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Oral manifestations of leukaemia: cooperation between dentist and haematologist

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Abstract

Many systemic diseases can manifest in the oral mucosa. Leukaemia is the most common neoplastic disease of white blood cells. Common symptoms of leukaemia in the oral cavity include mucosa pallor, bleeding gums, gingival enlargement, ecchymosis, oral infections and ulcerations.

A dentist should know how to recognize the first signs of leukaemia and may be responsible for a prompt referral to an adequate professional to improve patient outcomes. A dentist must participate in a patient's process of treatment when the plan includes complex therapy of the oral cavity. In many cases, this procedure enables the implementation of appropriate therapy and the possibility of recovery and can even save the patient's life.

The study aimed to present the cooperation between the dentist and haematologist in the example of a 52-year-old female with oral symptoms of leukaemia.

Key words: leukaemia, early diagnosis, oral mucosa, oral manifestations, dental care

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Introduction

Leukaemias are malignancies of the haematopoietic system, characterized by the presence of a clone of transformed blast cells representing early developmental stages of haematopoiesis, which are dominant in the marrow and blood and can also infiltrate various organs. Leukaemia is more common in men than in women [1]. Acute leukaemia accounts for about 40% of all adult leukaemias [2]. Acute leukaemias are divided into acute myeloid leukaemia (AML) and acute lymphoblastic leukaemia (ALL), accounting for 80% and 20%, respectively [1]. Based on the Polish Adult Leukaemia Group (PALG) initiative, in 2003 a registry of acute leukaemia morbidity in adults has been established in the Institute of Haematology and Transfusion Medicine (IHT, *Instytut Hematologii i Transfuzjologii*), collecting reports sent in the form of questionnaires by haematology centres in Poland. Based on the obtained data, the structure of AML and ALL incidence was analysed, as well as the incidence rate and survival time were estimated. Patients diagnosed with AML in the years 2004–2010 accounted for over 80% of all patients. The age-specific analysis showed that AML incidence increased with age. Among patients with ALL, the most numerous population included patients under 30 years of age [3].

According to literature data, about 65% of patients with leukaemia develop mucosal surface lesions in the oral cavity, including gingivitis, spontaneous bleeding, ulcerated lesions, ecchymoses (especially in areas exposed to injuries), pallor of the mucosa, ulcerative gingivitis and inflammation of the oral mucosa, atrophic inflammation of the oral mucosa, angular cheilitis, toothache and pain in the bones of the jaws and the mandible without

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noticeable radiological finding, paraesthesia, and dysgeusia [4]. Very often patients with the above-mentioned symptoms come to the dentist's office seeking advice or searching for the dental cause of the signs and symptoms. In such cases, the dentist's experience has a great influence on the early diagnosis and referral to the specialistic clinic. General practitioners must make their patients aware of the need for regular visits to the dentist because only periodic dental examinations will allow early detection of developing neoplastic lesions or systemic disease symptoms in the oral cavity.

A case report

A 52-year-old female patient came to the Periodontal Disease Clinic of the University Dental Clinic in Krakow due to pain and swelling of the gums in both dental arches. During her medical history, she denied the presence of systemic diseases, chronic drug use, addictions or family burdens. The patient reported the onset of mouth lesions about a month earlier. During this time, the patient used commercially available rinses and toothpaste, but without any improvement. The patient had episodes of elevated (above 37°C) body temperature. After consulting a dentist in the local clinic, she was referred to the specialized clinic for consultation and treatment. The physical examination revealed significant gingival hyperplasia, necrotic lesions of the gingival papillae, and severe bleeding during probing of the gingival pockets and *fetor ex ore* (Figure 1). An orthopantomographic image showed a horizontal bone loss and a periapical lesion at tooth 37. According to the local lesions in the mouth, the patient was referred for an urgent complete blood count with a smear. The results are presented in Table 1.

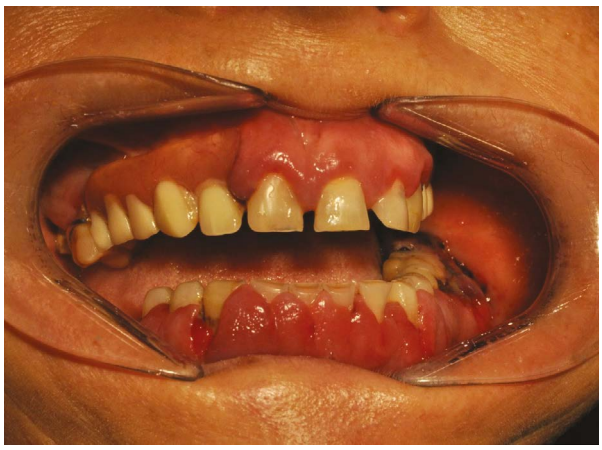

Figure 1. Oral manifestation of leukaemia

Table 1. Patient's blood test results

Parameter	The patient's result	Laboratory standard
WBC	1.8 G/L	4.0–10.0 G/L
Lymphocytes	67.8% (1.2 G/L)	20.0–45.0% (0.8–4.5 G/L)
Monocytes	27.2% (0.49 G/L)	0–12.0% (0–1.2 G/L)
Neutrophils	4.4% (0.1 G/L)	45.0–65.0% (1.6–6.5 G/L)
Eosinophils	0% (0 G/L)	0–5% (0–0.5 G/L)
Basophils	0.6% (0.01 G/L)	0.0–1.00% (0–0.1 G/L)
RBC	10.7 g/dL	11.5–15.7 g/dL
HGB	34.9%	35.0–45.0%
MCV	86.8 fL	80.0–95.0 fL
MCH	26.6 pg	25.0–33.0 pg
MCHC	30.7 g/dL	31.0–37.0 g/dL
RDW-CV	17.5%	11.0–16.0%
RDW-SD	54.0 fL	37.0–57.0 fL
PLT	31 G/L	150–400 G/L

Blue marks the results which are higher than normal; **red marks** the results which are lower than the normal; Hb — hemoglobin; MCH — mean cell haemoglobin; MCHC — mean corpuscular hemoglobin concentration; MCV mean corpuscular volume; PLT — platelets; RBC — red blood cells; RDW-CV — red blood cell distribution width; RDW-SD — red blood cell distribution width, standard deviation; WBC — white blood cells

Due to significant deviations from the norm, the patient was urgently referred to the Department of Haematology. As the oral symptoms made it difficult for the patient to perform hygienic procedures, rinsing the mouth with 0.2% chlorhexidine solution was recommended. The diagnostics conducted at the Department of Haematology of the University Hospital in Krakow confirmed acute myeloid leukaemia (AML). The scheduled treatment included necessary oral cavity sanation, performed at the University Dental Clinic in Krakow, followed by bone marrow transplantation.

Discussion

A patient suspected of having acute leukaemia should be immediately referred to a haematology centre. Physical examination may show hepatosplenomegaly and less commonly lymph node enlargement. The basic lab tests include a complete blood count with smear evaluation in light microscopy. Blood tests most often show leukocytosis, blast cells in blood smear, increased erythrocyte sedimentation rate (ESR), thrombocytopenia, and

anaemia. To deepen the diagnostics, a cytological examination of bone marrow is performed, which is usually the basis for the initial diagnosis and morphological subtype classification. The treatment of AML depends on prognostic factors, mainly including the patient's age, general condition as well as cytogenetic and molecular risk [4].

The clinical manifestation of AML is not very characteristic, with usually sudden onset symptoms. Half of the patients indicate the first symptoms of increasing fatigue, dizziness and fainting. Occasionally, patients report bone pain, weight loss, nonspecific cough, and excessive sweating. Symptoms of haemorrhagic diathesis appear in the form of petechiae on the skin, oral mucosa, bleeding from the nose and gums, and prolonged bleeding time [5].

The presented patient reported a feeling of fatigue lasting more than 1 month and, above all, pain in the jawbone, which prompted her to visit the dentist's office. Gingival hyperplasia along with bleeding may have been misdiagnosed as chronic gingivitis.

Patients with AML show symptoms resulting from pancytopenias such as weakness, easy fatigue, various infections and changes related to blood system disorders, e.g. bleeding from the gums, skin ecchymosis, epistaxis, and prolonged menstruation. Unlike other types of leukaemias, patients with AML almost always show characteristic mouth lesions in the form of pallor of the mucosa, ecchymosis on the mucosa, spontaneous gingival bleeding and gingival hypertrophy caused by blasts infiltration. Ulcers resulting from neutropenia are also frequent. Recurrent viral, bacterial or fungal infections may occur as a consequence of immunosuppression [6]. Oncological vigilance of dentists is of great importance, thanks to which they can diagnose the early onset of the disease based on the symptoms in the oral cavity and the information that can be obtained from the patient during the medical history. It is important to perform additional tests as soon as possible and refer the patient to a haematologist.

Lesions in the oral cavity in patients with leukaemia can be divided into primary (closely related to haematological disorders and blast infiltrates), secondary (microbial infections) and treatment-related.

The primary lesions in the oral cavity during AML include:

- leukaemia cell infiltrates manifested by gingival hypertrophy as well as paraesthesia and numbness of the lower lip of unclear cause;
- spontaneous bleeding;
- neutropenia-related ulcers;
- thrombocytopenia-related ecchymoses (especially in places exposed to injuries — bite line on the mucosa of the cheeks, lower lip);
- pallor of the mucosa;
- exfoliative cheilitis;
- atrophic mucositis;
- ulcerative inflammation of the gums and oral mucosa;
- angular cheilitis;
- bone and tooth pain with no radiological findings [4].

The literature data showed that almost 65% of leukaemia patients have oral lesions. The most common are gingival hyperplasia, ulcerations, bleeding gums, ecchymosis, and superinfections with *Herpes* viruses [7]. Spontaneous gingival bleeding (56%) or ulceration on the mucosa (53%) are observed in more than half of the patients [8].

Patients may also develop arthritis of the temporomandibular joint, osteolytic changes in the bones of the maxilla and mandible, pigmentation changes on the palate, haemorrhagic blisters, swelling of the salivary glands or increased mobility and toothache [9–12]. Gingival hypertrophy mainly affects the interdental papillae and the marginal gingiva (it can be generalized or local). Gingival hyperplasia can be of various degrees, and sometimes even involve the entire clinical crowns of the teeth [6]. It often leads to the formation of pseudo-pockets, which promotes the development of gingivitis and periodontitis [13]. Gingival enlargement may result from neutropenia or direct infiltration with immature leukocytes, or as a secondary symptom of thrombocytopenia [14, 15]. Thrombocytopenia symptoms usually develop when the platelet count falls below 50,000 cells/mm^3. There may be bruising, ecchymosis on the soft and hard palate, and spontaneous bleeding from the gums [16]. The dentist should remember that significant gum enlargement, profuse bleeding, and tooth mobility may be early symptoms of disorders of the white blood cell system [17]. Gingival hyperplasia with reddening or bluish discolouration and necrotic lesions is one of the most common symptoms in patients with early-stage acute leukaemia [18].

The results of studies conducted in the groups of patients suffering from leukaemia indicate a high frequency of pathological lesions in the oral mucosa, a high index of caries and deepening inflammatory processes within the periodontium, especially in patients with AML. The 2017 study by Busjan et al. [19] assessed various dental

indicators and lesions in the oral cavity in a group of patients with AML. Microbiological examination of samples collected from periodontal pockets revealed the presence of *Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis, Tannerella forsythia, Treponemadenticola, Prevotella intermedia (Pi), Parvimonas micra, Fusobacterium nucleatum, Campylobacter rectus, Eubacterium nodatum, Eikanella corrodens and Capnocytophaga.* In 82.4% of patients, periodontal disease was diagnosed, and the bleeding on probing (BOP), periodontal pocket depth (PD) and clinical attachment loss (CAL) indices were statistically higher than in the control group [19].

During oncological treatment, patients very often experience reduced salivation or dry mouth, which may lead to tooth decay [20]. The build-up of tartar and plaque predisposes to gingival overgrowth, periodontal disease, tissue necrosis or gingival bleeding. Insufficient oral hygiene increases the risk of systemic infections in patients undergoing chemotherapy, therefore it is very important to educate both patients and haematologists on the prevention of oral cavity diseases during oncological treatment [21]. Proper oral hygiene during the treatment of leukaemia reduces the risk of changes in the oral cavity and also causes a decrease in Gram-negative bacteria and *Candida albicans*, and above all minimizes the risk of sepsis [22].

Based on the results of published randomized clinical trials, current guidance of management and own experience, recommendations were issued which constitute the opinion of a team of experts in the field of oncological radiotherapy, clinical oncology, palliative medicine, haematology, paediatric oncology and haematology, periodontics, maxillary surgery, dental prosthetics, clinical nutrition and oral cavity medicine, which are part of the Polish Group of Specialists for the Prevention and Treatment of Complications in the Oral Cavity. It is very important to prevent complications before commencing oncological treatment. Patients should be referred for a dental consultation and informed about the need to follow the rules of oral hygiene: brushing teeth 3 times a day with a very soft toothbrush made of nylon bristles, rinsing the mouth with physiological saline solution (0.9% NaCl) or baking soda, using dental floss. Daily use of preparations based on chlorhexidine is intended to improve oral hygiene, and in immunosuppressive patients to reduce the risk of fungal superinfection. The use of removable prosthetic restorations should be limited and fixed orthodontic appliances should be removed. Patients are strictly forbidden to smoke or drink alcohol during treatment and should also receive dietary recommendations: avoiding foods and drinks containing simple sugars, spicy, acidic, hot foods or carbonated drinks, excluding fruit and fruit juices and hard foods from the diet. The nutritional status of each patient should be assessed. The dentist should assess the condition of the oral cavity based on a clinical and radiological examination. If possible, before starting oncological treatment, the oral cavity should be sanitized, which includes conservative treatment (including endodontic treatment), periodontal treatment, removal of teeth that are a potential source of infection, and assessment of current prosthetic restorations and removal of fixed orthodontic appliances. During leukaemia therapy, the patient may be exposed to various opportunistic infections and chemotherapy-induced mucositis. Therefore, such conservative measures as e.g. acyclovir, nystatin, chlorhexidine, oral hygiene preparations and treatments can be used to minimize the risk of complications. Good cooperation between dentists and haematology specialists plays a very important role in preparing the patient for the treatment of the underlying disease. A patient after oral cavity sanitation has a lower risk of dental complications even before starting oncological therapy. Good communication with the haematologist allows to perform procedures in the oral cavity, and after appropriate preparation by the attending physician, also those associated with greater postoperative bleeding.

Both daily hygiene procedures performed by the patient at home and professional management in the dentist's office can prevent the development of gingivitis or resolve the lesions that have already appeared. Periodontal treatments, if indicated, should be performed with prophylactic antibiotic coverage. Any more extensive periodontal surgery procedures should be postponed until remission of the underlying disease is achieved. In the case of abscesses, treatment should be conducted with prophylactic antibiotic coverage and lead to drainage and pain relief. Preparation of carious lesions does not require the use of an antibiotic. In young children and non-cooperating patients, dental treatment under general anaesthesia is often required [8, 23–25]. As many as 90% of juvenile AML patients have abnormalities in the structure and number of teeth after the end of treatment. The disorders depend on the patient's age and the stage of odontogenesis in which haematological treatment was performed. Curious damaged teeth should be rebuilt, and missing teeth should be re-

Table 2. Therapy of oral mucositis

Therapy	The most important results	Recommendations
Professional oral hygiene	Decrease by 1/3 of the number of patients with mucositis [29]	Sanitation of the oral cavity before treatment and maintaining proper hygiene during treatment
Palifermin	Slight reduction in the severity of oral mucositis [30]	Administration before and during treatment
Benzydamine	It reduces the frequency and severity of oral mucositis [31–33]	Rinsing the mouth during and 2 weeks after the end of therapy
Caphosol	No statistical differences from other topical preparations [34, 35]	Rinsing the mouth during treatment
Cryotherapy	Reducing the severity of oral mucositis and delaying the onset of inflammation; low cost of therapy [36]	Application of ice cubes to the patient's mouth during the administration of chemotherapy
Manuka honey	It does not affect the possibility of oral mucositis, but it reduces the incidence of bacterial superinfections [37]	Apply topically several times a day for several weeks
Zinc	It reduces the severity of oral mucositis and alleviates pain [38]	Rinse with a concentration of 37 mg/dL ZnC 4 times a day
Chamomile	It has anti-inflammatory and antibacterial properties, reduces pain [39]	For rinsing the mouth with a cool infusion or in the form of oral gels
Aloe	It has a moisturizing, anti-inflammatory effect, is a source of amino acids, vitamins and fatty acids [40, 41]	To be applied to the mucosa in the form of a gel
Superoxide dismutase	It reduces the severity and duration of oral mucositis [42]	Oral administration prior to irradiation
Chlorhexidine	It causes a 40% reduction in pain and reduces the risk of bacterial superinfections by up to 50% [43]	Topically as a mouthwash or in the form of a gel
Povidone-iodine	It reduces the risk of oral mucositis by over 60% [44]	For rinsing the mouth at a dilution of 1:8
Tissue coatings (e.g. sucralfate, non-absorbed aluminium salt)	They reduce pain by 40–66.5%, and the severity of oral mucositis by more than 60%, create a protective barrier, increasing mucus production and blood flow to the mucosa [45]	For topical use in the mouth
Sodium bicarbonate	It neutralizes the acidic environment in the oral cavity, has an antiseptic effect [46]	For rinsing the mouth after dilution

placed [20, 26]. Wang et al. [27] report that minor ALL patients have a higher risk of caries and oral dysbiosis. This phenomenon highlights the need for personalized oral health prophylaxis in patients undergoing chemotherapy.

Oral mucositis is one of the side effects of radiotherapy and chemotherapy used to treat cancer. It affects 20–100% of cancer patients. Clinical manifestations include erythematous and painful ulcerations in the oral mucosa. It can lead to dysphagia, dysgeusia, weight loss and secondary infections [28]. Table 2 presents the prevention and treatment of oral mucositis. Oral mucositis may complicate the course of oncological treatment and reduce patients' quality of life. It should be remembered that the prevention of oral mucositis plays a key role. Therefore, cooperation between oncological centres and dentists is very important to provide patients with dental care, including the prevention of oral mucositis and possible treatment of complications related to lesions in the oral cavity [41].

Conclusions

The mouth may be the site of the first manifestation of AML symptoms. Mucosal lesions can cause discomfort that prompts patients to visit a dentist. Therefore, a dentist may contribute to the early diagnosis of the disease [19]. In the new classification of periodontal diseases developed in 2017 by the American Academy of Periodontology and the European Federation of Periodontology, the subcategory of gingivitis modified by general and local factors, including haematological disorders, was distinguished. It should be remembered

that the early detection of the causes of gingival hyperplasia speeds up the correct diagnosis and treatment initiation. Suspicion of a haematological disease confirmed by the dentist and referral of the patient to the appropriate centre means that the patient is referred to a specialist in the early stages of the disease, and treatment can be started as soon as possible. The cooperation of the haematologist and the dentist enables the maintenance of oral cavity health and reduces the risk of intraoral complications related to the general therapy of the underlying disease.

References

1. Dmoszyńska A, Robak T, Hus I. Podstawy hematologii. Wydanie III. Wydawnictwo Czelej, Lublin; 2015: 227–270.
2. Wysocka-Słowik A, Dorocka-Bobkowska B, Gil L. Ostra białaczka szpikowa w praktyce lekarza dentysty. Dent Forum. 2016; 44(1): 97–102.
3. Wetzler M, Byrd JC, Bloomfield CD. Ostra i przewlekła białaczka szpikowa. Onkologia i Hematologia. 2009; 6(104): 738–742.
4. Francisconi CF, Caldas RJ, Oliveira Martins LJ, et al. Leukemic oral manifestations and their management. Asian Pac J Cancer Prev. 2016; 17(3): 911–915, doi: 10.7314/apjcp.2016.17.3.911, indexed in Pubmed: 27039811.
5. Deliverska E, Krasteva A. Oral Signs of leukemia and dental management — literature data and case report. Journal of IMAB — Annual Proceeding (Scientific Papers). 2013; 19(4): 388–391, doi: 10.5272/jimab.2013194.388.
6. Zimmermann C, Meurer MI, Grando LJ, et al. Dental treatment in patients with leukemia. J Oncol. 2015; 2015: 571739, doi: 10.1155/2015/571739, indexed in Pubmed: 25784937.
7. López-Valverde N, López-Valverde A, Gómez-de Diego R, et al. Gingival hyperplasia as an early manifestation of acute myeloid leukemia. A retrospective review. J Clin Exp Dent. 2019; 11(12): e1139–e1142, doi: 10.4317/jced.56214, indexed in Pubmed: 31824594.
8. Cammarata-Scalisi F, Girardi K, Strocchio L, et al. Oral manifestations and complications in childhood acute myeloid leukemia. Cancers (Basel). 2020; 12(6), doi: 10.3390/cancers12061634, indexed in Pubmed: 32575613.
9. Lupi SM, Rodriguez Y Baena A, Cervino G, et al. Long-Term effects of acute myeloid leukemia treatment on the oral system in a pediatric patient. Open Dent J. 2018; 12: 230–237, doi: 10.2174/1874210601812010230, indexed in Pubmed: 29760815.
10. Chowdhri K, Tandon S, Lamba AK, et al. Leukemic gingival enlargement: A case report and review of literature. J Oral Maxillofac Pathol. 2018; 22(Suppl 1): S77–S81, doi: 10.4103/jomfp.JOMFP_205_17, indexed in Pubmed: 29491612.
11. Ratre MS, Gulati R, Khetarpal S, et al. Regular oral screening and vigilance: can it be a potential lifesaver? J Indian Soc Periodontol. 2018; 22(2): 171–173, doi: 10.4103/jisp.jisp_136_18, indexed in Pubmed: 29769773.
12. Chapple ILC, Mealey BL, Van Dyke TE, et al. Periodontal health and gingival diseases and conditions on an intact and a reduced periodontium: Consensus report of workgroup 1 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. J Periodontol. 2018; 89 (Suppl 1): S74–S84, doi: 10.1002/JPER.17-0719, indexed in Pubmed: 29926944.
13. Shankarapillai R, Nair MA, George R, et al. Periodontal and gingival parameters in young adults with acute myeloid leukaemia in Kerala, South India. Oral Health Prev Dent. 2010; 8(4): 395–400, indexed in Pubmed: 21180678.
14. Zwaan CM. van den Heuvel-Eibrink MM. Pediatric acute myeloid leukemia. In: Antica M. ed. Acute leukemia — the scientist's perspective and challenge. InTech, London 2011: 235–276.
15. Maloney KW, Giller R, Hunger SP. Recent advances in the understanding and treatment of pediatric leukemias. Adv Pediatr. 2012; 59(1): 329–358, doi: 10.1016/j.yapd.2012.04.010, indexed in Pubmed: 22789585.
16. Misirlioglu M, Adisen MZ, Yilmaz S. Diagnosis of acute myeloid leukemia in a dental hospital; report of a case with severe gingival hypertrophy. Niger J Clin Pract. 2015; 18(4): 573–576, doi: 10.4103/1119-3077.151803, indexed in Pubmed: 25966736.
17. Dean AK, Ferguson JW, Marvan ES. Acute leukaemia presenting as oral ulceration to a dental emergency service. Aust Dent J. 2003; 48(3): 195–197, doi: 10.1111/j.1834-7819.2003.tb00032.x, indexed in Pubmed: 14640374.
18. Singh-Rambiritch S, Wood NH. Post-chemotherapeuticresolution of acute myeloid leukaemia-induced gingivalenlargement: a case report. SADJ. 2012; 67(7): 344–347.
19. Busjan R, Hasenkamp J, Schmalz G, et al. Oral health status in adult patients with newly diagnosed acute leukemia. Clin Oral Investig. 2018; 22(1): 411–418, doi: 10.1007/s00784-017-2127-x, indexed in Pubmed: 28536781.
20. Lauritano D, Petruzzi M. Decayed, missing and filled teeth index and dental anomalies in long-term survivors leukaemic children: a prospective controlled study. Med Oral Patol Oral Cir Bucal. 2012; 17(6): e977–e980, doi: 10.4317/medoral.17955, indexed in Pubmed: 22926470.
21. Allareddy V, Prakasam S, Allareddy V, et al. Poor Oral Health Linked with Increased Risk of Infectious Complications in Adults with Leukemia. J Mass Dent Soc. 2015; 64(3): 38–42, indexed in Pubmed: 26727815.
22. Djuric M, Hillier-Kolarov V, Belic A, et al. Mucositis prevention by improved dental care in acute leukemia patients. Support Care Cancer. 2006; 14(2): 137–146, doi: 10.1007/s00520-005-0867-7, indexed in Pubmed: 16041502.
23. Ellegaard B, Bergmann OJ, Ellegaard J. Effect of plaque removal on patients with acute leukemia. J Oral Pathol Med. 1989; 18(1): 54–58, doi: 10.1111/j.1600-0714.1989.tb00734.x, indexed in Pubmed: 2746518.
24. McGaw W, Belch A. Oral complications of acute leukemia: prophylactic impact of a chlorhexidine mouth rinse regimen. Oral Surgery, Oral Medicine, Oral Pathology. 1985; 60(3): 275–280, doi: 10.1016/0030-4220(85)90311-1, indexed in Pubmed: 3862040.
25. Reenesh M, Munishwar S, Rath SK. Generalised leukaemic gingival enlargement: a case report. J Oral Maxillofac Res. 2012; 3(3): e5, doi: 10.5037/jomr.2012.3305, indexed in Pubmed: 24422017.
26. Lupi SM, Rodriguez Y Baena A, Cervino G, et al. Long-term effects of acute myeloid leukemia treatment on the oral system in a pediatric patient. Open Dent J. 2018; 12: 230–237, doi: 10.2174/1874210601812010230, indexed in Pubmed: 29760815.
27. Wang Y, Zeng X, Yang X, et al. Oral health, caries risk profiles, and oral microbiome of pediatric patients with leukemia submitted to chemotherapy. Biomed Res Int. 2021; 2021: 6637503, doi: 10.1155/2021/6637503, indexed in Pubmed: 33532491.

28. Daugėlaitė G, Užkuraitytė K, Jagelavičienė E, et al. Prevention and treatment of chemotherapy and radiotherapy induced oral mucositis. Medicina (Kaunas). 2019; 55(2), doi: 10.3390/medicina55020025, indexed in Pubmed: 30678228.
29. Kashiwazaki H, Matsushita T, Sugita J, et al. Professional oral health care reduces oral mucositis and febrile neutropenia in patients treated with allogeneic bone marrow transplantation. Support Care Cancer. 2012; 20(2): 367–373, doi: 10.1007/s00520-011-1116-x, indexed in Pubmed: 21328006.
30. Bradstock KF, Link E, Collins M, et al. Australasian Leukaemia and Lymphoma Group. A randomized trial of prophylactic palifermin on gastrointestinal toxicity after intensive induction therapy for acute myeloid leukaemia. Br J Haematol. 2014; 167(5): 618––625, doi: 10.1111/bjh.13086, indexed in Pubmed: 25142189.
31. Kazemian A, Kamian S, Aghili M, et al. Benzydamine for prophylaxis of radiation-induced oral mucositis in head and neck cancers: a double-blind placebo-controlled randomized clinical trial. Eur J Cancer Care (Engl). 2009; 18(2): 174–178, doi: 10.1111/j.1365-2354.2008.00943.x, indexed in Pubmed: 19267733.
32. Rastogi M, Khurana R, Revannasiddaiah S, et al. Role of benzydamine hydrochloride in the prevention of oral mucositis in head and neck cancer patients treated with radiotherapy (>50 Gy) with or without chemotherapy. Support Care Cancer. 2017; 25(5): 1439–1443, doi: 10.1007/s00520-016-3548-9, indexed in Pubmed: 27987094.
33. Sheibani KM, Mafi AR, Moghaddam S, et al. Efficacy of benzydamine oral rinse in prevention and management of radiation-induced oral mucositis: a double-blind placebo-controlled randomized clinical trial. Asia Pac J Clin Oncol. 2015; 11(1): 22–27, doi: 10.1111/ajco.12288, indexed in Pubmed: 25471468.
34. Wong KH, Kuciejewska A, Sharabiani MTA, et al. A randomised controlled trial of Caphosol mouthwash in management of radiation-induced mucositis in head and neck cancer. Radiother Oncol. 2017; 122(2): 207–211, doi: 10.1016/j.radonc.2016.06.015, indexed in Pubmed: 27393218.
35. Murdock JL, Reeves DJ. Chemotherapy-induced oral mucositis management: a retrospective analysis of MuGard, Caphosol, and standard supportive care measures. J Oncol Pharm Pract. 2020; 26(3): 521–528, doi: 10.1177/1078155219850298, indexed in Pubmed: 31142234.
36. Vokurka S, Bystricka E, Scudlova J, et al. The risk factors for oral mucositis and the effect of cryotherapy in patients after the BEAM and HD-l-PAM 200 mg/m(2) autologous hematopoietic stem cell transplantation. Eur J Oncol Nurs. 2011; 15(5): 508–512, doi: 10.1016/j.ejon.2011.01.006, indexed in Pubmed: 21310656.
37. Bardy J, Molassiotis A, Ryder WD, et al. A double-blind, placebo--controlled, randomised trial of active manuka honey and standard oral care for radiation-induced oral mucositis. Br J Oral Maxillofac Surg. 2012; 50(3): 221–226, doi: 10.1016/j.bjoms.2011.03.005, indexed in Pubmed: 21636188.
38. Hewlings S, Kalman D. A review of zinc-l-carnosine and its positive effects on oral mucositis, taste disorders, and gastrointestinal disorders. Nutrients. 2020; 12(3), doi: 10.3390/nu12030665, indexed in Pubmed: 32121367.
39. Szałek E. Zapalenie błony śluzowej jamy ustnej — istotny problem terapeutyczny w onkologii. Farmacja Współczesna. 2018; 11: 8–14.
40. Sahebjamee M, Mansourian A, Hajimirzamohammad M, et al. Comparative efficacy of aloe vera and benzydamine mouthwashes on radiation-induced oral mucositis: a triple-blind, randomised, controlled clinical trial. Oral Health Prev Dent. 2015; 13(4): 309–315, doi: 10.3290/j.ohpd.a33091, indexed in Pubmed: 25431805.
41. Stawarz-Janeczek M, Szczeklik K, Pytko-Polończyk J. Oral mucositis (OM) — a common problem for oncologists and dentists. Nowotwory J Oncol. 2020; 70: 253–259.
42. Guo H, Seixas-Silva JA, Epperly MW, et al. Prevention of radiation-induced oral cavity mucositis by plasmid/liposome delivery of the human manganese superoxide dismutase (SOD2) transgene. Radiat Res. 2003; 159(3): 361–370, doi: 10.1667/0033-7587(2003)159[0361:porioc]2.0.co;2, indexed in Pubmed: 12600239.
43. Manoharan V, Fareed N, Battur H, et al. Effectiveness of mouthrinses in prevention and treatment of radiation induced mucositis: A systematic review. J Cancer Res Ther. 2020; 16 (Suppl): S1–S10, doi: 10.4103/jcrt.JCRT_176_18, indexed in Pubmed: 33380645.
44. Rahn R, Adamietz IA, Boettcher HD, et al. Povidone-iodine to prevent mucositis in patients during antineoplastic radiochemotherapy. Dermatology. 1997; 195 Suppl 2: 57–61, doi: 10.1159/000246032, indexed in Pubmed: 9403257.
45. Etiz D, Erkal HŞ, Serin M, et al. Clinical and histopathological evaluation of sucralfate in prevention of oral mucositis induced by radiation therapy in patients with head and neck malignancies. Oral Oncol. 2000; 36(1): 116–120, doi: 10.1016/s1368-8375(99)00075-5, indexed in Pubmed: 10889930.
46. Majdaeen M, Babaei M, Rahimi A. Sodium bicarbonate containing mouthwash for preventing radiotherapy-induced oral mucositis in patients with locally advanced head and neck cancer. Rep Radiother Oncol. 2015; 2(2), doi: 10.17795/rro-3721.