

The dentist's role in improving the life's quality of children with leukemia

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Abstract

Background: Leukemia is a malignant hematopoietic tissue. Because of its high mortality rate, timely diagnosis and appropriate medical therapy are Necessary. Early symptoms of leukemia may be detected in the mouth or neck. This paper is refers to all oral and neck manifestations in these patients (Before or after the detection of disease). Oral lesions are more commonly appear in patients with AML.

Method and materials: This research was accomplished using the keywords "leukemia" and "oral manifestation" to finding the current literature. The related assays were searched in IDL, Pubmed and Medline from 1990 to 2010 .

Results: Common oral symptoms are: gingival Swelling (usually the first sign), mucositis, oral ulceration, spontaneous gingival bleeding, petechiae, pale mucosa, xerostomia, atrophic glossitis, herpetic infections and candidiasis. General symptoms are fever, fatigue, anorexia, weight loss, lymphadenopathy, laryngeal pain and generally flu-like with bone pain, joint

pain. Atypical oral manifestations are: cracked lips, presence of hemorrhagic bulla, pain in tooth, ANUG, gingival hyperplasia.

Discussion: The fact that gingival hyperplasia is sometimes the first manifestation of the disease. Gingival overgrowth in it is edematous, soft, tender to touch and show tendency to bleed. The dentist has an important role in improving the quality of life for children with leukemia. He can be the first person who finds leukemia in children and can help speed up treatment process.

Key words: leukemia, oral manifestation, gingival bleeding, mucositis

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Introduction

Leukemia is the malignancy of white blood cells (WBC) precursors that according to global statistics annually from 8 to 10 cases per 100,000 people are affected. Oral cavity and gingival are the primary areas that will be affected (1, 2).

Leukemia has rooted in Latin language, means "white blood". It disrupts the body's natural immunity and erythropoiesis. Leukemia causes the accumulation of cells outside the bone marrow, forming masses in vital organs of the body such as the brain, lymph node, spleen and liver (3, 4).

Leukemia is the most common cancer in children (3). Leukemia than other cancers are more prevalent in the Middle East and the Eastern Mediterranean and based on the severity and rate of progression of the disease process, be divided in two categories: acute and chronic (1).

Acute Leukemia: It is rapid growth along with large number of immature white blood cells and the time interval between the onset of the disease and its spread is very short (1).

Chronic Leukemia: It is slow growth along with Cancer cells become more mature and there is a long time to manifest symptoms (1).

Leukemia also based on the type of WBC that has cancer can be divided into two categories: lymphocytic and myelogenous.

According to the above classification, the most common forms of leukemia are divided into four groups as follows:

1. Acute lymphoid leukemia (ALL): The large number of lymphocytes is disorders. Proliferation of blood lymphocytes is reduced the number of other cells such as red blood cells (RBC) and platelets. This causes anemia, bleeding and lack of blood coagulation. ALL is the most common type of leukemia in children and often presents in children aged 2 to 6 years. Other age groups who are vulnerable to the disease than others, people over 75 years.

2. Acute myeloid leukemia (AML): This type of cancer has several subtypes, and the average age is 64 years. This type of leukemia seen in children is less. But the first three years of life in children with Down syndrome are more prone to it.

3. Chronic lymphoid leukemia (CLL): Most frequent type of leukemia in adults. This type of leukemia is extremely slow growth and often presents in elderly. The average age of onset is 60 years. The risk of that at ages below 30 years is very unusual. This type of leukemia is more frequent in men over 50 years and is often diagnosed accidentally.

4. Chronic myeloid leukemia (CML): It's kind of an acquired disorder caused by an abnormality of chromosome 22 in bone marrow cells. It is more common in men ages 40 to 60 years. People who have been under ionizing radiation or contact with benzene and its derivatives are most at risk (1).

Warning Signs of Leukemia:

- General ill feeling
- Spots appear pomegranate seeds subcutaneous skin (petechiae)
- Not coagulated blood in a wound or incision
- Weakness and fatigue
- Numerous and recurrent infections
- Bone and joint pain
- Breathlessness due activity
- Fever, chills, and flu-like symptoms
- Progressive paleness
- Swollen and enlarged lymph nodes, spleen and liver
- Feeling of fullness and anorexia
- Anemia

- Sleepiness
- Frequent nose bleeding
- Swollen and bleeding gums
- Atrophy and weakness continuous

In addition to these symptoms, side effects may occur in patients that can be related to the spread of cancer cells to other body organs. Such as headache, nausea and vomiting, Loss of consciousness, seizures, Double vision, paralysis of the brain, Lack of maintains balance and swelling in area of neck and face (4).

Oral manifestations of leukemia:

- Mouth ulcers
- Mucositis
- Xerostomia
- Infections
- Gingival bleeding
- Gingival enlargement
- Petechiae
- Erythema
- Mucosal pallor
- Atrophic glossitis
- Herpes infection
- Candidiasis (5)
- Cracked lips (Less common)
- Hemorrhagic bullosa in anterior tongue or buccal mucosa and labial (Less common)
- Tooth pain (Less common)
- ANUG (Less common) (6)

Oral manifestations in type of acute disease are the most common (5). In many cases, these symptoms can lead to the initial diagnosis by the dentist so these are important.

Materials and Methods

Related articles on electronic sources Med line, Pub Med, IDL between 1990 and 2010 were reviewed. The key words "oral manifestations" and "leukemia" and "leukemia in children" is used.

Results

Periodontal disease is the most common oral problems in patients with leukemia and in many cases; the first symptom of leukemia is it. Gingival enlargement in 21% of patients with AML, ALL was observed (7, 8).

Oral manifestations of AML are an inflammation of the gums (usually the first symptom), mouth sores, spontaneous bleeding gums, petechiae, mucosal pallor, atrophic glossitis, herpes infection, and candidiasis induced thrombocytopenia (4).

Another study suggests that only 10-17% of children with leukemia have gingivitis (9, 10). Increasing volume of gingival can prevent from plaque control. Over time, this plaque itself as an aggressive factor in gingival enlargement acts. In another study reported that gingival infiltration may cause pain in the gingival (11). Gingival bleeding due to thrombocytopenia is a usual symptom of leukemia patients. It is said that this is first symptom in 17% of cases with the acute form and in 4% of patient whit chronic form (12).

In a person with leukemia, the increase periodontal disease due fungal infections, bacterial and viral infections may also be seen. Of course, often occur after chemotherapy and radiotherapy (8). Increased alveolar bone loss and tooth mobility can be seen in leukemia patients (12).

Many studies show that herpes simplex infections are the most common reason in development of oral lesions among leukemic patients (13, 14).

Research showed that 40% of patients with acute leukemia during the treatment are affected to oral ulcers that are caused by infection with herpes (15).

Other studies showed that in both of the overall evaluation of periodontal diseases and gingivitis, periodontitis in its resolution, there is a significant relationship between periodontal disease and leukemia (16).

Oral finding of acute leukemia:

Early symptoms of leukemia can occur in the mouth and neck. Lesions associated with acute leukemia include: mucosal paleness, mucosal purpura, lymphadenopathy, bleeding gingiva and petechia (17, 18).

Gingivitis is seen mostly in patients with acute myeloblastic leukemia (AML) and ALL is

uncommon (19, 20). The rapid enlargement in gingiva can be the first symptom of AML (21).

Demirer reported that 17-year-old girl as if the severe and rapid increase in size of gingiva with bleeding gingiva in 2 weeks was shown. After a full medical examination determined that she is suffering from acute monocytic leukemia (21). The other oral symptoms associated with leukemia can be note swollen tonsillar node and symptoms of yeast infection (22).

The dentist must be knowledge these symptoms with intermittent fever, paleness, lethargy and weakness, anorexia and weight Loss. When the patient does not respond to routine treatment as increases oral hygiene and periodontal treatment, blood disorder may be considered (22).

Common oral problems following cancer treatment:

Mucositis: One of the most common side effects of chemotherapy and radiotherapy is mucositis (Prevalence of 40% - 76%). Mucositis is the inflammation of the mucosa in the form erythema, ulcer, bleeding, swelling and pain occurs (23, 24, 25).

Mucositis can cause many problems for the person. Various studies have shown that 11% the patients due to severe oral mucositis require changing the treatment Method. And in some cases were patients require hospitalization (26). Early symptoms of mucositis are xerostomia and paresthesia that after 5-7 days of begin treatment, resulting in a direct effect on the oral mucosa, starts. And After 2-4 weeks of completion of therapy slowly disappears (27).

The main strategy for prevention is oral hygiene, because is reducing the growth of microorganisms and Develop mucositis. Use mouthwash is recommended in various studies such as Chlorhexidine %0/12, Sodium bicarbonate, Hydrogen peroxide, Saline solution %0/9, Nystatin and Sodium fluoride %0/05 (28).

One way to new therapies for the treatment of mucositis is low power laser that can significantly reduce pain and mucositis (29, 30). Even reported that the laser is well tolerated by patients and it has the positive effects on mucositis and improves quality of patient's life (31).

Xerostomia: It is one of the most common side effects of radiotherapy in the head and neck. Xerostomia result of a defect in the function of the salivary glands caused by radiotherapy (32, 33, 34). It has been shown that there is a direct relationship between radiation dose and the extent of the changes in salivary glands (34, 35). Xerostomia is causing difficulty in speaking, swallowing and chewing. Furthermore, it increases the risk of candidiasis,

periodontal disease and caries (23, 33,36).

Recommended way of treatment for xerostomia is the use of artificial saliva based on carboxy methyl cellulose, saliva stimulants and topical fluoride (30). Recently, the application of Pilocarpine is also recommended (37).

Osteoradionecrosis: This is one of the most serious and severe oral complications of head and neck radiotherapy (38, 39). It because decreased vascular tissue and hypoxic conditions are created. This problem affects bone structure. Signs and symptoms of it are including pain, Intra-or extraoral fistula, local infection, pathologic fracture and difficulty in chewing (39, 40).

Some researchers believe that despite improvements in oral care before radiotherapy however, incidence of osteo radio necrosis has not decreased in recent years. This is done while others believe that improving oral hygiene, dental care before and after radiotherapy, advanced radiotherapy techniques, correct diagnosis and improving therapeutic approaches is reduced osteonecrosis (41).

Dental care before treatment of leukemia:

Parents of children with cancer diagnosis are confused. And all their attention to be focused on their child's medical treatment disease and not show no attention to the child's oral care.

Proper dental care should not be overlooked, because oral and dental infection may make trouble in oncology treatment. Trauma associated with oral function and damage to the mucosa increases the risk of bleeding (42).

Thus the dental consultation in child newly diagnosed her disease, should be done so immediately. Until have sufficient time to complete dental care before starting treatment for leukemia (43).

Since infection due to neutropenia is the most common cause of mortality in patients with leukemia, consequently, every effort should be made until minimize risk of infection (17, 44). Therefore, in these patients should avoid performing pulpotomy in primary teeth (45, 46). But there is controversy about the root canal therapy of permanent teeth (18, 45, 46).

It seems that prevention of sepsis during chemotherapy is very important from retains patient's more teeth. It seems extracting teeth with risk of infection is more wisely. Extraction

should be done at least 10-14 days before chemotherapy (47).

Dental care during treatment of leukemia:

Oral lesions caused by chemotherapy in children are very painful. Brushing and even speaking sometimes is impossible. Recommends the use of chlorhexidine mouthwash is very important (47). Some researchers have recommended a mouthwash of steroids, antifungal agents, local anesthesia and antibiotics (47, 48).

Nystatin solution (100,000 u/ml) should be used 4 times a day if necessary. Recommended to children where they can keep this solution in your mouth before swallowing (47). Herpetic lesions (By name cold sore) are usually seen in children undergoing chemotherapy. In case of severe infection in these lesions, systemic acyclovir is recommended.

The saliva of these children is less, viscous and acidic. Therefore recommend artificial saliva. Using 5% sodium bicarbonate is suggested. This substance helps to saliva buffering and Treat mucositis (49).

In situations where the patient has a central venous cateter, the use of antibiotics against endocarditis is recommended (Prophylactic antibiotics); even if the patient is receiving antibiotics to prevent systemic infection. Prolonged bleeding in childhood cancer may be caused via certain drugs, coagulation abnormalities associated with leukemia and myeloid suppression induced by radiotherapy. Dental treatments can be performed when the platelet count is more than 40,000 mm³. Of course with prolonged bleeding control methods (50).

Children who have a full recovery can be take dental treatment like normal children. If it is necessary to perform an aggressive treatment, complete blood tests may be needed .Dental care during the child's recovery period should be focused on her dental health (47).

Discussion

The dentist has an important role in improving the quality of life for children with leukemia. He can be the first person who finds leukemia in children and can help speed up treatment process. Also during treatment he can have significant effect on a child's life with reduces pain and infection in their mouth and teeth. Finally, we hope this paper also is a step towards improving the lives of these lovely innocent children.

References

1. Little JW, Falace DA, Miller GS, et al. Dental management of medically compromised patient. 6th ed Philadelphia: CV Mosby Co;2008;370.
2. Newman MG, Takei HH, Carranza FA. Clinical periodontology. 9th ed. Philadelphia: W.B. Saunders Co;2002;214.
3. Josephine WU, Fantasia JE, Kaplan R. Oral manifestations of acute myelomonocytic leukemia: A case Report and Review of the classification of leukemias. J periodontol 2002;73:664-68 .
4. Greenberg MS, Glick M. Burket oral medicine diagnosis & treatment. 10th ed. Spain: BC Decker; 2008;443.
5. Goldman L, Bennet JC. Cecil textbook of medicine. 21th ed. Philadelphia: WB, Saunders co; 2006;954.
6. Djuric M, Pavlica D, Jankovic L, Milasin J, Jovanovic T. Presence of herpes simplex virus type I on the oral mucosa in patients undergoing chemotherapy. Scott Med J 2007;52:28-31.
7. Lynch MA, Ship II. Initial oral manifestations of leukemia. J Am Dent Assoc 2004;75:932-40.
8. Meyer U, Klein Heinz J, Handschel J, et al. Oral findings in three different groups of immune compromised patients. J Oral Pathol & Med 2008;29:153-58.
9. Curtis AB: Childhood leukemia's: Initial oral manifestations. J Am Den Assoc 2001; 83: 159-64 .
10. Michaud M, Baehner RL, Bixler D, et al. Oral manifestations of acute leukemia in children. J Am Dent Assoc. 2002;95:1145-50.
11. Sydney SB, Serio F. Acute monocytic leukemia diagnosed in a patient referred because of gingival pain. J Am Dent Assoc 2003;103:886-7 .
12. Vural F, Dzcan MA. Gingival involvement in patient with CD56+, chronic myelomonocytic leukemia. Leuk lymphoma 2004;4:415-18.
13. Tilliss TS, McDowell JD. Differential Diagnosis: is it Herpes or Aphthous? J Contemp Dent Pract 2002;3:1-15.
14. Sepulveda E, Brethauer Meier U, Jiménez Moraga M, Morales Figueroa R, Rojas Castro J, Le Fort, Canales P. Herpes simplex virus type I detection in oral mucosa lesions in patients undergoing oncologic therapy. J Oral Med 2003;8:329-333.
15. Barrett AP. A long prospective clinical study of oral complications during conventional chemotherapy for acute leukemia. Oral Surg Oral Med Oral Pathol 2002;63:313-316.

16. Lafzi A, Asvadi Kermani E, Ghanbari H, Raadi E. Clinical comparison of the prevalence and type of the periodontal diseases in leukemic patients hospitalized in Tabriz through 2004-2005. *Journal of Dentistry. Mashhad University of Medical Sciences* 2005;29:123-130.
17. Scully C, Cawson RA. *Medical problems in dentistry*. 3rd ed. Oxford: Wright; 1993.
18. Cousin GC. Oral manifestation of leukaemia. *Dent Update* 1997;24:67-70.
19. Lynch MA, Ship H. Initial manifestation of leukemia. *J Am Dent Assoc* 1967;75:932-40.
20. Genc A, Atalay T, Gedikoglu G, Zulfikar B, Kullu S. Leukemic children: clinical and histopathological gingival lesions. *J Clin Pediatr Dent* 1998;22:253-6.
21. Demirer S, Özdemir H, Şencan M, Marakoğlu I. Gingival Hyperplasia as an Early Diagnostic Oral Manifestation in Acute Monocytic Leukemia: A Case Report. *Eur J Dent* 2007;2:111-114.
22. Cho SY, Cheng AC, Cheng MCK. Oral care for children with leukaemia. *HKMJ* 2000;6:203-8.
23. Lokhart PB, Clark JR. Oral complication following neoadjuvant chemotherapy in patients with head and neck cancer. *NCI Monogr* 1990;(9):99-101.
24. Fleming P. Dental management of the pediatric oncology patient. *Curr Opin Dent* 1991;1(5):577-82.
25. Herrstedt J. Prevention and management of mucositis in patient with cancer. *Int J Antimicrob Agents*. 2002;16(2):161-3.
26. Bonan PRF, Lopes MA, Alves FA, Almeida OP. Clinical, biological, histological features and treatment of oral mucositis induced by radiation therapy: a literature review [in portuguese]. *Rev Bras Cancerol*. 2005;51(3):235-42.
27. Scully C, Epstein J, Sonis S. Oral mucositis: a challenging complication of radiotherapy, chemotherapy, and radiochemotherapy. Part 2: diagnosis and management of mucositis. *Head Neck*. 2004;26(1):77-84.
28. Emidio TC, Maeda YC, Caldo-Teixeira AS, Puppim-Rontani RM. Oral manifestations of leukemia and antineoplastic treatment – a literature review (part II). *Braz J Health*, 2010;1:136-149.
29. Kroetz FM, Czulniak GD. Oral alterations in juvenile patients submitted to radiotherapy and chemotherapy. *Publ UEPG Biol Health Sci*. 2003;9(2):41-8.
30. Camargo JD, Batistella FID, Ferreira SLM. Immediate oral complications of infant oncotherapy: identification, prevention and treatment. [in portuguese, in spanish] *JBP – Rev Ibero-am Odontopediatr Odontol Bebe*. 2004;36(7):177-84.

31. Kelner N, Lisboa de Catro JF. Low-energy laser in the management of radiation-induced oral mucositis: report of two cases [in portuguese]. *Revista Brasileira de Cancerologia*. 2007;53(1):29-33.
32. Pavlatos J. Oral care protocols for patients undergoing cancer therapy. *Gen Dent*. 2008;56(5):464-78.
33. Chambers MS, Garden AS, Kies MS, Martin JW. Radiation-induced xerostomia in patients with head and neck cancer: pathogenesis, impact on quality of life, and management. *Head Neck*. 2004;26(9):796-807.
34. Jensen SB, Pedersen AM, Reibel J, Nauntofte B. Xerostomia and hypofunction of the salivary glands in cancer therapy. *Support Care Cancer*. 2003;11(4):207-25.
35. Lima AAS, Figueiredo MAZ, Krapf SMR, Souza FR. Salivary flow rate and pH after radiotherapy of the head and neck region. *Rev Bras Cancerol*. 2004;50(4):287-93.
36. Leggott PJ. Oral complications in the pediatric population. *NCI Monogr*. 1990;(9):129-32.
37. Belfield PM, Dwyer AA. Oral complications of childhood cancer and its treatment: current best practice. *Eur J Cancer*. 2004; 40(7):1035-41.
38. Jereczek-Fossa BA, Orecchia R. Radiotherapy-induced mandibular bone complications. *Cancer Treat Rev*. 2002;28(1):65-74.
39. Harrison JS, Dale RA, Haveman CW, Redding SW. Oral complications in radiation therapy. *Gen Dent*. 2003;51(6):552-60.
40. Curi MM, Dib LL, Kowalski LP, Landman G, Mangini C. Opportunistic actinomycosis in osteoradionecrosis of the jaws in patients affected by head and neck cancer: incidence and clinical significance. *Oral Oncology*. 2000;36(3):294-9.
41. Grimaldi N, Sarmiento V, Provedel L, Almeida D, Cunha S. Dental care in prevention and treatment of osteoradionecrosis: literature review [in portuguese] *Rev Bras Cancerol*. 2005; 51(4):319-24.
42. Margolin JF, Steuber CP, Poplack DG: Acute lymphoblastic leukemia. In: Pizzo PA, Poplack DG, editors. *Principles and Practice of Pediatric Oncology*, 4th ed. Philadelphia, Lippincott Williams & Wilkins, 2002.
43. Schubert MM, Epstein JB, Peterson DE: Oral complications of cancer therapy. In: Yagiela JA, Neidle EA, Dowd FJ, editors. *Pharmacology and Therapeutics for Dentistry*, 4th ed. St. Louis, Mosby Year Book, 1998.
44. Fayle SA, Curzon ME. Oral complications in pediatric oncology patients. *Pediatr Dent* 1991;13:289-95.
45. Cameron AC, Widmer RP. *Handbook of pediatric dentistry*. London: Mosby; 1997.

46. Fayle SA, Duggal MS, Williams SA. Oral problems and the dentist's role in the management of paediatric oncology patients. *Dent Update* 1992;19:152-9.
47. Cho SY, Cheng AC, Cheng MCK. Oral care for children with leukaemia. *HKMJ* 2000;6:203-8.
48. Simon AR, Roberts MW. Management of oral complications associated with cancer therapy in pediatric patients. *J Dent Child* 1991;58:384-9.
49. Carl W. Local radiation and systemic chemotherapy: preventing and managing the oral complications. *J Am Dent Assoc* 1993;124:119-23.
50. Little JW, Falace DA, Miller CS, Rhodus NL: *Dental management of the medically compromised patient*, 6th ed. St. Louis, Mosby, 2002.