Case Report

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Dentistry Section

Periodontal Management of Leukocyte Adhesion Deficiency Type-I with Photodynamic Therapy-A Case Report

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ABSTRACT

Leukocyte Adhesion Deficiency type I (LAD-I) is a rare autosomal recessive disorder affecting the immune system which is characterised by defects in white blood cell integrin receptors leading to impaired adhesion and chemotaxis with increased susceptibility to recurrent infections, delayed wound healing and periodontitis. A case of aggressive form of generalised periodontitis in a 19-year-old girl with LAD-I is presented in this case report. The medical diagnosis was made on the basis of characteristic clinical and laboratory findings suggestive of LAD, particularly the total absence of Cluster of Differentiation (CD)18, CD11a, CD11b and CD11c which were determined by flow cytometry. After non surgical periodontal therapy, photodynamic therapy with Low Level Laser Therapy (LLT) was performed. After three months, reduced inflammatory signs and improved periodontal health was observed. This report highlights the importance of the differential diagnosis of severe immunodeficiency disorders. It also emphasises the joint role of medical and dental specialists to control oral infections and thereby preventing tooth loss.

Keywords: Aggressive periodontitis, Diode laser, Gingival inflammation, Leucocytosis

CASE REPORT

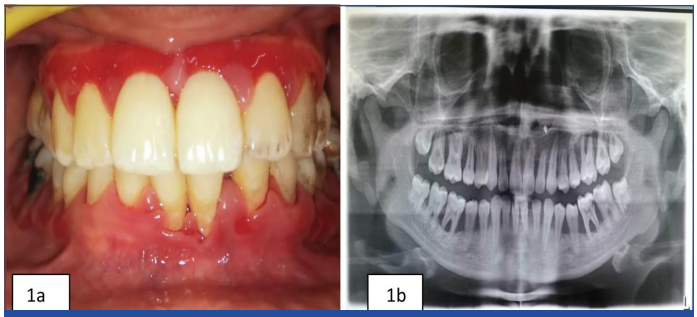
A 19-year-old female patient reported to the Department of Periodontology in a dental institution with the chief complaint of swollen gums with bleeding while brushing and mobility of her teeth since two years. Past medical history revealed that the patient had a history of recurrent infections, recurrent fever, cytopenia, anaemia, leucocytosis, generalised weakness, easy fatiguability, abdominal discomfort for six years. Patient was under medication for vitamin D and folic acid deficiency.

On observing the family history, her parents had a fifth degree consanguineous marriage. General physical examination revealed that the patient was thin, poorly nourished and cooperative. The lymph nodes in the submandibular region on either side were palpable, tender, firm and movable. Intraoral examination showed the presence of generalised diffuse inflammatory associated gingival enlargement.

Colour of the gingiva appeared bright red with rounded marginal gingiva and bulbous interdental papilla. On palpation, the consistency of gingiva was soft and oedematous and spontaneous bleeding on probing was observed. Oral ulcers were present in buccal mucosa with irregular margins. Full mouth plaque index score was 3.1 (Silness J and Loe H, 1964), gingival index scores was 2.7 (Loe H and Silness J, 1963) [1,2].

Generalised deep periodontal pockets with average probing pocket depth score was 6.7 mm and clinical attachment level was 7.4 mm was present [Table/Fig-1a]. Generalised mobility of teeth with (grade-I and grade II) was observed. Orthopantomogram (OPG) showed generalised moderate to severe bone loss with crestal bone height located at the apical one-third of tooth which is horizontal in nature was observed [Table/Fig-1b]. On hard tissue examination, mandibular molars and maxillary molars were carious due to lack of proper oral hygiene. Three molar teeth namely maxillary left first molar, mandibular left first molar and mandibular right first molar (irt 26,36,46) with furcation involvement presented with grade III mobility were planned for extraction due to poor prognosis.

Complete blood picture investigations revealed neutrophilic leucocytosis (white blood cell count-17,100 cells/cumm) with mild hypochromic normocytic anaemia, mild prolonged bleeding time, clotting time, Prothrombin Time (PT) and with normal level of coagulation factors [Table/Fig-2].



[Table/Fig-1]: (a) Intraoral view showing sites of intense gingival redness in maxillary and mandibular anterior region; (b) Orthopantamogram (OPG) view showing generalised moderate to severe bone loss with crestal bone height located at the apical one third of tooth which is horizontal in nature.

Blood sample	Observed value	Normal range
RBC count*	3.58 million/cu mm;	3.5-4.5 million/cu mm
Haemoglobin %‡	9.6 gm/dL	12-15 gm/dL
Total WBC count‡	17,100 cells/cu mm	4000-11000 cells/cu mm
Neutrophils‡	77%	40-75%
Lymphocytes‡	18%	20-45%
Monocytes‡	3%	2-10%
Eosinophils‡	2%	0-7%
Platelets‡	1,77,000/cu. mm	1,50000-400000/cu mm
Mean Corpuscular Volume (MCV)*	86.9 fL	80-96 fL
Mean Corpuscular Haemoglobin (MCH)*	28.9 pg	27-31 pg
Mean Corpuscular Haemoglobin Concentration (MCHC)*	33.2 g/dL	32-37 gm/dL
Erythrocyte Sedimentation Rate* (ESR)	105 mm;	Below 10 mm
Packed Cell Volume* (PCV)	31.1 vol%;	36-54 vol%
Serum folic acid levels*	12.2 ng/mL	3.1-20 ng/mL
Serum ferritin levels*	26.7 ng/mL	12-90 ng/mL

Serum vitamin D-levels*	16.38 ng/mL	30-80 ng/mL
Total iron binding capacity TIBC*	324	135-392
Serum vitamin B-12*	1250 pg/mL	211-940 pg/mL
Activated partial thromboplastin time‡	36.8 sec	25.2-38 sec
Random blood sugar level*	82 mg/dL	80-140 mg/dL
Bleeding time*	3 min	2-6 min
Clotting time*	4 min 21 sec	8-15 min
Prothrombin time‡	12.6 sec	8-11.2 sec
Thrombin time‡	13.7 sec	12-16 sec
Factor VII C‡	40%	50-150%
Factor VIII C‡	105.8%	50-150%
Factor IX C‡	88.1%	50-150%
Factor XI C‡	67.2%	50-150%
Fibrinogen‡	343 mg/dL	150-450 mg/dL
Von willebrand antigen‡	136.2	61.3-157.8 µ/dL

[Table/Fig-2]: Haematological investigations.
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†Ampath Central Reference Laboratory Serlingampally Hyderabad
‡Christian Medical College Vellore

The patient was given a provisional diagnosis of stage-III, grade C periodontitis associated with a genetic risk factor based on the clinical and radiological data. Primary immunodeficiency was assessed using peripheral blood examination by flow cytometry. Investigations revealed an abnormal increase in IgG Immunoglobulin levels along with increase in absolute lymphocyte count, absolute CD3 counts and absolute CD3+, CD4+ counts. A deficiency of CD 18, CD 11a, CD 11b was determined suggesting the condition as LAD type-I [Table/Fig-3].

Immunological tests	Observed value	Reference value
Immunoglobulin M	348.3 mg/dL	40-230 mg/dL
Immunoglobulin G	3599.6 mg/dL	700-1600 mg/dL
Immunoglobulin E	74.6 mg/dL	<100 mg/dL
Immunoglobulin A	380mg/dL	70-400 cells/µL
Absolute lymphocyte count	4.9×10^3/µL	1,000-4,800/µL
Absolute CD3 count (T cells)	4277 cells/µL	527-2846 cells/µL
CD 3%	87.24%	49-81%
Absolute CD19+ count (B cells)	361 cells/µL	78-899 cells/µL
CD 19+%	7.36%	7-23%
Absolute CD56+ count (NK cells)	219 cells/µL	67-1134 cells/µL
CD56+%	4.46%	6-29%
Absolute CD3+, CD4+ counts	1970 cells/µL	332-1642 cells/µL
CD4%	40.19%	28-51%
CD4/CD8 ratio	0.94%	0.7-3.5%
CD11a	Deficient	
CD11b	Deficient	
CD18	Deficient	

[Table/Fig-3]: Immunological investigations.†
†Ampath Central Reference Laboratory Serlingampally Hyderabad

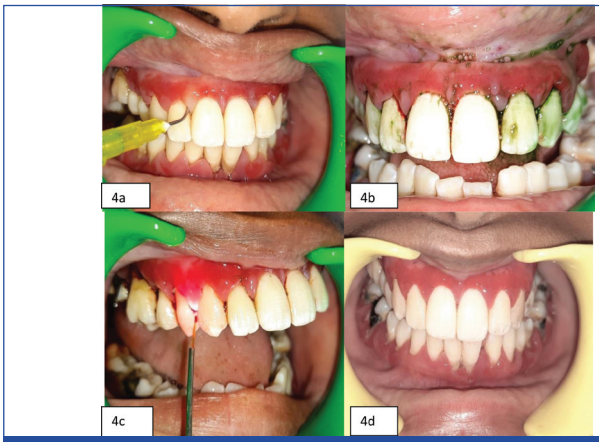
A final diagnosis of stage-III, grade C periodontitis associated with LAD type-I was recommended for this case [3]. Due to the presence of generalised severe gingival inflammation and deep periodontal pockets, subgingival scaling and root planning followed by laser assisted pocket therapy was planned. Amoxicillin 500 mg thrice daily was prescribed for five days.

Initial phase-I therapy including scaling and root planning was performed using hand and ultrasonic instruments twice at 14 days interval. Postoperative oral hygiene instructions were given including brushing techniques and 0.2% chlorhexidine mouthwash were prescribed. After four weeks, patient was recalled for re-evaluation of phase-I therapy. Gingival inflammation was seen to be persistent after one month post-therapy, hence photodynamic therapy was planned.

In a three-visit plan the entire procedure was performed and photodynamic therapy was performed twice. Photodynamic therapy with LLT using a diode laser at 810 nm wavelength and 0.8W power output in continuous mode was planned as it has advantages of antibacterial and anti-inflammatory effect [Table/Fig-4].

Intrapocket delivery of 0.5-1 mL of Indocyanin Green (ICG) was done using a blunt needle [Table/Fig-4a]. After one minute the pockets were thoroughly irrigated to eliminate the residual photosensitiser from the pocket with saline solution [Table/Fig-4b]. After irrigation, a probe tip was positioned at the depth of the pocket and placed circumferentially around the tooth for one minute using a diode laser with an 810 nm wavelength and 0.8W power output in continuous mode [Table/Fig-4c].

At third month recall visit clinical parameters observed showed reduced inflammatory signs and improved periodontal health with reduced bleeding on probing [Table/Fig-4d].



[Table/Fig-4]: (a) Intrapocket delivery of 0.5-1 mL of Indocyanin green was done using a blunt needle; b) After a period of 60 sec pocket was thoroughly rinsed using saline solution to remove excess photosensitiser from the pocket; c) Diode laser with 810 nm wavelength and 0.8W power output in continuous mode equipped with probe tip was placed at depth of the pocket and moved circumferentially around the tooth for one min; d) Intraoral postoperative view after three months.

Plaque index, gingival index scores, mean probing pocket depth and mean clinical attachment level scores showed improvement postoperatively after three months [Table/Fig-5].

Parameter	Before	Three months postop
Plaque index [1]	3.1	1.7
Gingival index [2]	2.7	1.9
Probing pocket depth	6.7 mm	4.8 mm
Clinical attachment level	7.4 mm	5.6 mm

[Table/Fig-5]: Clinical parameters three months post photodynamic therapy.

The patient is currently under regular recall for dental and medical treatment and further regenerative procedures are being planned for patient.

DISCUSSION

Periodontitis is a host driven bacterial condition where genetic, environmental and other systemic factors play a critical role in disease occurrence as well as in disease progression [4]. Genetic disorders are related to the development of severe form of periodontitis associated with single gene diseases or syndromes. There are several reported cases of aggressive periodontitis in prepubertal children associated with inheritance pattern in those syndromes [5,6]. The term LAD was coined by Anderson DC and Springer TA, is a rare group of disorders of leukocyte function transmitted by an autosomal recessive pattern of inheritance effecting one out of 10 million newborns [7]. Failure of leukocyte adhesion to the vessel

wall endothelium and subsequent migration to the extravascular space is its distinguishing traits [8].

Four distinct forms of leukocyte adhesion deficiencies that have so far been discovered and are referred to as LAD I, LAD II, LAD III, and LAD IV, respectively, based on the sequence in which they were discovered [9]. The Lymphocyte Function-Associated antigen 1 (LFA-1) is composed of two integrins, an αL-integrin and a β2-integrin, each of which has three subunits: a short intracellular domain, a single α-helical transmembrane domain and a large N-terminal extracellular domain. Mutations in the ITGB2 gene, located on chromosome 21q22.3 and encodes for CD18, result in Leukocyte Adhesion Defect-I (LAD I) [10].

Leukocyte β2-integrin is a heterodimer comprising of CD11 subunit and CD18 subunits essential for extravasation of the neutrophils to peripheral tissues. Springer TA et al., hypothesised that the primary defect was in the β2 subunit, which was essential for endothelial cell adhesion [11]. The patient in this case had a history of leukocytosis and recurrent fever, which is consistent with LAD type-I. Flow cytometry revealed deficiency of leucocyte integrin antigens CD11a, CD11b, CD18 confirming the diagnosis and categorising the case as LAD-I. Recurrent skin and mucous membrane infections were the major manifestations, according to a clinical profile of seven patients of LAD type I published by Madkaikar M et al., during a period of three years [12].

In another similar investigation, 15 cases of LAD type-I were diagnosed over a span of 14 years in Iran. The patients' ages ranged from 10 months to 14 years; (10 of them were male and five of them were female) and 93% of the parents were married consanguineously [13]. A recent case report with significant LAD type-I was also reported in a 9-year-old Iranian child with extensive alveolar bone loss and aggressive periodontitis was reported [14].

Dababneh R et al., reported a 10-year-old Jordanian girl with history of recurrent skin infections involving the hands and feet, urinary tract infections, otitis media, oral ulcerations, oral candidiasis and periorbital cellulitis. They reported no significant improvement in gingival inflammation and mobility after Scaling and Root Planing (SRP) performed at multiple recall visits [15]. Roberts MW and Atkinson JC, described that traditional methods of SRP to control periodontitis and intraoral infections associated with the primary and permanent dentitions in a child with LAD-I for 5-years were largely unsuccessful [16].

In the present study, SRP was performed along with antimicrobial mouthwash of 0.2% chlorhexidine which was prescribed to reduce plaque and calculus. Although, plaque scores were reduced significantly, gingival inflammation was seen to be persistent after one month post-therapy. As patient was not medically fit to undergo surgical periodontal therapy, LLT assisted photodynamic therapy with ICG was planned. In a two-visit plan procedure was performed and showed decreased gingival inflammation, probing pocket depth and gain in clinical attachment level.

The patient's periodontal therapy, which involved repeated visits to motivate and educate the patient about maintaining proper oral hygiene, was somewhat successful.

CONCLUSION(S)

Various syndromes are associated with aggressive periodontitis including Papillon-Lefevre syndrome, LAD type I and type II, Haim-Munk syndrome, Ehlers-Danlos syndrome, cyclic neutropenia, cyclic familial neutropenia, Chediak-Higashi syndrome. The present report describes a case of severe periodontal destruction involving mobility or loss of teeth. Periodontal therapy performed in aggressive periodontitis has been shown to be successful in the control of gingival inflammation and disease progression. This case demonstrates that the aggressive forms of periodontitis condition associated with unusual immunological condition can be managed with SRP followed by photo biomodulation using LLT application in reducing gingival inflammation and enhanced wound healing after three months of the procedure. Regular recall visits with oral hygiene maintenance are necessary for good periodontal health in cases with aggressive periodontitis.

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