra and subgingival scaling done periodically at each visit. In addition, the patient was given strict oral hygiene instructions and prescribed chlorhexidine mouthwash 0.12% daily (due to the child's ability to expectorate). Restoration of decayed primary molars was planned following control of the patient's periodontal disease, to some extent. The patient was scheduled to be seen at least once a month.

An immunologist was contacted to discuss the patient's medical history, precautions that needed to be taken for the first dental appointment, and the type of antibiotic therapy required to prevent the development of local or systemic infection. A preoperative dose of amoxicillin (50mg/kg) one hour before the procedure was recommended. It should be mentioned that different prophylaxis protocols have been stated in the literature for immunocompromised patients, such as a postoperative course of clindamycin for two weeks[1] or cefaclor or amoxicillin two hours prior to dental treatment.[3] A standard guideline applicable for all is yet to be proposed.

The child attended two treatment sessions, once a month after the initial examination. By the second visit it was obvious that the plaque index had improved and gingival bleeding and inflammation

had reduced to a great extent. Unfortunately he failed to return to the dental clinic. In fact, due to the chronic condition of illness adequate compliance may be difficult to achieve in these patients. Several attempts were made to contact the patient and it was determined that he had been hospitalized due to several episodes of pneumonitis in addition to colonic obstruction due to the use of cotrimoxazole and was thus unable to continue dental treatment. Five months later the child returned for a dental visit. At this time he was in poor condition with weight loss and lethargy. Oral assessment revealed loss of periodontal attachment, severe bone loss, and diffuse gingival inflammation on both the maxilla and mandible. Spontaneous gingival bleeding and pain were severe, and his oral hygiene was poor. As a result of the child's poor condition and lack of cooperativeness, the only treatment done was meticulous prophylaxis. It was emphasized to continue oral hygiene instructions.

Discussion

We describe a case of the moderate form of LAD-I in a five year-old boy with periodontitis as a manifestation of the systemic disease. Progressive periodontal disease in children with LAD-I may cause severe systemic infections and death; early diagnosis with appropriate intervention is crucial to the prognosis.[3]

The pathologic basis of LAD appears to be fully expressed in periodontal tissues. A possible mechanism may be related to the active process of tooth eruption whereby tissues that promote inflammation are involved.[14] Because of poor wound healing and defective neutrophil function, healthy gingiva are difficult to maintain. Therapeutic strategies in these patients should include prevention of local (dental) and systemic infections. However, despite optimal prophylaxis against systemic infections, oral disease remains a problem in patients with LAD-I and warrants specific measures. These include reinforcement of oral hygiene, prevention of local infections through the use of chlorhexidine, and monitoring of periodontal disease.[3] Clinicians, who confront children with aggressive periodontitis in the primary teeth, must decide between a conservative treatment approach avoiding extractions and a radical treatment approach that involves extractions. In general, aggressive periodontitis in the primary teeth may be successfully treated by a conservative approach that includes local (prophylaxis, scaling, curettage, and antiseptic rinses) and systemic therapy in patients with good compliance. According to the eruption of permanent teeth as a possible mechanism of aggravating periodontal disease, full mouth extractions may be proposed early enough to prevent periodontitis as been indicated in the literature.[1,7]

In the present case, analysis of variables indicated a conservative approach. Despite the significant amount of inflammation present, tooth mobility was not considerable. The gingival tissues responded well to the treatment approach and the child was able to cooperate. In addition, a preventive regimen that included regular oral hygiene, frequent professional dental prophylaxis and chlorhexidine rinses proved to be successful in such cases.[1] We decided to improve the oral hygiene status, eliminate local irritants and control the periodontal pathogens. The preventive measures were successful in the first dental visits; unfortunately the general condition of the patient deteriorated which caused lack of compliance; an issue that has been cited in the literature.[3]

In summary, the present case emphasizes the need for cooperation between medical and dental professionals, and the substantial significance of the prevention or early treatment of gingival and periodontal disease that are related to systemic conditions. However, each case must be considered individually based on the severity and extent of the gingival and periodontal disease, the systemic condition of the patient, behavior management considerations, and compliance.

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