

Case Report

Aggressive periodontitis in a young Pakistani female with laryngo-onycho-cutaneous syndrome

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Abstract: The periodontal status of patients with laryngo-onycho-cutaneous syndrome is unknown. This study describes a case of severe aggressive periodontitis in a 19-year-old American-Pakistani female with laryngo-onycho-cutaneous syndrome. The patient showed abundant dental plaque and calculus accumulations, suppuration and hemorrhage from virtually all gingivae and interdental papillae, and extensive radiographic alveolar bone loss and vertical mobility of several teeth. Subgingival plaque samples revealed a variety of major periodontal pathogens. The patient was scheduled for full-mouth tooth extraction. (*J Oral Sci* 55, 359-362, 2013)

Keywords: aggressive periodontitis; laryngo-onycho-cutaneous syndrome; bacterial pathogens.

Introduction

Laryngo-onycho-cutaneous (LOC) syndrome is a homozygous recessive condition characterized by proliferation of dermal and mucosal granulation tissue and progressive scarring of the conjunctiva and cornea (1). LOC syndrome has been associated with mutation in the gene encoding laminin alpha-3a on chromosome 18q11.2 (2). LOC syndrome was initially described as an

inherited disease that occurred exclusively in children of the Punjab province of Pakistan (2).

LOC syndrome usually starts within two-weeks after birth and the affected children present with hoarseness in voice, dystrophic changes in nails, chronic bleeding, crusted lesions of facial skin and corneal scarring leading to blindness (1,2). The ulcers do not respond to medications including antibiotics, anti-tuberculosis drugs, dapsone or steroids. Respiratory tract complications of LOC syndrome are associated with erosions and subsequent formation of granulation tissue causing airway obstruction that may lead to premature death (3). Orofacial manifestations of LOC syndrome include enamel hypoplasia, dental caries, gingival ulcerations, mucosa-covered nodules of the hard palate, and erosion of the lower lip and nares (1-3).

To our knowledge, there are no reports in the indexed literature of the periodontal status of patients with LOC syndrome. In the present study, we describe a severe case of aggressive periodontitis in a young American-Pakistani female patient affected by LOC syndrome.

Case Report

In 2008, a 19-year-old American-Pakistani female and her legal guardian reported to the Department of Pediatric Dentistry at Eastman Institute for Oral Health at the University of Rochester NY, USA. The patient was referred from the Department of Pediatric Hematology of the University of Rochester Medical Center. The patient's chief complaints, as reported by her guardian, were pain in teeth and difficulty with chewing due to tooth mobility. The ethical committee of the Eastman Institute for Oral

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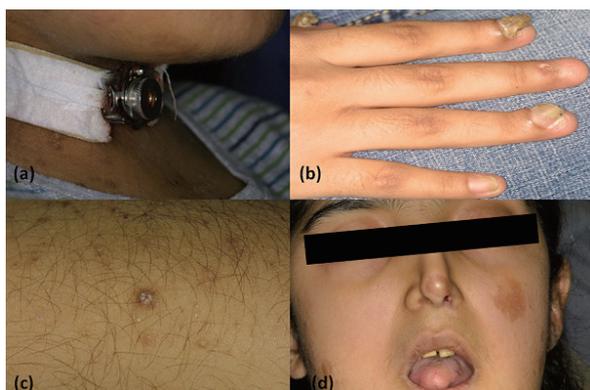


Fig. 1 Classical manifestations of laryngo-onycho-cutaneous syndrome: a) intact tracheostomy with regions of excoriation on adjacent skin; b) absence or thickening of nails; c-d) scarring and sclerosis of skin.

Health approved the study.

Medical history

The medical history, obtained from the Hematology Clinic at the University of Rochester Medical Center, revealed (a) severe iron deficiency and intravenous iron administration; (b) hemoglobin ranges from 4.5 to 7.1; and (c) mean corpuscular volume (MCV) of ~45 femtoliters (fl). No history was reported of severe skin infections. The patient was visually impaired. In 2000, a medical examination at the Boston Children's Hospital, Boston MA, USA suggested the tentative diagnosis of polydysplastic epidermolysis bullosa. In 2001, the patient underwent tracheostomy due to severe airway impingement during a bronchoscopy examination (Fig. 1a).

The family history had a twin brother and two younger siblings, who were currently healthy. Her 12-year-old sister had leukemia at 3-years of age. A paternal cousin has epidermolysis bullosa, which may be related to a family history of thalassemia trait.

Physical medical examination

The physical examination revealed a height of 155 cm, weight of 44 kg, body temperature of 37.3°C, heart rate of 130 beats per min, respiratory rate of 18 breaths per min, blood pressure of 108/69 mm Hg. The eyes presented corneal clouding and limited light reflex. The neck demonstrated intact tracheostomy with regions of excoriation on adjacent skin (Fig. 1a). Her extremities showed absence of nails in multiple fingers and toes while other nails were thickened and/or avulsing (Fig. 1b). The skin presented scarring and sclerosis (Figs. 1c and 1d), but no ulcerations or blistering. The patient was very quiet and smiled occasionally.



Fig. 2 Oro-dental manifestations of laryngo-onycho-cutaneous syndrome: a) limited mouth opening; b-c) swollen gingivae and interdental papillae with suppuration and extensive dental plaque and calculus accumulations; d) subgingival plaque sampling using sterile paper points.

Hematologic tests and metabolic profile

Hematologic tests (performed 7 months previously) demonstrated: (a) white blood cells [WBC] 7,100/ μ L; (b) normal differential and normal lymphocyte subsets; (c) IgG 2,860 mg/dL (hi); (d) hematocrit 24%; (e) mean corpuscular volume [MCV] 47 femtoliters (fl); (f) red blood cell distribution width (RDW) 22.6%; (g) reticulocyte count 1.6%; (h) platelet count 401,000/ μ L; (i) prothrombin time and partial thromboplastin times were normal (12-13 s and 60-70 s respectively); (j) serum iron 6 μ mol/L; (k) total iron binding capacity 364 μ g/dL; (l) transferrin sat% 2; (m) chemistry panel within normal limits.

The most recent hematological report showed following results: (a) WBC 6,000/ μ L; (b) red blood cells [RBC] 6 (high); (c) hemoglobin 7.9 g/dL (low); (d) hematocrit 9% (low); (e) MCV 48 fl (low); (f) mean corpuscular hemoglobin 13 picograms/cell (low); (g) mean corpuscular hemoglobin concentration 27% (low); (h) RDW 24% (high); (i) platelet count 378,000/mL (normal); (j) neutrophils 59.5% (normal); (k) lymphocytes 29% (normal); (l) monocytes 8.5% (normal); (m) eosinophils 2.2% (normal) and (n) basophils 0.8% (normal). The morphology of the red blood cells showed presence of anisocytosis, microcytic, hypochromic cells with polychromasia, fragmentation, tear-drop cells and ovalocytes. The reticulocyte count was high (2.1%).

The comprehensive metabolic profile examination presented (a) a relatively low creatinine (0.3 mg/dL); (b) low calcium (8.8 mg/dL); (c) low alanine aminotransferase (9 u/L); (d) normal bilirubin (0.2 mg/dL); (e) high globulin levels (5 g/dL); total protein (8.8 g/dL). The international normalized ratio (INR) was 1.2 (reference, 0.9-1.1) and the reticulocyte count was higher than normal.

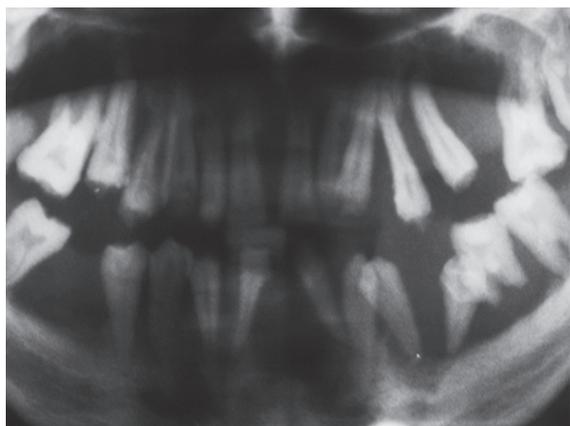


Fig. 3 Panoramic radiograph showing severe alveolar bone loss in several teeth.

All other parameters were within normal limits.

At the latest physical examination, the patient displayed classical signs of LOC syndrome including corneal scarring (blindness), dystrophic changes in the nails, crusted lesions of the skin of face, and excessive dermal granuloma particularly on the elbows. The patient was referred to the Eastman Institute for Oral Health for specialist consultation.

Periodontal examination

Upon visual examination, the patient exhibited a poor oral hygiene with abundant plaque and calculus accumulations (Figs. 2a-2d). The gingivae and interdental papillae were generally inflamed with suppuration. Mean full-mouth scores for plaque index (PI) and gingival index (GI) were 3 and 3, respectively. Several teeth exhibited Grade-III (vertical) mobility. Panoramic and periapical radiographs were obtained. Mesial and distal marginal bone loss was measured from the cemento-enamel junction (CEJ) to the crest of the apical bone using a vernier caliper. Overlapping teeth and teeth where the CEJ was unclear were excluded. Mesial and distal marginal bone loss was at least 10 mm in most teeth in both arches (Fig. 3).

Microbiological analysis

The microbiological analysis was carried out according to established procedures at the Oral Microbiology Testing Laboratory of the University of Southern California (<https://dentists.usc.edu/dental-practitioners/oral-microbiology>). Plaque samples were collected from three subgingival sites (teeth #11, 34, and 43) using sterile paper-points (Fig. 2d). Four paper points were inserted to the depth of each of the three periodontal pockets studied and kept in place for 10 s. Two paper points were placed

Table 1 Microbiota of periodontitis lesions associated with the laryngo-onycho-cutaneous syndrome

Bacteria	Tooth #11	Tooth #34	Tooth #43
<i>Porphyromonas gingivalis</i>	2.3*	1.5	—
<i>Prevotella intermedia</i>	—	—	3.8
<i>Tannerella forsythia</i>	—	1.5	3.1
<i>Fusobacterium</i> species	3.8	2.3	3.1
<i>Peptostreptococcus micros</i>	3.1	3.1	3.1
<i>Campylobacter</i> species	3.8	2.3	—
Gram-negative enteric rods	4.6	6.9	6.2
Total viable counts/mL	39×10^6	325×10^6	33×10^6

*Percent of total cultivable microbiota.

in a glass vial with transport medium (for culture), and two paper points in an empty plastic vial (for DNA probe analysis).

The percentage of total cultivable microbiota from teeth #11, 34, and 43 are shown in Table 1.

Treatment strategy

Preoperative medications (antibiotics [ciprofloxacin and metronidazole, 500 mg of each, twice daily for 10 days and non-steroidal anti-inflammatory drugs [ibuprofen 400 mg once daily]) were prescribed. Periodontal scaling was performed and a full-mouth tooth extraction (under general anesthesia) was recommended. Oral hygiene instructions for the patient were given to the parents and the patient was scheduled for follow-up treatment in 4 weeks. However, the parents elected not to pursue further dental treatment for the patient.

Discussion

The present patient case clearly demonstrates that oral health, and particularly the periodontal health status, can be severely jeopardized in young individuals with LOC syndrome. There is little doubt that the advanced periodontitis associated with LOC syndrome results from a combination of genetically determined host defense-deficiencies and periodontopathic bacteria. That hypothesis places emphasis on preventive measures against dental plaque formation and colonization of pathogenic bacteria. As LOC syndrome can be diagnosed prior to tooth eruption, the caregiver can start the preventive periodontal therapy early in a child's life.

In the present case-report, classical bacteria associated with aggressive periodontitis (*Prevotella intermedia* and *Porphyromonas gingivalis*) were isolated from sub-gingival plaque samples. Amongst these, prote-

ases produced by *P. gingivalis* have been reported to degrade the human alpha- and beta- defensins (hBD-1 and hBD-2 respectively) that exhibit antimicrobial and anti-inflammatory properties (4-6). *P. gingivalis* trypsin-like proteinase exhibit the potential to cleave an intact laminin-332 γ 2-chain into smaller fragments and eventually promote the formation of periodontal pockets (4,7).

A direct relationship between low hemoglobin level and periodontitis has been proposed (8,9). Persistent anemia in the patient presented in our case-report seems to have further compromised immunity of the patient towards infection and facilitated the growth of pathogenic microbes including those in the periodontal pockets. This suggests that the pathogenesis of aggressive periodontitis as seen in the present case comprises of a network of events including laminin-332 γ 2 chain mutation, fragmentation of laminin-332 by periodontopathic bacteria, destruction of hBD-1 and hBD-2 and persistent anemia. The interplay of these conjoint factors may be held responsible for aggressive periodontitis in patients with LOC syndrome. Nevertheless, the role of poor oral hygiene maintenance in aggravating periodontal inflammation cannot be disregarded.

It is suggested that early diagnosis and comprehensive periodontal treatment in combination with treatment for LOC syndrome may help exert a positive influence on the overall health of patients with LOC disease.

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