

Oral Manifestations of Leukemia at the Time of Diagnosis

DOI doi: <https://doi.org/10.32635/2176-9745.RBC.2018v64n2.82>

Manifestações Oraís da Leucemia no Momento do Diagnóstico

Manifestaciones Orales de Leucemia en el Momento del Diagnóstico

Michele Formighieri Antonini¹; Leticia Tainá de Oliveira Lemes²; Carolina Barreto Mozzini³

Abstract

Introduction: Leukemia is a pathology that consistent with modifications derived from hematopoietic stem cells, which can generate signs and symptoms in the patient's body. **Objective:** To verify the oral manifestations of leukemia at the time of diagnosis. **Method:** A review of the integrative literature was carried out in May and June of 2018 from the PubMed and BIREME databases, using the words registered in the MESH and the DeCS (Health Descriptors), respectively, in English leukemia AND diagnosis AND oral manifestations. We included studies evaluating oral alterations in leukemic patients at the time of diagnosis, published in the bases cited in Portuguese and English, with any study design, except revision of narrative literature and articles published between 1950 to 2018. We excluded articles that did not address the subject of the study, which included individuals other than leukemic patients, with absence of oral manifestations in leukemic patients and articles not found in its full version. **Results:** Through the search, 353 articles were found, of which 318 were excluded. Thus, 35 articles remained. **Conclusion:** According to the articles found, the surgeon-dentist has great importance at the time of diagnosis of leukemia, since the first manifestations of this disease occur in the oral cavity, such as gingival bleeding, hyperplasia, gingival swelling, oral ulceration and petechiae.

Key words: Leukemia; Diagnosis; Oral Manifestations.

Resumo

Introdução: A leucemia é uma patologia com modificações malignas nas células-tronco hematopoiéticas, podendo gerar sinais e sintomas no organismo do paciente. **Objetivo:** Verificar as manifestações orais de leucemia no momento do diagnóstico. **Método:** Foi realizada uma revisão de literatura integrativa em maio e junho de 2018, a partir das bases de dados PubMed e BIREME, por meio das palavras cadastradas no MESH e no DeCS (Descritores em Saúde), respectivamente, em inglês *leukemia AND diagnosis AND oral manifestations*. Foram incluídos estudos avaliando as alterações bucais em pacientes leucêmicos no momento do diagnóstico, publicados nas bases citadas, nas línguas portuguesa e inglesa, com qualquer desenho de estudo, exceto revisão de literatura narrativa e artigos publicados entre 1950 a 2018. Foram excluídos os artigos que não abordam o tema do estudo, que incluíram outros indivíduos, além de pacientes leucêmicos, com ausência de manifestações orais em pacientes leucêmicos, e artigos não encontrados em sua versão completa. **Resultados:** Foram encontrados 353 artigos; destes, 318 foram excluídos. Assim, restaram 35 artigos. **Conclusão:** Conforme descrito nos artigos encontrados, o cirurgião-dentista tem grande importância no momento do diagnóstico da leucemia, já que as primeiras manifestações dessa doença ocorrem na cavidade oral, tais como sangramento gengival, hiperplasia, inchaço gengival, ulceração oral e petéquias.

Palavras-chave: Leucemia; Diagnóstico; Manifestações Buciais.

Resumen

Introducción: La leucemia es una patología con modificaciones de las células madre hematopoyéticas, las cuales pueden generar signos y síntomas en el organismo del paciente. **Objetivo:** Verificar las manifestaciones orales de leucemia en el momento del diagnóstico. **Método:** Se realizó una revisión de literatura integrativa en mayo y junio de 2018 a partir de las bases de datos PubMed y BIREME, por medio de las palabras catastradas en el MESH y en el DeCS (Descritores en Salud), respectivamente, en inglés *leucemia AND diagnóstico AND oral manifestaciones*. Se incluyeron los estudios que evalúan las alteraciones orales en pacientes leucémicos el momento del diagnóstico, publicados en las bases mencionadas en portugués y en Inglés, con cualquier diseño de estudio, excepto la narrativa revisión de la literatura y artículos publicados entre 1950 e 2018. Se excluyeron los artículos que no abordan el tema del estudio, que incluyeron a otros individuos además de pacientes leucémicos, con ausencia de manifestaciones orales en pacientes leucémicos y artículos no encontrados en su versión completa. **Resultados:** A través de una búsqueda realizada encontraron 353 artículos, de éstas, 318 fueron excluidos. Así, quedaron 35 artículos. **Conclusión:** Según los artículos encontrados, el cirujano dentista tiene gran importancia en el momento del diagnóstico de la leucemia, ya que las primeras manifestaciones de esta enfermedad ocurren en la cavidad oral, tales como sangrado gingival, hiperplasia, hinchazón gingival, ulceración oral y petequias.

Palabras clave: Leucemia; Diagnóstico; Manifestaciones Bucuales.

¹ Dentist. Faculdade Especializada na Área de Saúde. Passo Fundo (RS), Brazil. E- mail:micheleformighieri@gmail.com. Orcid ID: <https://orcid.org/0000-0003-0612-6045>

² Student in the Graduate Studies Program in Dentistry, Faculdade Meridional (IMED). Passo Fundo (RS), Brazil. E-mail: leticiatlemes@hotmail.com. Orcid ID: <https://orcid.org/0000-0002-6525-5368>

³ Preceptor, Multidisciplinary Residency in Health, Hospital da Cidade de Passo Fundo. Passo Fundo (RS), Brazil. E-mail: carolmozzini@gmail.com. Orcid ID: <https://orcid.org/0000-0003-4360-2936>

Corresponding authors: Polus Care Centro Clínico. Rua Bento Gonçalves 900, sala 101, Centro. Passo Fundo (RS), Brazil. CEP 99020-060.



This article is published in Open Access under the Creative Commons Attribution license, which allows use, distribution, and reproduction in any medium, without restrictions, as long as the original work is correctly cited.

INTRODUCTION

Leukemia is a hematological disorder characterized by the differentiation and proliferation of malignant leukocytes, which destroy the bone marrow, generating the multiplication of leukemia cells¹⁻⁷.

According to Silva et al.⁸, leukemia represents one-third of all childhood cancers, and 75% of pediatric patients suffer acute lymphoblastic leukemia, which can originate in the B or T cells.

The causes of this disease are unknown and uncertain, although it is associated with radiation exposure, chromosomal anomalies, chemical lesions, and viral infections and may be caused by a combination of environmental and genetic factors^{2,9}.

Leukemias are classified according to their clinical course (acute or chronic) and histogenetic origin (lymphoid or myeloid). Chronic leukemia tends to show relatively high leukocyte concentrations and its evolution is slower, while acute leukemia presents with more rapid progression^{2,5,10-12}.

The alterations are associated with the compromise to the hematopoietic system, generating systemic signs and symptoms in the patient, such as fatigue and dyspnea, besides alterations in the oral cavity, with gingival swelling, petechiae, bruising, spontaneous bleeding/hemorrhage, ulcers, lichen planus, hyperplasia, erythema multiforme, lupus erythematosus, pemphigus vulgaris, and mucositis¹³⁻²⁴.

The current study thus aims to investigate the oral manifestations of leukemia at the time of diagnosis and thus contribute to knowledge through the detection of alterations in the mouth that indicate diseases than dental problems. The study also aims to verify the age with the highest rate of involvement of the oral cavity as well as the dentist's role at the time of diagnosis.

METHOD

This study is an integrative literature review on the oral manifestations of leukemia at the time of diagnosis. We consulted the PubMed (MEDLINE) and Virtual Health Library (BIREME) databases. The review was conducted in May and June 2018 using a search strategy that addressed *MeSH* and *entry terms* in PubMed and the keywords registered in DeCS in BIREME.

The search strategy was the following: in PubMed via *MeSH* and *entry terms* - "*Leukemia*"[Mesh] OR "*Leukemias*" OR "*Leucocythaemia*" OR "*Leucocythaemias*" OR "*Leucocythemia*" OR "*Leucocythemias*" AND "*Oral Manifestations*"[Mesh] OR "*Manifestation, Oral*" OR "*Manifestations, Oral*" OR "*Oral Manifestation*" AND

"*Diagnosis*"[MeSH] OR "*Diagnoses*" OR "*Diagnoses and Examinations*" OR "*Examinations and Diagnoses*" OR "*Antemortem Diagnosis*" OR "*Antemortem Diagnoses*" OR "*Diagnoses, Antemortem*" OR "*Diagnosis, Antemortem*". The search in BIREME used the words registered in DeCS: "*leukemia*" AND "*diagnosis*" AND "*oral manifestations*". The search was expanded to "*leukemia*" AND "*diagnosis*" AND "*oral manifestation*"; the term "*oral manifestation*" is not registered in DeCS.

Inclusion criteria were: studies reporting oral manifestations in leukemia patients at the time of diagnosis; published in Portuguese and English in the above-mentioned databases; any study design except narrative literature review; and published from 1950 to 2018. Exclusion criteria were: articles that did not address the study theme; that included individuals other than leukemia patients; that did not report oral manifestations in leukemia patients; and that were not found in full text format, even after requesting them for purchase/acquisition.

The studies were analyzed by two independent researchers based on the titles and abstracts, according to the inclusion and exclusion criteria. After the articles were included, they were submitted to an analysis of the full text according to the eligibility criteria. The extracted data were related to oral manifestations, patients' age, and the dentist's role in the leukemia diagnosis.

RESULTS

The search yielded 353 articles, selected via the inclusion and exclusion criteria. A total of 35 articles were included. Chart 1 provides details on the included studies.

DISCUSSION

Clinical manifestations of patients with chronic leukemia are related to the decrease in the production of blood cells, which can lead to anemia, neutropenia, and thrombocytopenia^{4,17}.

The oral alterations most frequently reported in the literature in leukemia cases confirm the review's findings and are reported in different studies, such as gingival bleeding^{3,16,18-24}; gingival swelling^{3,11,23,25,26}; oral ulcers^{2,5,13,15,25,27-30}; petechiae^{2,5,27,28,31,32}; and hyperplasia^{5,10,21,27,29,31,33,34}.

The review also verified pain in the maxillary and/or mandibular region^{2,3,18,20,32,33}.

Other manifestations were reported, including mobility of the lower front teeth⁹; lymphadenopathy^{1,23,31,32}; and tenderness on palpation of bilateral submandibular lymph nodes⁷.

Chart 1. Description of eligible articles

References	Patient assessment procedures	Oral manifestations	Patients' age	Dentist's approach
Alessandrini et al. (2012)	Intraoral tests, CT, complete blood count, immunohistochemistry, biopsy, and extraoral tests	Swelling in upper left vestibule, painful firm mass on palpation, with smooth, elastic consistency	74 years	---
Anil et al. (1996)	Intraoral and extraoral tests, blood test, and biopsy	Gingival enlargement and difficulty chewing	34 years	After performing intra and extraoral tests and ordering blood tests, which came back normal, the dentist performed a gingivectomy and sent sample for biopsy, suspecting leukemia
Appel and Miggantz (1988)	Intraoral tests, x-ray, biopsy of inter-molar papilla, bone marrow biopsy, and laboratory tests	Pain in right mandibular region, reddish-purple alveolar mucosa, erythema, papillae and gingiva with purulent appearance. Right lower molar showed advanced periodontal destruction and subgingival calculus. Generalized horizontal bone loss, caries in third lower right molar, subgingival calculus, and periodontal pocket of 8 to 10 mm	59 years	Dentist performed first treatment for patient, then referred to periodontist, who ordered biopsy of the buccal papilla between lower left teeth and first and second molars. Patient was then referred to hospital for treatment with oncologist
Aronovich and Connolly (2008)	Complete blood count, clinical tests, biopsy, histopathology, and intraoral tests	Pain in left posterior region, pain and gingival bleeding, edema on the left around lower maxilla, trismus, and localized erythema	18 years	--
Babu et al. (2014)	Extraoral and intraoral tests and complete blood count	Bleeding and gingival swelling, deep bilateral submandibular cervical lymphadenopathy; erythematous gingiva, dental plaque and calculus, generalized enlargement of maxilla and mandibular gingiva with buccolingual involvement	43 years	After ordering extraoral, systemic, and intraoral tests and complete blood count, dentist instructed patient to use a soft toothbrush and perform mouthwash with chlorhexidine (0.2%) 3 times a day and referred immediately to cancer center
Boddu et al. (2017)	Extraoral and intraoral tests, CT, and biopsy	Gingival pain and oral lesions, sublingual ulcers	62	--
Brenneis, Mattson and Commers (1988)	Clinical and blood tests	Cyanotic gingiva with hyperplasia, bilateral cervical lymphadenopathy, enlarged and erythematous tonsillar tissue	43 years	Dentist ordered blood tests, since patient presented typical signs of leukemia
Bressman et al. (1982)	Clinical tests, x-ray, hematological assessment, physical tests, and bone marrow aspiration	Gingival pain and bleeding in right maxilla in premolar region, fibrotic marginal gingiva, teeth with extensive restorations and bone loss	36 years	Patient referred to regular physician with a special request for hematological assessment
Cale, Freedman, and Lumerman (1988)	Extraoral and intraoral tests	Hemorrhagic bullae on the anterior dorsum of tongue and spontaneous gingival bleeding	45 years	Upon receiving patient, dentist treated first with vitamin C and amoxicillin, without ordering any tests

Chart 1. cont.

References	Patient assessment procedures	Oral manifestations	Patients' age	Dentist's approach
Chavan et al. (2010)	Intraoral clinical tests and blood tests	Painful swelling and gingival bleeding, altered color of gingiva and marginal papillae, gingival ulceration, bruising on the mucosa of hard and soft palate	35 years	Dentist ordered a hematological assessment due to the severity and extent of the gingival alterations. After diagnosis, referred to an oncologist
Chung et al. (2011)	Physical tests, complete blood count, intraoral test, x-ray, CT, and biopsy	Pain in posterior right mandible and mobility of lower front teeth	35 years	Dentist took a complete history, including oral history, and requested hospital admission for systemic assessment of the patient
Claus and Denver (1954)	Laboratory and physical tests	--	37 years	--
Cooper, Loewen, and Shore (2000)	Intraoral tests, x-ray, blood tests, and biopsy	Hyperplasia and gingival bleeding	35 years	--
Dean, Ferguson, and Marvan (2003)	Extraoral and intraoral tests, complete blood count, and x-ray	Pain, gingival and mucosal ulcers, petechiae	22 years	Medicated the patient and referred to a specialist
Demirer et al. (2007)	Clinical tests, x-ray, complete blood count, and bone marrow biopsy	Gingival hyperplasia, erythematous areas on gingiva	17 years	--
Fatahzadeh and Krakow (2008)	Clinical tests, x-ray, intra and extraoral tests, complete blood count, bone marrow biopsy and peripheral blood test, smear test	Intermittent pain, generalized gingival bleeding, swollen and erythematous gingiva, plaque, tartar, submandibular lymphadenopathy	26 years	--
Guan and Firth (2015)	Extraoral and intraoral tests, blood tests	Spontaneous gingival bleeding	49 years	--
Gordon, O'Neal, and Woodyard (1985)	Clinical tests, urine test, complete blood count, serum glutamic oxaloacetic transaminase	Pale oral mucosa, firm, non-transcendent gingiva with normal physiological contours	42 years	After dentist treated the periodontitis with radicular scraping and smoothing, patient underwent periodontal surgery. One month after surgery, patient returned with symptoms of respiratory infection, was medicated, and blood tests were ordered. With the results, patient was referred to hospital
Gowda et al. (2013)	Extraoral, intraoral, and laboratory tests	Gingival swelling, pain, and bleeding, bilateral submandibular lymphadenopathy, localized necrosis and desquamation involving interdental papilla, and discoloration of marginal gingiva	28 years	--

Chart 1. cont.

References	Patient assessment procedures	Oral manifestations	Patients' age	Dentist's approach
Katz and Peretz (2002)	Extraoral and intraoral tests, panoramic radiograph, blood tests	Trismus, tenderness on palpation of submandibular nodules bilaterally	6 years	After initial assessment of patient, dentist ordered blood tests due to patient's debilitated state
Keene, Hussman, and Bruner (1972)	Radiographs and intraoral tests	Gingival hyperplasia, pain, diffuse erythema, generalized bone loss, gingival bleeding	54 years	Dentist ordered a complete blood count before performing periodontal treatment
Komono et al. (2015)	Intra and extraoral tests and blood tests	Oral and esophageal candidiasis	47 years	--
Menezes and Rao (2012)	Intraoral tests, laboratory tests, complete blood count, and bone marrow biopsy	Pain, swelling, and bleeding of maxillary and mandibular gingiva, enlarged and edematous gingiva, gingival necrosis at the margins of teeth	34 years	Dentist ordered routine blood workup that revealed alteration suggestive of leukemia
Pogrel (1978)	Clinical tests, radiographs, and biopsy	Severe hypertrophy on incisal mandible, purplish hypertrophic area, bleeding, mobility of lower incisors, and gingival lesion	32 years	Dentist performed a biopsy of the hypertrophic region of the incisal mandible
Ratre et al. (2018)	Intra and extraoral tests, and blood tests	Swollen gingiva and difficulty eating	51 years	--
Reenesh, Munishwar and Rath (2012)	Physical, intraoral, and blood tests	Gingival pain and bleeding, bluish gingiva with bruising	32 years	--
Shimizu et al. (2017)	Physical, intraoral, and blood tests and CT	Severe edema in right vestibular area. Enlarged right maxillary sinus on CT	12 years	
Sepúlveda et al. (2012)	Intraoral and blood tests	Hyperplasia and gingival bleeding, petechiae and bruising, lymphadenopathies	6 years	--
Sharma and Bhalla (2011)	Intra and extraoral tests and blood tests	Painful herpetiform lesions on extraoral region adjacent to redness on lower lip, ulcers covered with whitish spots. Loss of normal contours and dotted gingiva	16 years	--
Shen et al. (2018)	Intra and extraoral tests	Gingival swelling, chronic periodontitis, and epulis	41	--
Silva et al. (2008)	Physical tests, biopsy of genital ulcer, ancillary tests, complete blood count, cytogenetics, and immunophenotyping	Multiple, recurrent, difficult-to-heal oral ulcers and gingivitis	10 years and six months	--

Chart 1. cont.

References	Patient assessment procedures	Oral manifestations	Patients' age	Dentist's approach
Silva et al. (2012)	Clinical history, extraoral and intraoral tests, myelogram, bone marrow biopsy, and immunophenotyping	Swelling, painless fibrotic consistency on palpation	10 years	Dentist referred patient to the Department of Odontology at the Mato Grosso Hospital to expedite assessment and thus the treatment
Stoopler et al. (2004)	Intra and extraoral tests, CT, blood tests, bone marrow biopsy, and cytometry analysis	Ulcerations, oral erythema, neutropenic ulcers, chronic intraoral herpes, and fungal infection	50 years	--
Tag-Adeen et al. (2018)	Clinical and laboratory tests	Painful ulcers on the mouth	49 years	--
Wu, Fantasia and Kaplan (2002)	Blood tests and biopsy	Gingival swelling, enlarged maxillary and mandibular gingiva involving the floor of mouth, lingual and palatal aspects, pale, bulbous gingiva, palatal petechiae, besides skin nodules involving face and forehead	53 years	--

Note: -- Study did not provide this information

Aronovich and Connolly¹¹ report an inflammatory condition that occurs in impacted or partially erupted teeth, known as pericoronitis. This manifestation normally occurs in third molars at the time of eruption, where bacterial plaque and food remnants adhere below the gingiva, providing a substrate and medium for infection.

Sepúlveda et al.²³ report that leukemia is a neoplasia that occurs most frequently in children under 15 years of age. Meanwhile, Brenneise et al.²⁴ report that the highest prevalence of acute lymphocytic leukemia is in children 15 years of age, while chronic lymphocytic leukemia predominates in patients over 60 years of age.

Oral lesions are often the first sign or symptom of leukemia, leading patients to seek dental care in the belief that they have a local rather than systemic problem. The dentist thus plays a crucial role in the patient's initial workup, assisting with the diagnosis and prognosis^{2,8}. Patient education and an emphasis on prevention and improvements in routine oral hygiene are some of the relevant attitudes^{10,13,22}.

The dentist's assessment consists basically of performing intraoral and extraoral tests. Dentists thus use various tools to assist them, such as biopsy of suggestive areas or bone marrow.

Intraoral and extraoral tests are reported in most of the articles, while biopsy, a simple, safe, and less invasive alternative, was only reported by a few studies^{1,2,19,20,23,25,31,33}. However, the articles did not appear

to follow a set parameter for patient assessment. No criteria were reported, nor did the articles specify how the physical, extraoral, or intraoral assessment was performed in the reported cases.

As for imaging tests, periapical and panoramic radiography did not reveal any abnormality according to some authors^{2,10,22}, while other authors showed bone loss using radiography^{20,23,27,33,34}.

In addition to performing proper initial care for the patient, the dentist should thus be alert not only to the manifestations, but also to the patient's follow-up, being aware of the different systemic diseases versus more benign conditions.

Any invasive dental procedures in these patients should be performed with caution due to the high risk of hemorrhage and infection.

The studies were limited in their designs, since virtually all were case reports. We found no observational study with a larger sample of patients. There was thus a relative shortage of consistent information. There were also constant publications involving reports on the same disease and approached in similar ways.

CONCLUSION

Based on the above, leukemia tends to present its first manifestations in the oral cavity, and the most frequent alterations are gingival bleeding, hyperplasia, gingival

swelling, oral ulcers, and petechiae. Age with the highest incidence of leukemia and oral manifestations was 32 to 37 years. Dentists play a crucial role in rapid and early diagnosis of the disease, since they are the first health professionals patients turn to when they experience alterations in the oral cavity. The dentist is thus the first health professional to see the signs and symptoms of leukemia and can order tests to confirm the suspicion of a possible alteration, thus allowing a rapid and early diagnosis and favoring better prognosis for patients. In the multidisciplinary oncology team, the dentist contributes to the medical team before, during, and after medical treatment.

CONTRIBUTIONS

All the authors contributed equally to all phases of the study.

CONFLICT OF INTEREST:

None.

REFERENCES

- Babu K, Kashyap VP, Sivaranjani P, Agila S. An undiagnosed case of acute myeloid leukemia. *Journal of Indian Society of Periodontology*. 2014;18(1):95-97.
- Dean AK, Ferguson JW, Marvan ES. Acute leukaemia presenting as oral ulceration to a dental emergency service. *Australian Dental Journal*. 2003;48(3):195-197.
- Menezes L, Rao JR. Acute myelomonocytic leukemia presenting with gingival enlargement as the only clinical manifestation. *Journal of Indian Society of Periodontology*. 2012;16(4):597-601.
- Reenesh M, Munishwar S, Rath SK. Generalised Leukaemic Gingival Enlargement: a Case Report. *J Oral Maxillofac Res*. 2012;3(3):e5.
- Shen Y, Zhao L, Yafei WUY, HUANG P. Multifocal occurrence of intraoral isolated MS in a patient without leukemic presentation: A case report and literature review. *Oral Medicine, New York*, 2018;125(3):42-48.
- Silva BA, Siqueira CRB, Castro PHS, Araujo SS, Volpato LER. Oral manifestations leading to the diagnosis of acute lymphoblastic leukemia in a young girl. *Journal of Indian Society of Pedodontics and Preventive Dentistry*. 2012;30(2):166-8.
- Chung W, KIM S, CHOI JR. Osteolytic mandible presenting as an initial manifestation of an adult acute lymphoblastic leukaemia. *Int. J. Oral Maxillofac. Surg*. 2011;40:1438-1440.
- Demirer S, Özdemir H, Mehmet Ş, Marakçolu I. Gingival Hyperplasia as an Early Diagnostic Oral Manifestation in Acute Monocytic Leukemia: A Case Report. *European Journal of Dentistry*. 2007;1(2):111-114.
- Silva K, Higa M, Terreri MTS, Borsato ML, Hilário MOE. Ulcerações orais e genitais como manifestação inicial de leucemia em criança. *Rev Paul Pediatr*. 2008;26(1):84-87.
- Ratre MS, Gulati R, Khetarpal S, Parihar A. Regular oral screening and vigilance: can it be a potential lifesaver? *J Indian Soc Periodontol*, 2018;22(3):171-173.
- Aronovich S, Connolly TW. Pericoronitis as an Initial Manifestation of Acute Lymphoblastic Leukemia: A Case Report. *J Oral Maxillofac Surg*. 2008;66(4):804-808.
- Fatahzadeh M, Krakow AM. Manifestation of acute monocytic leukemia in the oral cavity: a case report. *Spec Care Dentist*. 2008;28(5):190-194.
- Boddu P, Chenb PL, Nagarajan P, Priet VG, Won A, Chambers M, et al. Necrotizing fungal gingivitis in a patient with acute myelogenous leukemia: Visible yet obscure. *Journal of Oral and Maxillofacial Surgery*, 2017;30(1):50-54.
- Alessandrini M, Micarelli A, Mugnaini F, De-Padova A, Pavone I, Bruno E. Unusual case of oral chronic lymphocytic leukemia presenting as recurrent epistaxis and asymptomatic intraoral swelling. *Rev Stomatol Chir Maxillofac*. 2012;113:455-457.
- Cale AE, Freedman PD, Lumerman H. Acute promyelocytic leukemia appearing as spontaneous oral hemorrhage: report of case. *JADA*. 1988;116(6):671-672.
- Bressman E, Decter JA, Chasens AI. Acute myeloblastic leukemia with oral manifestations. *Oral Surg*. 1982;54(4):401-403.
- Cooper CL, Loewen R, Shore T. Gingival hyperplasia complicating acute myelomonocytic leukemia. *J Can Den Assoc*. 2000;66(2):78-79.
- Gowda TM, Thomas R, Shanmukhappa SM, Agarwal G, Mehta D. Gingival enlargement as an early diagnostic indicator in therapy-related acute myeloid leukemia: A rare case report and review of literature. *Journal of Indian Society of Periodontology*, 2013;17(2):248-252.
- Pogrel MA. Acute leukemia an atypical case presenting with gingival manifestations. *Int. J. Oral Surg*. 1978;7(4):119-122.
- Chavan M, Subramaniam A, Jhaveri H, Khedkar S, Durkar SD, Argwal A. Acute myeloid leukemia: a case report with palatal and lingual gingival alterations. *Braz J Oral Sci*. 2010;9(1):67-69.
- Wu J, Fantasia JE, Kaplan R. Oral manifestations of acute Myelomonocytic Leukemia: A Case Report and Review of the Classification of Leukemias. *J. Periodontol*. 2002;73(6):664-668.

22. Stoopler ET, Pinto A, Alawi F, Raghavendra S, Boycr-Junior R, Porter D, *et al.* Granulocytic sarcoma: an atypical presentation in the oral cavity. *Spec Care Dentist.* 2004;24(2):65-69.
23. Sepúlveda E, Brethauer U, Fernández E, Cortés G, Mardones C. Oral Manifestations as First Clinical Sign of Acute Myeloid Leukemia: Report of a Case. *Pediatric Dentistry.* 2012;34(5):418-21.
24. Brenneise CV, Mattson JS, Commers JR. Acute myelomonocytic leukemia with oral manifestations: report of case. *Jada.* 1988;117(7):835-837.
25. Keene JJ, Hussman L, Bruner G. Terminal Oral Manifestations of Acute Lymphoblastic Leukemia. 1972;27(4):117-119.
26. Appel BN, Miggantz R J. Acute Nonlymphocytic Leukemia, Monocytic Variant Report of a Case. *J. Periodontol,* 1988;59(7):464-468.
27. Anil S, Smaranayake LP, Nair RG, Beena VT. Gingival enlargement as a diagnostic indicator in leukemia. Case report. *Australian Dental Journal.* 1996;41(4):235-237.
28. Claus EC, Denver C. Oral Manifestations in a case of myelogenous leukemia and leukopenia. *Oral Surg Oral Med Oral Pathol.* 1954;7(6):616-619.
29. Sharma U, Bhalla S. Oral Manifestations of a Systemic Disease. *J Can Dent Assoc.* v. 2011;77:b71.
30. Komeno Y, Uryu H, Iwata Y, Hatada Y, Sakamoto J, Iihara K, *et al.* Esophageal Candidiasis as the Initial Manifestation of Acute Myeloid Leukemia. *Intern Med.* 2015;54(7):3087-3092.
31. Guan G, Firth N. Oral manifestations as an early clinical sign of acute myeloid leukaemia: a case report. *Send to Aust Dent J.* 2015;60(1):123-7.
32. Katz J, Peretz B. Trismus in a 6-year-old child: a manifestation of leukemia? *J Clin Pediatr Dent.* 2002;26(4):337-339.
33. Tag-Adeen M, Hashiguchi K, Akazawa Y, Ohnita K, Yasushi S, Daisuke N. *et al.* An unusual presentation of adult T-cell leukemia/lymphoma. *Ecancermedicalscience.* 2018;12:801.
34. Shimizu R, Ohga N, Miyakoshi M, Asaka T, Sato J, Kitagawa Y. Unusual maxillary osteoblastic and osteolytic lesions presenting as an initial manifestation of childhood acute myeloid leukemia: A case report. *Quintessence Int.* 2017;48(2):149-153.
35. Gordon MR, O'neal RB, Woodyard SGA. Variation from classic oral manifestations associated with acute myeloblastic leukemia. A case report. *J Periodontol.* 1985;56(5):285-7.

Recebido em 28/6/2018
Aprovado em 31/7/2018