## Cíntia de Souza Alferes Araújo <sup>1</sup>\*© Carolina Eurich Mazur <sup>2</sup> Vitória Maria de-Melo Nardino <sup>1</sup> Hanagleicy Souza <sup>1</sup> Roberta Targa Stramandinoli-Zanicotti <sup>2</sup>

Mirella Lindoso Gomes

Edimar Rafael Oliveira<sup>2</sup>

José Miguel Amenábar 2

Campos 3

# Crohn's disease: Low-Level Laser Therapy (LLLT) as an adjuvant treatment of oral lesions

## **Abstract:**

Classified as a chronic inflammatory bowel disease, Crohns disease (CD) has a multifactorial etiology. Individual with CD can present signs/symptoms such as abdominal pain, fever, diarrhea with a serious risk of hemorrhagic progression, weight loss, anemia and malnutrition. Extra-intestinal complications of CD such as at mouth are probable in some cases. In the mouth, it may presents ulcers, verrucous lesions, swelling of the lips, recurrent aphthous stomatitis, and predisposition to fungal, bacterial and viral infections. In view of the patient's clinical condition, oral manifestations variable, painful symptomatology and challenge in the choice of oral lesions treatment, this study presents a case of Chron's Disease's oral manifestations and its management with Low-Level Laser Therapy (LLLT).

Keywords: Crohn Disease, Mouth, Laser Therapy

#### Correspondence to:

Cintia de Souza Alferes Araújo. E-mail: cintia@prof.unipar.br

Article received on December 3, 2018. Article accepted on December 7, 2018.

DOI: 10.5935/2525-5711.20180026



<sup>&</sup>lt;sup>1</sup> Universidade Paranaense, Odontologia -Umuarama - Paraná - Brasil.

<sup>&</sup>lt;sup>2</sup> Universidade Federal do Paraná - UFPR, Departamento de Estomatologia - Curitiba -Paraná - Brasil.

<sup>&</sup>lt;sup>3</sup> Universidade do Sagrado Coração - USC, Curso de Odontologia - Bauru - São Paulo -

### INTRODUCTION

Inflammatory bowel diseases (IBD) are a group of chronic inflammatory diseases that involve the gastrointestinal tract. This group is composed of Crohn's Disease (CD) and ulcerative colitis. Diagnosis and management of these diseases can be a challenge for health professionals, since they present similar clinical features as abdominal pain, fever, anemia, diarrhea, bleeding, weight loss and malnutrition<sup>1-3</sup>.

CD is identified by chronic inflammation of the intestinal tract that can affect small and/or large intestine, the initial part of the colon and distal ileum. Its severity and extension are variables and generates a segmental inflammatory process. Etiology is multifactorial, its occurrence varies according to environmental, genetic and external factors such as food, smoking, oral contraceptives, intestinal microbiota, which may lead to the appearance of a possible infectious enteric agent that stimulates an inflammatory process of the wall's gut<sup>3,4</sup>.

Extra-intestinal manifestations may occur prior to or concurrent with gastrointestinal symptoms, including oral lesions. Clinical findings are ulcers, verrucous lesions, mucositis and gingivitis, swelling lips, infections such as candidiasis and herpes lesions, usually located on the palate, gingival tissue, lips, tongue and the lingual and buccal mucosa<sup>5-8</sup>

Currently, there are no therapeutic resources considered the gold standard for CD's treatment, since its follow a chronic recurrence course, with drug treatment (topical or systemic) and does not always represent positive results, since the oral lesions present a self-limiting course, following the course of the disease<sup>6,9,10</sup>

Adjuvants or complementary therapies could be used in this case, such as Low-Level Laser Therapy (LLLT), since can help both on the repair activity and pain relief 11,12

Therefore, the purpose of this paper is to present the case of a patient with CD's oral manifestations e and laser therapy's use as an adjunctive treatment for lesions regression and consequent decrease of the symptoms.

### **CASE REPORT**

A 44-year-old white woman was attended at Dental Clinic of a University of the Paraná state (Brazil) with oral lesions, which were related to a history of intestinal disease. She presented a diagnosis of ulcerative colitis, which was initially treated with mesalazine (Mesacol®), without regression of the condition for 10 months. The therapeutic protocol was changed for azathioprine and purinethol, with intense symptomatology yet. After 18 months of diagnosis, with disease's persistence and in immunosuppression, she reported the onset of oral lesions, which contributed to the quality of life's alteration, also presented anorexia, inappetence and hospitalization for seven days, resulting in a loss of thirteen pounds in that period.

In the mouth examination, there were multiple symptomatic ulcerations and papillomatous lesions distributed on the palate, tongue dorsum, buccal and labial mucosa (Figures 1 and 2).

To relieve symptomatology and lesions repair, the patient underwent three weekly sessions of LLLT with InGaAIP laser (Therapy XT, DMC®) 660nm length, 2J / cm² density and 100mW, in all oral mucosa, 20 seconds per point, performed on alternate days, with improvement of symptoms and signs (Figures 3 to 5), that allowed the ingestion of food and improve the quality of life.

After 2 months, the patient returned with a persistence of intestinal changes and oral lesions recurrence. There were multiple symptomatic ulcerations and papillomatous lesions distributed on the palate, gum and buccal mucosa (Figure 6). An incisional biopsy of buccal mucosa was performed. Histopathological examination suggested Herpes Virus Type 1 (HSV-1) infection. The patient was medicated with oral Acyclovir 200mg 8/8 hours during 15 days. The same protocol of LLLT was performed and the oral lesions regressed. In use of azathioprine, a colonoscopy was requested, lead to the diagnosis of CD. After the final diagnosis, the medication was changed to a monoclonal antibody Adalimumab



Figure 1. Initial oral lesions: Ulcers on the palate.



**Figure 2.** Initial oral lesions: papulomatous and verrucous lesions in the buccal mucosa.



Figure 3. Ulcers on palate after first LLLT's session.

(Humira®). 21 months after the treatment, the patient was asymptomatic in relation to oral and intestinal lesions, in followed up with the dental team.



Figure 4. Lesions on buccal mucosa after first LLLT'S session.



Figure 5. Ulcers on palate after third LLLT's session.



**Figure 6.** Oral lesions recurrence: Diffuse papulomatous lesions on the palate.

## **DISCUSSION**

IBD's incidence has been expressive on a global scale, requiring attention in diagnosis by health

professionals, due not only to local lesions but also, in other organs such as the mouth, for example<sup>2</sup>. Etiology of IBD is complex and partially understood. However, it is believed that result from an inappropriate Activation the of immune system of gastrointestinal tract. Clinical findings similarity, can generate controversy in diagnosis since for definitive diagnosis it is important to consider a correlation of clinical, radiographic, endoscopic and histopathological findings<sup>1,3</sup>. As in the Reported case, which was initially diagnosed as ulcerative colitis and at a later time, the diagnosis of CD was established.

Often, extra-intestinal manifestations detection could prevent the onset of IBD. Gionchetti et al. <sup>13</sup> demonstrate that about 25% of individuals have a combination of more than five different types of extra intestinal manifestations during the natural history of the disease.

CD treatment usually includes sulfa drugs, diet therapy and immunosuppressive agents such as systemic steroids, azathioprine (AZA), methotrexate, or anti-TNF alpha antibodies. These treatments aim at the clinical and laboratory control of the inflammatory disease, but may not present positive results<sup>1,3,14</sup>, as in the case of this study, in which several drugs were prescribed without satisfactory results.

At the case reported, the difficult of systemic disease treatment may also have contributed to oral lesions recurrence. CD management in the mouth is complex, since in addition to the pain caused by injuries, the difficulty of feeding and communication aggravate the individual's quality of life.

A study by Tomazoni & Benvegnú $^{15}$  demonstrate that 61.7% of CD patients present symptoms of anxiety and / or depression, concluding that this disease has an impact on quality of life.

Oral lesions are significant and may precede gastrointestinal lesions in up to 30% of CD cases. <sup>16</sup> Variety of oral lesions have been reported in CD individuals, including diffuse and nodular swelling of oral tissues, deep granulomatous ulcers, among others <sup>16-18</sup>

Treatment depends symptoms on severity, type and number of painful ulcerated lesions. Can be used topical and systemic corticosteroid, topical anesthetic, mouthwashes and non-steroidal anti-inflammatory creams<sup>19</sup>. Adjuvants therapies such as LLLT may be indicated for pain relief and to accelerate wound healing. LLLT is performed through a laser that emits a monochromatic, intense, collimated and coherent light source, which can be divided into two categories: low power and high power. LLLT's application has been encouraging health professionals, since it presents beneficial results both in the medical and dentistry area. It does not affect the tissue thermally, however the speed of injured tissue repair is increased. When applied to the wounds, LLLT can promote physiological effects such as neoangiogenesis, antiinflammatory resolution, collagen synthesis and deposition, epithelial and fibroblast proliferation, revascularization and wound contraction 12,20.

As a consequence of immunosuppression, patients with IBD are at increased risk for opportunistic infections. After oral lesions recurrence, HSV-1 infection was detected in this case. Studies have shown that azathioprine's use was related to an increased risk of HSV infection. <sup>21,22</sup>.

Although topical immunosuppression is used for the treatment of CD oral lesions, in this case, due to the suspicion of viral infection, LLLT presented as an alternative, since unlike topical corticotherapy, LLLT does not promote local immunosuppression and contribute for tissue repair and symptom relief<sup>12</sup>.

### **CONCLUSION**

Concerning CD oral lesions features, LLLT can be used as adjuvant therapy for symptom relief and tissue repair.

#### **REFERENCES**

- Gajendran M, Loganathan P, Catinella AP, Hashash JG. A comprehensive review and update on Crohn's disease. Dis Mon. 2018;64:20-57. DOI: 10.1016/j.disamonth.2017.07.001
- 2. Feuerstein JD, Cheifetz AS. Crohn Disease: Epidemiology, Diagnosis, and Management. Mayo Clin Proc. 2017;92:1088-103. DOI: 10.1016/j.mayocp.2017.04.010

- Torres J, Mehandru S, Colombel JF, Peyrin-Biroulet L. Crohn's disease. Lancet. 2017;389:1741-55. DOI: 10.1016/S0140-6736(16)31711-1
- 4. Lucas López R, Grande Burgos MJ, Gálvez A, Pérez Pulido R. The human gastrointestinal tract and oral microbiota in inflammatory bowel disease: a state of the science review. APMIS. 2017;125:3-10. DOI: 10.1111/apm.12609
- Głowacka B, Radwan-Oczko M. Dental perspective on Crohn's disease: literature review. Wiad Lek. 70:860-4.
- Aguirre A, Nugent CA. Oral Manifestation of Crohn's Disease.
  N Engl J Med. 2015;373:1250. DOI: 10.1056/NEJMicm1413715
- O'Neill I, Scully C. Biologics in oral medicine: oral Crohn's disease and orofacial granulomatosis. Oral Dis. 2012;18:633-8. DOI: 10.1111/j.1601-0825.2012.01918.x
- Nishikawa J, Hosokawa A, Sugiyama T. Palatal ulcer as an initial manifestation of Crohn's Disease. Clin Gastroenterol Hepatol. 2014;12:e115-6. DOI: 10.1016/j.cgh.2014.07.026
- Szczeklik K, Pytko-Polończyk J, Cibor D, Owczarek D, Mach T. Oral mucosa lesions in patients with active Crohn's disease - a prospective study. Przegl Lek. 2017;74:57-61.
- Mortada I, Leone A, Gerges Geagea A, Mortada R, Matar C, Rizzo M, et al. Oral manifestations of inflammatory bowel disease. J Biol Regul Homeost Agents. 2017;31:817-21.
- 11. Giller JP, Vinciguerra M, Heller A, Kunken FR, Kahn E. Treatment of gingival Crohn's disease with laser therapy. N Y State Dent J. 1997;63:32-5.
- 12. Andrade Fdo S, Clark RM, Ferreira ML. Effects of low-level laser therapy on wound healing. Rev Col Bras Cir. 2014;41:129-33. DOI: 10.1590/S0100-69912014000200010
- Gionchetti P, Calabrese C, Rizzello F. Inflammatory Bowel Diseases and Spondyloarthropathies. J Rheumatol Suppl. 2015;93:21-3. DOI: 10.3899/jrheum.150628
- 14. Mentzer A, Goel R, Elliott T, Campbell H, Hullah E, Patel P, et al. Azathioprine is effective for oral involvement in Crohn's disease but not for orofacial granulomatosis alone. J Oral Pathol Med. 2016;45:312-8. DOI: 10.1111/jop.12379

- 15. Tomazoni EI, Benvegnú DM. Symptoms of anxiety and depression, and quality of life of patients with Crohn's disease. Arq Gastroenterol. 2018;55:148-53. DOI: 10.1590/S0004-2803.201800000-26
- 16. Eckel A, Lee D, Deutsch G, Maxin A, Oda D. Oral manifestations as the first presenting sign of Crohn's disease in a pediatric patient. J Clin Exp Dent. 2017;9:e934-e938. DOI: 10.4317/jced.53914
- Laranjeira N, Fonseca J, Meira T, Freitas J, Valido S, Leitão J. Oral mucosa lesions and oral symptoms in inflammatory bowel disease patients. Arq Gastroenterol. 2015;52:105-10. DOI: 10.1590/S0004-28032015000200006
- Laube R, Liu K, Schifter M, Yang JL, Suen MK, Leong RW. Oral and upper gastrointestinal Crohn's disease. J Gastroenterol Hepatol. 2018;33:355-64. DOI: 10.1111/jgh.13866
- 19. Muhvić-Urek M, Tomac-Stojmenović M, Mijandrušić-Sinčić B. Oral pathology in inflammatory bowel disease. World J Gastroenterol. 2016;22:5655-67. DOI: 10.3748/wjg.v22.i25.5655
- 20. Zecha JA, Raber-Durlacher JE, Nair RG, Epstein JB, Sonis ST, Elad S, et al. Low level laser therapy/photobiomodulation in the management of side effects of chemoradiation therapy in head and neck cancer: part 1: mechanisms of action, dosimetric, and safety considerations. Support Care Cancer. 2016;24:2781-92. DOI: 10.1007/s00520-016-3152-z
- 21. Seksik P, Cosnes J, Sokol H, Nion-Larmurier I, Gendre JP, Beaugerie L. Incidence of benign upper respiratory tract infections, HSV and HPV cutaneous infections in inflammatory bowel disease patients treated with azathioprine. Aliment Pharmacol Ther. 2009;29:1106-13. DOI: 10.1111/j.1365-2036.2009.03973.x
- 22. Haag LM, Hofmann J, Kredel LI, Holzem C, Kühl AA, Taube ET, et al. Herpes Simplex Virus Sepsis in a Young Woman with Crohn's Disease. J Crohns Colitis. 2015;9:1169-73. DOI: 10.1093/ecco-jcc/jjv149