

DENTAL CONSIDERATIONS FOR LEUKEMIC PEDIATRIC PATIENTS: AN UPDATED REVIEW FOR GENERAL DENTAL PRACTITIONER

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ABSTRACT

The early signs of leukemia can usually manifest in the oral cavity due to infiltration of leukemic cells or due to associated decline in normal marrow elements, especially in the acute phase of leukemia, as common lesions at this stage of the disease can be screened and diagnosed by the dentist. Therefore, the dental community should be aware of the oral manifestations of leukemia and oral complications of anticancer treatment. This can eliminate the oral symptoms of the disease and to improve quality of life for these patients. An extensive search in PubMed line using a combination of terms like "leukemia, children, dental, Acute lymphoblastic leukemia, pediatric" for last ten years was made. Reviews and case reports concerned about acute lymphoblastic leukemia in children were all collected and analyzed and data were extracted. Accordingly, the aim of this review is to highlight on the oral presentations of leukemia in children attending dental clinics and the management of its undesirable side effects.

Key words: Dental, leukemia, Pediatric, general dental practitioner.

1. INTRODUCTION

Leukemia is first recognized by Virchow and Bennet in 1845. (1). It is a malignant disease of blood-forming tissues such as the bone marrow and causes a large number of immature blood cells to be produced and enter the blood stream (2).

Leukemia is mainly classified according to the duration into (acute or chronic) and the type of cell affected (myeloid, lymphoid, or monocytic) (3). Leukemia is the most common childhood cancer in Saudi Arabia accounting for about 33.3% of all childhood cancer (4). Acute lymphoblastic leukemia (ALL) accounts for 1/4th of all childhood cancer and 3/4th of all malignant leukemias (5). It is considered as the most common childhood leukemias in Saudi Arabia representing 75% of all newly diagnosed leukemia (4).

Although the etiology of leukemia is still unknown. Genetic alteration and susceptibility, environmental factors, such as: parental smoking and alcohol consumption, chemicals, infections, and exposure to ionizing radiation, non-ionizing electromagnetic and electric fields are potential factors that may lead to development of childhood leukemia (6).

Diagnosis of leukemia is made by physical examination. Usually there is fever, fatigue and several enlarged lymph nodes, sometimes accompanied with hepatosplenomegaly (7). Com-

plete blood count (CBC) should be carried out (WBC, RBC and platelets). Additionally, a bone marrow biopsy should be made, to check the presence of leukemic cells in the bone marrow (8). Other tests are usually performed to determine the specific type of leukemia by assessment of chromosome abnormalities (cytogenetics) and lumbar puncture to investigate for the presence of leukemic cells in the cerebrospinal fluid (CSF) (9).

This disease is usually treated by chemotherapy, combined with radiation and bone marrow transplantation is applied in some cases (10).

1.1. Oral manifestations

Thrombocytopenia, neutropenia, or compromised granulocyte function are underlying conditions of leukemia that can lead to occurrence of oral manifestations or they may result from direct leukemic infiltration (11). Gingival bleeding, hyperplasia, opportunistic infections and bone alterations are common oral manifestations of leukemia (12). Leukemic infiltration can cause gingival swelling which may be the most constant findings of the disease. The gingival hyperplasia is usually generalized and differs in severity (13).

1.2. Oral complications of antineoplastic treatment

Multi agent chemotherapy and radiation therapy have greatly increased the chances of survival and are widely accepted (14).

However, these treatment modalities lead to oral complications and have an impact on the developing dentition and on orofacial growth (12).

Oral mucositis (OM) is the most common oral complications that follow chemotherapy and radiotherapy. The multi-agent chemotherapy includes three phases (induction phase, intensification phase and maintenance phase) (15). Several studies have reported significant incidence of various forms of oral mucosal inflammation.

In a study by Figliolia *et al.* 2008 where 169 pediatric patient of acute lymphoblastic leukemia (ALL) were examined and the association of oral mucositis with age, gender and leucocyte count were assessed. Forty-six percent of patients developed oral mucositis during chemotherapy. The study showed also that 48% of patients who developed oral mucositis OM were children <9 years while 39% were children between 10 and 18 years of age. Moreover, they also found that OM is more frequent among patient who had high leucocyte counts (9400-400000 leucocyte mm³) (16). Later, another study reported by Pels *et al.* 2012 have reported that the oral mucositis was present prior to anticancer therapy in 5% of a group of pediatric patients composed of 78 children aged (2-18) with ALL. Sixty-two percent of these patients have manifested OM after the induction of chemotherapy with average time of 10-16 days of chemotherapy (17).

Furthermore, a study have documented that Oral mucositis commonly arise in patients with Acute Lymphoblastic Leukemia (ALL) regardless of the chemotherapy protocol used for the treatment (18).

A predisposing factor of oral mucositis have been suggested by Bektaş-Kayhan *et al.* 2012, that children carrying the CT genotype are more likely to develop oral mucosal lesions and is more susceptible to the side effects of chemotherapy (19).

1.3. Oral Health

In a cross sectional study done by Kanchan *et al.* 2014 formed of 33 pediatric patient of both sexes range between (5-15 years) were undergoing chemotherapy in the induction phase particularly, they found that the oral health status, DMFT index and gingival findings was significantly deteriorated following the induction phase. This can be explained by change in quality and quantity of saliva due to anticancer treatment (20). Further studies by Cubukçu *et al.* 2008 (21), Nasim *et al.* 2007 (22) and Azher *et al.* 2013 (2) have reached similar results.

1.4. Dental abnormalities and maturity

Some studies correlate between ALL treatment and the frequency of dental anomalies. In three cross-sectional studies done by Minicucci *et al.* 2003 (23), Maciel *et al.* 2009 (24) and Khojastepour *et al.* 2014(25) performed on 76, 56 and 25 ALL pediatric patients respectively. The clinical and radiographic examination showed that 82%, 80% and 28% of the same patients had at least one dental anomaly, respectively. Therefore, this result lead us to conclude that the treatment of ALL significantly increase the number of dental anomalies. Moreover, Maciel *et al.* 2009 reported that agenesis, microdontia, tapering roots and short roots was considerably greater on the same group (24) Vasconcelos *et al.* 2009 stated that ALL treatment does affect the dental age maturity of the involved patients compared to their healthy counterparts (26).

1.5. Other complications

For pediatric patients who are undergoing bone marrow transplant and radiotherapy, they may develop graft-versus-host

disease (GVHD) after the transplantation approximately by 2-3 weeks, and it is induced by the cytotoxic effect of the donor T lymphocytes in the receiver tissues. Those patients may manifest oral signs such as: erythema, erosion, ulceration of the mucosa, lichenoid changes and xerostomia (27).

Some case reports studies have referred to rare oral complications of treatment of leukemia in children such as; leukemic infiltration in the mandible (11), trismus (28), mucormycosis (29) and oral aspergillosis (30).

1.6. Dental management of children with Leukemia and prevention

Several studies have discussed use of different modalities for treatment of mucositis and other oral complications of leukemia that could help those patients and enhance their quality of life:

2. ORAL MANAGEMENT BEFORE LEUKEMIC TREATMENT

Detailed dental examination should be performed by the dentist with the required radiographs. Extraction of teeth with questionable prognosis should be done at least 10-14 days before starting chemotherapy to allow adequate healing and to minimize the risk of oral and systemic complications (31). Dental scaling and preventive therapy such as fluoride application and pits and fissure sealant should be completed prior to initiation of the cancer treatment (32). All carious teeth need to be dressed with temporary fillings at this stage and final treatment should be postponed until the patient is in remission (33). Tooth brushing instructions must be given to parents and patient using soft brush twice daily and dental flossing. Gentle massage of teeth and gum after brushing is also beneficial (34).

3. ORAL MANAGEMENT DURING LEUKEMIC TREATMENT

Oral complications at this stage includes: mucositis, gingival bleeding, oral candidiasis, herpes simplex, xerostomia and bacterial infections (35).

The child may find that even tooth brushing is too painful. Thus, Rinsing with chlorohexidine 0.12% mouth wash for one minute twice a day is very important and proven to be very effective in prevention of oral mucositis (15, 36). Recently, some studies have confirmed the clinical efficiency of Palifermin (37), low level infra-red laser therapy (38) as well as Honey and mixture of Honey (39) in the treatment of mucositis in pediatric patients.

Fungal infections as candida should be treated by Nystatin suspension (100 000 units/ml four times daily. Also, it is essential to know that nystatin and chlorohexidine should not be used simultaneously because some studies suggest that they inhibit each other action. Thus, the patient should be instructed to allow a time gap between the two drugs (40).

Herpes simplex lesion (cold sore) is one of the lesions that usually found in the oral cavity of patients undergoing chemotherapy. For that, treatment with topical Acyclovir is quite effective. In severe infections, systemic Acyclovir is prescribed to those patients after consultation of their pediatrician (41). Artificial saliva and sugar-free chewing gum can be prescribed for treatment of xerostomia (33).

4. ORAL MANAGEMENT AFTER LEUKEMIC TREATMENT

Periodic follow-ups should be scheduled to monitor oral health with 3-6 months intervals (34). Children with leukemia during remission phase can be treated as normal patients, although, blood investigations is still necessary if invasive treatment is required. In addition, tooth brushing with fluoride toothpaste and 0.05% sodium fluoride mouthwash should be used instead of chlorohexidine mouthwash (42). The orofacial abnormalities in leukemic children includes enamel hypoplasia, arrested teeth development, tooth anomalies and tooth maturity disturbance. Some of these abnormalities may have significant impact on aesthetic and cause functional and occlusal disturbances. Therefore, Oral care for those patients may include aesthetic restorations, orthodontic appliances and endodontic procedures (32).

Some studies refer to risk of developing of mucoepidermoid carcinoma in previously treated leukemic children (43, 44, 45) and squamous cell carcinoma secondary to allogenic bone marrow transplant. So that dentists have an important role in the long term observation of this disease (46).

5. CONCLUSION

Dentists should be able to clearly recognize oral manifestations of leukemia as the dentist sometimes is the first health care professional that discovers acute leukemia in children. All the preventive and curative oral measures should be carried out with the consultation of hematologist or pediatric oncologist in charge. Parents need to be educated about the benefits of optimal oral hygiene for their children and the need to seek immediate care for mouth pain and lesions. Such a preventive and therapeutic approach may prevent associated life threatening oral and systemic complications, promote rapid and complete mucosal healing, alleviate pain and improve quality of life in children with leukemia.

CONFLICT OF INTEREST: NONE DECLARED.

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