Review Article

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Gingival Enlargement: A Review Article

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Abstract

Leukocytes are the major cellular essentials of inflammatory and immune reactions of the individual. Leukocyte alterations are the consequence of a disproportion between the formation of leukocytes in the bone marrow and its exclusion by the mononuclear phagocytic system. There is also a wide range of clinical manifestations that can result from them: from very insignificant symptoms to serious conditions.

Acute leukemias are a group of neoplastic diseases that are characterized by proliferation of immature white cells in the bone marrow and/or blood and are often associated with severe leukopenia, anemia and thrombocytopenia. In some cases oral manifestations will be the first signs and it will be the dentist's responsibility to recognize the underlying disorder leading to the diagnosis of the patient's condition. Oral bleeding, gingival enlargement, ulceration and infection in patients with leukemia have been described. Leukemic infiltrates in the gingiva are commonly seen in acute leukemia. The aim of this article is to review the literature concerning the oral manifestations of patients.

Keywords: Leukemia, Oral Manifestations, Gingival Hyperplasia.

Leukemia is a cancer of the blood cells. It starts in the bone marrow, the soft tissue within most bones. Bone marrow is where blood cells are made.[1-6]

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For some, the first signs of leukemia appear in an unexpected place: the oral cavity. In fact, a dentist may be the first to detect cancer. Leukemia, as well as subsequent chemotherapy, has a distinct effect on dental health, which means that dental hygiene should be a priority when you're fighting the disease. There are several dental symptoms to look out for when you

have leukemia, as well as ways to prevent any problems.[7]

How leukemia affects dental health

One of the first signs of leukemia can be gingivitis, or swelling and bleeding gums. Common oral findings in leukemia include spontaneous gingival bleeding and small petechial hemorrhages or bruising of the oral soft tissues secondary to thrombocytopenia. When a patient has gingivitis combined with feeling weak and losing weight for no apparent reason, the dentist will run blood tests for leukemia. If they are positive, he'll refer the patient to an oncologist for confirmation of the diagnosis and for treatment. It is not known exactly why leukemia affects the oral cavity this way, but some speculate that it could be due to how the disease alters the immune system. Leukemic patients are more prone to oral candidiasis, herpetic infections, and neutropenic ulceration. These ulcers are typically deep, punched-out lesions with a gray-white necrotic base. They occur most commonly after chemotherapeutics, related to mucosal trauma or opportunistic infections. Acute leukemias, particularly acute monocytic and myelogenous subtypes, cause infiltration of leukemic cells into oral soft tissue, especially gingival tissue, resulting in swollen, boggy hyperplastic gingivitis.[7-14]

When you are healthy, your bone marrow produces:

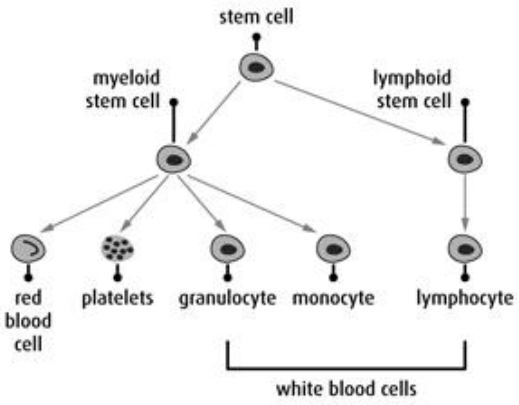
White blood cells, which help your body fight infection.

Red blood cells, which carry oxygen to all parts of your body.

platelets, which help your blood clot.[1-6]

Understanding normal blood cells

Blood cells form in the bone marrow. Bone marrow is the soft material in the center of most bones. Immature blood cells are called stem cells and blasts. Most blood cells mature in the bone marrow and then move into the blood vessels. The main cells of the immune system are derived from the lymphoid and myeloid arms of the hematopoietic system. In the bone marrow, the myeloid arm gives rise to peripheral dendritic cells, phagocytes (neutrophils and monocytes), mast cell precursors, basophils, eosinophils, platelets, and erythrocytes. In the bone marrow, the lymphoid arm gives rise to NK cells, B cells, and T cells.[1-6]



Understanding leukemia cells

In patients with leukemia, the bone marrow produces abnormal white blood cells, which are leukemia cells. They do not do the work of normal white blood cells, they grow faster than normal cells, and they do not stop growing when they should. At first, these cells act almost normally. Then, they may outnumber normal blood cells. This makes it hard for the white blood cells, red blood cells and platelets to carry out their functions.[15-22]

Lymphoid stem cells develop into lymphocytes. Lymphocytes are another type of white blood cells that are usually found in the lymph nodes and lymphatic system, such as the spleen and the blood. Some of the T cells migrate to the site of infection, where they help other phagocytic cells. Other activated T cells remain in the lymphoid organ and help B cells respond to the microbial antigens. The activated B cells secrete antibodies that circulate in the body and coat the microbes, targeting them for efficient phagocytosis.

Over time, leukemia cells can outnumber the normal blood cells. This can lead to serious problems such as anemia, bleeding, and infections. Leukemia cells can also spread to the lymph nodes or other organs and cause swelling or pain. Symptoms of leukemia can vary from person to person. Some patient symptoms may be very mild for a very long time until it is diagnosed by the doctor or spread and this kind of leukemia is called chronic leukemia while some other people may experience severe or acute symptoms classified as acute leukemia. Leukemia is said to affect other parts of the body and the lungs. The symptoms are the result of abnormal white cells that may gather in the brain or the spinal cord thus causing symptoms such as vomiting, headaches, unusual skin rashes, loss of muscle control and difficulty seeing. Other patients may develop sores in the eyes. People with leukemia are those whose bone marrow produces abnormal white cells called leukemia cells. Leukemias are also grouped by the type of white blood cells that are affected. Leukemia can arise in lymphoid cells or myeloid cells. Leukemia that affects lymphoid cells is called lymphocytic leukemia. Leukemia

that affects myeloid cells is called myeloid leukemia or myelogenous leukemia. Leukemia can be chronic or acute. In chronic leukemia the abnormal blood cell can still be functional and it will get worse slowly; acute leukemia will get worse quickly as the blood cells are very abnormal, resulting in difficulty carrying out their normal function.[23–35]

The symptoms of leukemia are fever and nocturnal sweats, feeling very tired and weak most of the time, having headaches quite often, frequent infections, pain in the bones and joints and bleeding in the gums and tiny red spots under the skins or purple patches in the skins. Most leukemia patients will find swollen lymph nodes in the neck or armpit and feel discomfort in the abdomen due to an enlarged spleen and weight loss. A doctor should be consulted if such symptoms are experienced as the doctor can diagnose the problem because such symptoms may not be leukemia and other infections might be involved.[23-35]

The early symptom of leukemia

Patients in the early stages of leukemia have no obvious symptoms and the symptoms do not stay very long; such patients may not have symptoms at all at the beginning. When leukemic blood cell increase with leukemia getting worse, it will result in a number of symptoms, referred to as acute leukemia. In such a case blood cells become very abnormal and cannot carry out their daily routines. Acute leukemia worsens when the number of abnormal cells increases rapidly.[36–43] Most of the symptoms of acute leukemia are vomiting, loss of muscle control, confusion and seizures. The cells can accumulate in the testicles causing them to swell. Leukemia also can affect the digestive tract, kidneys, lungs, or other parts of the body. Some patients develop sores in the eyes or on the skin.[44-48]

There are several different types of leukemia. In general, leukemia is grouped by how fast it develops and what kind of white blood cell it affects.

- It may be acute or chronic. Acute leukemia gets worse very fast and may make the patient feel sick right away. Chronic leukemia gets worse slowly and may not cause symptoms for years.
- It may be lymphocytic or myelogenous. Lymphocytic (or lymphoblastic) leukemia affects white blood cells called lymphocytes. Myelogenous leukemia affects white blood cells called myelocytes.

The four main types of leukemia are:

- Acute lymphoblastic leukemia, or ALL.
- Acute myelogenous leukemia, or AML.
- Chronic lymphocytic leukemia, or CLL.
- Chronic myelogenous leukemia, or CML.

Acute leukemias

With acute leukemia, immature white blood cells multiply quickly in the bone marrow. Over time, they outnumber healthy cells. (Patients may notice that they bleed a lot or suffer from infections as a result.) When these cells reach high

numbers, they can sometimes spread to other organs, causing damage. This is especially true in acute myeloid leukemia. The two main types of acute leukemia involve different types of blood cells:

- Acute lymphocytic leukemia (ALL) is the most common type of leukemia in children, mainly affecting those under 10. Adults sometimes develop ALL, but it is rare in people over 50. ALL occurs when primitive blood-forming cells called lymphoblasts reproduce without developing into normal blood cells. These abnormal cells outnumber healthy blood cells. They can collect in the lymph nodes and cause swelling.[44-50]
- Acute myeloid leukemia (AML) accounts for half of leukemia cases diagnosed in teenagers and in people in their twenties. AML occurs when primitive blood-forming cells called myeloblasts reproduce without developing into normal blood cells. Immature myeloblasts crowd the bone marrow and interfere with the production of normal blood cells. This leads to anemia, a condition in which a person does not have enough red blood cells. It can also lead to bleeding and bruising (due to a lack of blood platelets, which help the blood clot) and frequent infections (due to a lack of protective white blood cells).[51-55]

Both ALL and AML have multiple subtypes. The treatment and prognosis may vary somewhat, depending on the subtype.[44-48]

Chronic leukemias

Chronic leukemia is when the body produces too many blood cells that are only partially developed. These cells often cannot function like mature blood cells. Chronic leukemia usually develops more slowly and is a less dramatic illness than acute leukemia. There are two main types of chronic leukemia:

- Chronic lymphocytic leukemia (CLL) is rare in people under 30. It is more likely to develop as a person ages. Most cases occur in people aged 60–70. In CLL, abnormal lymphocytes cannot fight infection as well as normal cells can. These cancerous cells live in the bone marrow, blood, spleen, and lymph nodes. They can cause swelling, which appears as swollen glands. People with CLL can live a long life, even without treatment. Most often, CLL is discovered when a person has a routine blood test that shows elevated levels of lymphocytes. Over time, this type of leukemia can require treatment, especially if the person has infections or develops a high white blood cell count.[56–58]
- Chronic myeloid leukemia (CML) occurs most often in individuals aged 25–60. In CML, the abnormal cells are a type of blood cells called myeloid cells. CML usually involves a defective string of DNA called the Philadelphia chromosome. (This disease is not inherited; the change in DNA that causes it occurs after birth.) The genetic defect results in the production

of an abnormal protein. Drugs called tyrosine kinase inhibitors block the function of this abnormal protein, improving a person's blood counts. In some cases, the abnormal genetic defect even seems to disappear. Alternatively, some cases of CML can be cured with a bone marrow transplant.[44–48]

Both CLL and CML have subtypes. They also share some characteristics with other forms of leukemia. The treatment and prognosis may vary depending on the subtype.[36-43]

Rarer forms of leukemia

Lymphatic and myelogenous leukemias are the most common forms. However, cancers of other types of bone marrow cells can develop. For example, megakaryocytic leukemia arises from megakaryocytes, cells that form platelets. (Platelets help blood to clot.) Another rare form of leukemia is erythroleukima. It arises from cells that form red blood cells.

In adults, chronic lymphocytic leukemia (CLL) and acute myelogenous leukemia (AML) are the most common leukemias. In children, the most common leukemia is acute lymphoblastic leukemia (ALL). Childhood leukemias also include acute myelogenous leukemia (AML) and other myeloid leukemias, such as chronic myelogenous leukemia (CML) and juvenile myelomonocytic leukemia (JMML).

There are less common leukemias, such as hairy cell leukemia. There are also subtypes of leukemia, such as acute promyelocytic leukemia (a subtype of AML).[36–48]

Experts do not know what causes leukemia. But some factors are known to increase the risk of some kinds of leukemia, which are called risk factors. An individual is more likely to get leukemia if he or she:

- Is exposed to large amounts of radiation.
- Is exposed to certain chemicals at work, such as benzene.
- Have some types of chemotherapy to treat another cancer.
- Has Down syndrome or some other genetic problems.
- Smokes.

But most people who have these risk factors do not get leukemia; and most people who get leukemia do not have any known risk factors.[59–61]

What type of treatment the patient needs will depend on many factors, including what kind of leukemia he or she has, how far along it is, and age and overall health.

- If you have acute leukemia, you will need quick treatment to stop the rapid growth of leukemia cells. In many cases, treatment makes acute leukemia go into remission. Some doctors prefer the term "remission" to "cure," because there is a chance the cancer could recur.
- Chronic leukemia can rarely be cured, but treatment can help control the disease. If you have chronic lymphocytic leukemia, you may not need to be treated until you have symptoms. But chronic myelogenous

- leukemia will probably be treated right away.[62–66]

Treatments for leukemia include:

- Chemotherapy, which uses powerful medicines to kill cancer cells. This is the main treatment for most types of leukemia.
- Radiation treatments. Radiation therapy uses high-dose x-rays to destroy cancer cells and shrink swollen lymph nodes or an enlarged spleen. It may also be used before a stem cell transplant.
- Stem cell transplant. Stem cells can rebuild your supply of normal blood cells and boost your immune system. Before the transplant, radiation or chemotherapy may be given to destroy cells in the bone marrow and make room for the new stem cells. Or it may be given to weaken your immune system so the new stem cells can get established.
- Biological therapy. This is the use of special medicines that improve your body's natural defenses against cancer. For some people, clinical trials are a treatment option. Clinical trials are research projects to test new medicines and other treatments. Often people with leukemia take part in these studies. Some treatments for leukemia can cause side effects. Your doctor can tell you what problems are common and help you find ways to manage them.[63–69]

Protecting leukemia patient mouth

Once cancer treatment begins, dental problems can get worse. Chemotherapy alters the blood and makes it harder for blood to clot, so bleeding becomes a problem. The patient's mouth may also become more sensitive, becoming more susceptible to infections due to bacteria that originate in the oral cavity. If a patient is experiencing nausea and vomiting due to chemotherapy, the acidity of the vomit in the oral cavity can cause problems with the teeth. The patient can prevent these problems with good dental hygiene, and there are some precautions to help with a sore or sensitive mouth. Here's how:

Get dental work before treatment. Because chemotherapy can cause bleeding, it is best to get any dental work you need before you start treatment. Therefore, be sure to keep your dentist informed of your diagnosis and your treatment schedule.[70-80]

At the same time, it is important to let your physician know about your dental care.

Keep up with dental appointments during treatment. Continue to see your dentist for cleanings while you have leukemia and during treatment to keep your mouth healthy.

Be diligent about brushing and flossing at home. To keep your mouth in tip-top shape, brush and floss in the morning, before bed, and after meals.

Use gentle brushes or a sponge. Your mouth will probably bleed more easily during chemotherapy, so use a gentle toothbrush and take care not to cut your gums when you floss. Chemotherapy can also cause a sore and sensitive mouth, called mucositis, which is

like having sunburn in your mouth. It usually happens about four to seven days after treatment. When your mouth becomes too sensitive for your toothbrush, try using dental sponges, which you can buy at a pharmacy, to brush your teeth.

Use rinses regularly. Silverman recommends rinsing your mouth during the day with an antiseptic mouthrinse (which you can buy over-the-counter or get through a prescription from a doctor) or with your own solution of warm water and salt or warm water and baking soda. How often you do it depends on how many problems you are having. If you are having mouth problems, you may want to rinse your mouth four times a day, including after meals.

Treat infections promptly. If you do develop an infection in your mouth, be sure to see your doctor and get treated with an antibiotic.

The health of your mouth is something to take seriously when you have leukemia, and staying on top of your dental hygiene can prevent problems like infection.[70–80]

Increase in size of the gingiva is a common feature of gingival disease. The many types of gingival enlargement can be classified according to etiologic factors and pathologic changes as follows:

- Inflammatory enlargement
- Drug-induced enlargement
- Enlargement associated with systemic disease
- Neoplastic enlargement
- False enlargement

Leukemic enlargement may be diffuse or marginal, localized or generalized. It may appear as a diffuse enlargement of gingival mucosa, an oversized extension of the marginal gingiva or a discrete tumor-like interproximal mass. In leukemic enlargement the gingiva is generally bluish red and has a shiny surface. The consistency is moderately firm, but there is a tendency toward friability and hemorrhage, occurring either spontaneously or on slight irritation. Acute painful necrotizing ulcerative inflammatory involvement sometimes occurs in the crevice formed at the junction of the enlarged gingival and the contiguous tooth surfaces.

Patients with leukemia may also have a simple chronic inflammation without the involvement of leukemic cells and may present with the same clinical and microscopic features seen in patients without the disease. Most cases reveal features of both simple chronic inflammation and a leukemic infiltrate.

True leukemic enlargement occurs commonly in acute leukemia but may also be seen in subacute leukemia. It seldom occurs in chronic leukemia.

References

1. A. William Shafer. Etiology of Leukemia—A Review, Calif Med. 1966 March; 104(3): 161–165.

2. Saba N, Flaig T, Bone marrow transplantation for nonmalignant diseases. J

Hematother Stem Cell Res 2002 Apr;11(2):377-87. Review.

3. Zhdanova EV. [Prognosis of iron deficiency in women of reproductive age].Klin Lab Diagn 2002 Mar;(3):50-3. Russian.

4. Golovkina LL, Zotikov EA, [Platelet antigens (designation, structural molecular basis, incidence in population) (a literature review)].Klin Lab Diagn. 2002 Mar;(3):23-4, 33-5. Review. Russian.

5. DeNicola DB. Advances in hematology analyzers, Top Companion Anim Med 2011 May;26(2):52-61. Review.

6. Rabinovitch A. Hematology analyzers and body fluid analysis.Am J Clin Pathol 2010 Jul;134(1):167-8.

7. Pai A, Prasad S, Dyasanoor S. Acute leukemias: a dentist's perspective.Minerva Stomatol 2012 May;61(5):233-8. Review.

8. Ashok L, Sujatha GP, Hema G. Estimation of salivary amylase and total proteins in leukemia patients and its correlation with clinical feature and radiographic finding. Indian J Dent Res 2010 Oct-Dec;21(4):486-90.

9. Chi AC, Neville BW, Krayer JW, Gonsalves WC. Oral manifestations of systemic disease. Am Fam Physician 2010 Dec 1;82(11):1381-8. Review.

10. Tomlinson D, Ethier MC, Judd P, Doyle J, Gassas A, Naqvi A, et al. Reliability and construct validity of the oral mucositis daily questionnaire in children with cancer. Eur J Cancer 2011 Feb;47(3):383-8.

11. Ponce-Torres E, Ruíz-Rodríguez Mdel S, Alejo-González F, Hernández-Sierra JF, Pozos-Guillén Ade J.Oral manifestations in pediatric patients receiving chemotherapy for acute lymphoblastic leukemia. J Clin Pediatr Dent 2010 Spring;34(3):275-9.

12. Orbak R, Orbak Z. Oral condition of patients with leukemia and lymphoma. J Nihon Univ Sch Dent 1997;39:67-70.

13. Barrett AP. Gingival lesions in leukemia. A classification. J Periodontol 1984;55:585-588.

14. Bressman E, Decter JA, Chasens AI, Sackler RS. Acute myeloblastic leukemia with oral manifestations. A case report. Oral Surg Oral Med Oral Pathol 1982;54:401-403.

15. Drexler HG, MacLeod RA, Uphoff CC. Leukemia cell lines: in vitro models for the study of Philadelphia chromosome-positive leukemia. Leuk Res 1999 Mar;23(3):207-15.

16. Berényi E, Benko I, Vámosi G, Géresi K, Tárkányi I, Szegedi I, et al. In vitro and in vivo activity of 4-thio-uridylate against JY cells, a model for human acute lymphoid leukemia. Biochem Biophys Res Commun 2011 Jul 8;410(3):682-7. Epub 2011 Jun 13.

17. SCHREK R, LEITHOLD SL, FRIEDMAN IA, In vitro sensitivity of human leukemic cells to x-rays. Proc Soc Exp Biol Med 1957 Feb;94(2):250-3. No abstract available.

18. Han LY, Li YP, Ye MZ, Wang BW, Wang Q, Zhao SH, et al. Transduction of mesenchymal stem cells with multidrug resistance gene provides protection for bone marrow toxicity after being transplanted into a nude mice model. Chin Med J (Engl) 2012 Sep;125(18):3246-50.

19. Logan AC, Weissman IL, Shizuru JA, The road to purified hematopoietic stem cell transplants is paved with antibodies. Curr Opin Immunol 2012 Aug 29.

20. Lv F, Lu M, Cheung KM, Leung VY, Zhou G, Intrinsic properties of mesemchymal stem cells from human bone marrow, umbilical cord and umbilical cord blood (comparing the different sources of msc). Curr Stem Cell Res Ther 2012 Aug 30.

21. Moviglia GA, Blasetti N, Zarate JO, Pelayes DE, In vitro Differentiation of Adult Adipose Mesenchymal Stem Cells into Retinal Progenitor Cells. Ophthalmic Res 2012;48 Suppl 1:1-5. Epub 2012 Aug 21.

22. Ryu HH, Kang BJ, Park SS, Kim Y, Sung GJ, Woo HM, et al. Comparison of Mesenchymal Stem Cells Derived from Fat, Bone Marrow, Wharton's Jelly, and Umbilical Cord Blood for Treating Spinal Cord Injuries in Dogs. J Vet Med Sci 2012 Dec;74(12):1617-30.

23. Lins MM, Amorim M, Vilela P, Viana M, Ribeiro RC, Pedrosa A, Lucena-Silva N, Howard SC, Pedrosa F. Delayed Diagnosis of Leukemia and Association With Morbid-Mortality in Children in Pernambuco, Brazil. J Pediatr Hematol Oncol 2012 Aug 29.

24. Pai A, Prasad S, Dyasanoor S. Acute leukemias: a dentist's perspective. Minerva Stomatol 2012 May;61(5):233-8. Review.

25. Huang PK, Sanjay S. Visual Disturbance as the first Symptom of Chronic Myeloid Leukemia. Middle East Afr J Ophthalmol. 2011 Oct;18(4):336-8.

26. Temtap S, Nilmanat K. Symptom experience and management among people with acute myeloid leukaemia in Thailand. Int J Palliat Nurs 2011 Aug;17(8):381-6.

27. Tokuda Y, Chinen K, Obara H, Joishy SK. Intervals between symptom onset and clinical presentation in cancer patients. Intern Med 2009;48(11):899-905. Epub 2009 Jun 1.

28. Elbahrawy A, Hamdy M, Morsy MH, Ragab R. Chronic neutrophilic leukaemia: an Egyptian case. BMJ Case Rep 2009;2009. pii: bcr11.2008.1277. Epub 2009 Jun 24.

29. Chang PH, Lai YH, Shun SC, Lin LY, Chen ML, Yang Y, et al. Effects of a walking intervention on fatigue-related experiences of hospitalized acute myelogenous leukemia patients undergoing chemotherapy: a randomized controlled trial. J Pain Symptom Manage 2008 May;35(5):524-34.

30. Williams PD, Piamjariyakul U, Ducey K, Badura J, Boltz KD, Olberding K, et al. Cancer treatment, symptom monitoring, and self-care in adults: pilot study. Cancer Nurs 2006 Sep-Oct; 29(5):347-55.

31. Bilavsky E, Scheuerman O, Marcus N, Hoffer V, Garty BZ. Facial paralysis as a presenting symptom of leukemia. Pediatr Neurol 2006 Jun;34(6):502-4.

32. Gedaly-Duff V, Lee KA, Nail L, Nicholson HS, Johnson KP. Pain, sleep disturbance, and fatigue in children with leukemia and their parents: a pilot study. Oncol Nurs Forum 2006 May 3;33(3):641-6.

33. Banaś M, Kotulska A, Kucharz JE, Kyrcz-Krzemień S, Hołowiecki J. Musculoskeletal manifestations as the first symptom of acute lymphoblastic leukemia. A case report]. Pol Arch Med Wewn 2005 Jul;114(1):681-3.

34. Yao PY, Cao LF, Xu LY, Lu YM. [Misdiagnosis of acute leukemia presenting with arthralgia as primary symptom: report of 7 cases]. Zhongguo Dang Dai Er Ke Za Zhi 2006 Feb;8(1):77-8. Chinese.

35. Udani A, Mahalingam V, Nageswaran P, Ekambaram S. Chronic myeloid leukemia in a child with IgA nephropathy. Indian Pediatr 2012 Aug 8;49(8):668-70.

36. Travella A, Ripollés L, Aventin A, Rodríguez A, Bezares RF, Caballín MR, Slavutsky I. Structural alterations in chronic lymphocytic leukaemia. Cytogenetic and FISH analysis. Hematol Oncol 2012 Sep 7. doi: 10.1002/hon.2025.

37. Jabbour E, Mathisen MS, O'Brien S. 10 years of progress in chronic myelogenous

leukemia.J Natl Compr Canc Netw 2012 Sep 1;10(9):1049-53.

38. Abraham I, Macdonald K. Why are patients with chronic myeloid leukaemia (non-)adherent? Br J Cancer 2012 Sep 4;107(6):901-3. doi: 10.1038/bjc.2012.349.

39. Rohon P, Vondrakova J, Jonasova A, Holzerova M, Jarosova M, Indrak K. Treatment of chronic myelomonocytic leukemia with 5-azacytidine: case reports. Case Report Hematol 2012;2012:369086. Epub 2012 May 28.

40. Ferdinand R, Mitchell SA, Batson S, Tumur I. Treatments for chronic myeloid leukemia: a qualitative systematic review. J Blood Med 2012;3:51-76. Epub 2012 Aug 3.

41. Sharma A, Bahl A, Raina V, Kumar L, Gupta R. Dasatinib in chronic myeloid leukemia: A limited Indian experience. Asia Pac J Clin Oncol 2012 Jul 6. doi: 10.1111/j.1743-7563.2012.01557.x.

42. Słabicki M, Zenz T. Improving treatment for chronic lymphocytic leukemia by rational use of monoclonal antibodies. Leuk Lymphoma 2012 Sep 3.

43. Raca G, Larson RA. Acute myeloid leukemia: the challenge of unfavorable cytogenetics. Oncology (Williston Park) 2012 Aug;26(8):724,726-7.

44. Schnerch D, Yalcintepe J, Schmidts A, Becker H, Follo M, Engelhardt M, Wäsch R. Cell cycle control in acute myeloid leukemia. Am J Cancer Res 2012;2(5):508-28. Epub 2012 Aug 20.

45. Kini S, Amarapurkar A, Balasubramanian M. Small Intestinal Obstruction with Intussusception due to Acute Myeloid Leukemia: A Case Report. Case Rep Gastrointest Med. 2012;2012:425358. Epub 2012 Aug 14.

46. Silva BA, Siqueira C, Castro P, Araújo SS, Volpato L. Oral manifestations leading to the diagnosis of acute lymphoblastic leukemia in a young girl. J Indian Soc Pedod Prev Dent 2012 Apr;30(2):166-8.

47. Rakheja D, Konoplev S, Medeiros LJ, Chen W.IDH mutations in acute myeloid leukemia. Hum Pathol 2012 Aug 20.

48. Venegas P, Rivera J. Cytogenetic studies in children with Acute Lymphocitic Leukemia-B in Costa Rica].Rev Biol Trop 2004 Sep;52(3):551-8. Spanish.

49. González-Martín MC, Muñóz Villa A, García-Miguel P, Herrero Díez A, Hurtado Ruano T, Fernández Epifanio JL. [Long-term survival in childhood acute lymphocitic leukemia (author's transl)]. An Esp Pediat. 1978 Jun-Jul;11(6-7):453-60. Spanish.

50. Pagano L, Caira M. Risks for infection in patients with myelodysplasia and acute leukemia. Curr Opin Infect Dis 2012 Sep 7.

51. Ungewickell A, Medeiros BC. Novel agents in acute myeloid leukemia. Int J Hematol 2012 Aug;96(2):178-85. Epub 2012 Aug 6.

52. Fadoo Z, Mushtaq N, Alvi S, Ali M. Acute myeloid leukaemia in children: experience at a tertiary care facility of Pakistan. J Pak Med Assoc. 2012 Feb;62(2):125-8.

53. Kourelis TV, Boruchov A, Hull D, Polio J, Scholes J, Moustakakis M, Bilgrami SF. Acute myeloid leukemia following solid organ transplantation: case report and comprehensive review. Conn Med. 2012 Mar;76(3):151-4. Review.

54. Lin TL, Levy MY, Acute myeloid leukemia: focus on novel therapeutic strategies. Clin Med Insights Oncol 2012;6:205-17. Epub 2012 May 16.

55. Minden MD, Ubelhart R, Schneider D, Wossning T, Bach MP, Buchner M, Hofmann D, Surova E, Follo M, Köhler F, Wardemann H, Zirlik K, Veelken H, Jumaa H.

Chronic lymphocytic leukaemia is driven by antigen-independent cell-autonomous signalling. Nature 2012 Aug 12. doi: 10.1038/nature11309.

56. Park J. Large cell lymphoma as initial presentation of undetected chronic lymphocytic leukemia. Korean J Hematol 2012 Jun;47(2):90. Epub 2012 Jun 26.

57. Xu ZS, Zhang JY, Zhan R, Zheng ZH, Wu SQ, Chen ZZ. [Clinical analysis on 40 patients with chronic lymphocytic leukemia]. Zhongguo Shi Yan Xue Ye Xue Za Zhi 2012 Jun;20(3):583-6. Chinese.

58. Krille L, Zeeb H, Jahnen A, Mildenberger P, Seidenbusch M, Schneider K, Weisser G, Hammer G, Scholz P, Blettner M. Computed tomographies and cancer risk in children: a literature overview of CT practices, risk estimations and an epidemiologic cohort study proposal. Radiat Environ Biophys 2012 May;51(2):103-11. Epub 2012 Feb 5. Review.

59. Rodriguez GH, Ahmed SI, Al-Akhrass F, Rallapalli V, Safdar A. Characteristics of, and risk factors for, infections in patients with cancer treated with dasatinib and a brief review of other complications.Leuk Lymphoma. 2012 Aug;53(8):1530-5. Epub 2012 Feb 21.

60. Miles RR, Arnold S, Cairo MS. Risk factors and treatment of childhood and adolescent Burkitt lymphoma/leukaemia. Br J Haematol 2012 Mar;156(6):730-43.

61. Kourelis TV, Boruchov A, Hull D, Polio J, Scholes J, Moustakakis M, Bilgrami SF. Acute myeloid leukemia following solid organ transplantation: case report and comprehensive review. Conn Med 2012 Mar;76(3):151-4. Review.

62. Liang C, Chan KH, Yoon PJ, Lovell MA. Clinicopathological Characteristics of Extramedullary Acute Megakaryoblastic Leukemia (AMKL): Report of a Case with Initial Mastoid Presentation and Review of Literature to Compare Extramedullary AMKL and Non-AMKL Cases. Pediatr Dev Pathol 2012 Jun 5.

63. Parikh SA, Tefferi A. Chronic myelomonocytic leukemia: 2012 update on diagnosis, risk stratification, and management. Am J Hematol 2012 Jun;87(6):610-9. doi: 10.1002/ajh.23203. Review.

64. Zhang L, Zhu X. Epidemiology, diagnosis and treatment of acute promyelocytic leukemia in children: the experience in china. Mediterr J Hematol Infect Dis 2012;4(1):e2012012. Epub 2012 Mar 10.

65. Kwong YL. Pathogenesis and treatment of leukemia: an Asian perspective. Expert Opin Ther Targets 2012 Mar;16 Suppl 1:S37-43. Epub 2012 Feb 7. Review.

66. Büchner T, Schlenk RF, Schaich M, Döhner K, Krahl R, Krauter J, Heil G, Krug U, Sauerland MC, Heinecke A, Späth D, Kramer M, Scholl S, Berdel WE, Hiddemann W, Hoelzer D, Hehlmann R, Hasford J, Hoffmann VS, Döhner H, Ehninger G, Ganser A, Niederwieser DW, Pfirrmann M. Acute Myeloid Leukemia (AML): Different Treatment Strategies Versus a Common Standard Arm--Combined Prospective Analysis by the German AML Intergroup. J Clin Oncol 2012 Sep 10.

67. Liew E, Atenafu EG, Schimmer AD, Yee KW, Schuh AC, Minden MD, Gupta V, Brandwein JM. Outcomes of adult patients with relapsed acute lymphoblastic leukemia following frontline treatment with a pediatric regimen. Leuk Res 2012 Aug 30.

68. Flatt T, Neville K, Lewing K, Dalal J. Successful treatment of fanconi anemia and T-cell acute lymphoblastic leukemia. Case Report Hematol 2012;2012:396395. Epub 2012 Apr 1

69. Rohon P, Vondrakova J, Jonasova A, Holzerova M, Jarosova M, Indrak K. Treatment of chronic myelomonocytic leukemia with 5-azacytidine: case reports. Case Report Hematol 2012;2012:369086. Epub 2012 May 28.

70. Imamura T, Iwamoto S, Kanai R, Shimada A, Terui K, Osugi Y, Kobayashi R, Tawa A, Kosaka Y, Kato K, Hori H, Horibe K, Oda M, Adachi S. Outcome in 146 patients with paediatric acute myeloid leukaemia treated according to the AML99 protocol in the period 2003-06 from the Japan Association of Childhood Leukaemia Study. Br J Haematol 2012 Aug 28.

71. Hassan S, Popalzai M, Yu E, Wrzolek M, Odaimi M. A 61-year-old man presented with myopathy, neuropathy, and inflammatory dermatitis responsive to chronic lymphocytic leukemia treatment. Int J Gen Med 2012;5:647-53. Epub 2012 Jul 31.

72. Gao C, Zhao XX, Li WJ, Cui L, Zhao W, Liu SG, Yue ZX, Jiao Y, Wu MY, Li ZG. Clinical features, early treatment responses, and outcomes of pediatric acute lymphoblastic leukemia in china with or without specific fusion transcripts: A single institutional study of 1,004 patients. Am J Hematol 2012 Jul 9

73. Júlio César Cordova Maciel, Cláudio Galvão de Castro J, Algemir Lunardi Brunetto, Luciane Pons Di Leone, Heloisa Emília Dias da Silvei, Pediatric Blood & Cancer Volume 53, Issue 3, pages 361–365, September 2009.

74.Garfunkel AA, Glick M. Common oral findings in two different diseases--leukemia and AIDS: Part 2. Compendium 1992 Jul;13(7):550, 552-3, 556 passim.

75. Cheng KK. Association of plasma methotrexate, neutropenia, hepatic dysfunction, nausea/vomiting and oral mucositis in children with cancer. Eur J Cancer Care (Engl). 2008 May;17(3):306-11.

76.Beiraghi S, Sanders B. Oral complications in a patient with acute lymphocytic leukemia: a report of case. Spec Care Dentist 1988 Jan-Feb;8(1):13-5.

77. Naithani R, Mahapatra M. Parotid involvement in acute myelomonocytic leukemia. Indian J Pediatr 2007 Oct;74(10):965-6.

78. Dogan MC, Leblebisatan G, Haytac MC, Antmen B, Surmegozler O. Oral mucormycosis in children with leukemia: report of 2 cases. Quintessence Int 2007 Jun;38(6):515-20.

79. Nasim VS, Shetty YR, Hegde AM. Dental health status in children with acute lymphoblastic leukemia. J Clin Pediatr Dent 2007 Spring;31(3):210-3.

80. Yuki F, Kawaguchi T, Hazemoto K, Asou N. [Preventive effects of oren-gedoku-to on mucositis caused by anticancer agents in patients with acute leukemia]. Gan To Kagaku Ryoho 2003 Sep;30(9):1303-7. Japanese.