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Oral manifestations in acute leukemia as the first sign; the interdisciplinary approach of diagnosis and treatment

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Running title: Oral manifestations in acute leukemia
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Abstract

Systemic diseases often present associated oral signs and symptoms, which can occur either from the beginning of the disease or during its evolution. In some cases the oral manifestations reveal an undetected and severe disease, like leukemia. According to the encountered oral signs and symptoms and their response to topical/dental treatment, the dentist and physician should take into account specific additional tests, which could highlight a possible associated systemic disease.

The most frequent oral manifestations associated with leukemia are represented by paleness of oral mucosa/local abnormal colour of the gum, gingival petechiae, ecchymosis, bleeding associating painless gingival hyperplasia, hemorrhages, ulcerative necrotic lesions and buccal infections. We presented in this paper the relevant literature data in respect to the oral manifestations encountered in leukemia, exemplified with two suggestive cases.

As a conclusion, dentists should be advised not only to recognize and treat the encountered oral lesions but also to refer the patient to specialized professionals for additional investigations, especially in the situation when suspect a severe systemic disease that require a precocious diagnosis or in the case when the establishment of diagnosis exceed the possibilities of the usual tests. Chemotherapy
administration in association with topical/ oral solutions often leads to total or partial remission of the oral signs and symptoms.

**Introduction**

Many systemic diseases associate various signs and symptoms related to oral cavity. In some cases these oral manifestations are the only ones that are present or detectable, so that they often contribute to diagnosis of the corresponding systemic disease. Periodontal lesions are relatively frequent encountered in patients with various forms of leukemia, occurring from the beginning or during the evolution of the disease.

According to oral manifestations that could be encountered, the physicians in general and dentists in particular can establish or direct towards a possible diagnosis of the systemic disease. The most frequent oral signs and symptoms encountered in acute leukemia are represented by paleness of oral mucosa/ local abnormal colour of the gum, gingival petechiae, ecchymosis, bleeding associating painless gingival hyperplasia, hemorrhages, ulcerative necrotic lesions and buccal infections.

Due to their clinical prognosis and significance, the oral signs and symptoms require a special attention of the dental physicians. The aim of this paper is to present some peculiarities of the oral manifestations in leukemic patients, as contributing factors for a precocious diagnosis of this systemic disease, and the interdisciplinary approach of diagnosis and treatment in patients with undiagnosed leukemia but with various manifestations at the level of oral cavity.

**Discussion**

Leukemia is a group of malignant hematologic diseases with mesenchymal (myeloid or lymphoid) origin originating from the bone marrow, which generates a high numbers of abnormal hematopoietic cells in respect to their proliferation, differentiation and programmed cell death (apoptosis) (1).
The etiology of leukemia is poorly defined, most authors considering that it is multifactorial. Thus, the risk factors are represented by smoking, ionizing radiation exposure, viral infections (Epstein-Barr), chemical compounds (benzene), chromosomal abnormalities (Down syndrome), or families with leukemic history/members (2).

The classification of leukemia is according to clinical-behavioural and histopathological criteria, in: acute and chronic lymphoid leukemia, and in acute and chronic myeloid leukemia, respectively (3). The genesis of leukemic cells in detriment of normal hematopoietic cells lines leads to marrow deficiency, with decreasing of the blood cell count and subsequently complications such infection, (internal or external) bleeding and finally death. All these symptoms are due to lacking of normal blood cells (4).

The decreasing of platelets leads to blood clotting and petechiae. The decreasing of white blood cells exposes the patient to frequent infection, such as tonsils, oral sores, pneumonia, etc. Yet, the deficiency of the red blood cells causes anaemia and subsequently dyspnea and pallor. It can be present headaches, migraines, seizures, when leukemic cells invade the brain (5).

Usually the diagnosis is founded on blood tests and bone marrow biopsy. Therapeutic approach of leukemia involves chemotherapy, radiotherapy, bone marrow transplantation, and supportive/palliative care. Usually the most common applied is chemotherapy, but other additional therapeutic supports could be also necessary: transfusions of red blood cells or platelets, treatment with antibiotics to combat side effects of chemotherapy, etc. Chemotherapy involves most times three distinct steps: induction, followed by consolidation and finally the step of maintenance. Depending by case/form of leukemia, the duration of chemotherapy can prolong until 2 years (6, 7).

In contrast to acute leukemia, the oral manifestations are non-specific and less common in patients diagnosed with chronic leukemia. The most frequent oral symptom encountered is gingival
enlargement, in some cases as the first symptom of acute leukemic disease, which alerts the patient who seek a dental consultation that leads to precocious diagnosis of leukemia (8). The oral lesions in acute leukemia can be explained through: a direct infiltration with leukemic cells of local tissues, through immunodeficiency, thrombocytopenia and anaemia.

In addition to gingival enlargement that is the most frequent, other oral manifestations could be represented by: local abnormal colour of the gum, gingival petechiae, ecchymosis, and/or haemorrhage, mucosal ulceration and buccal infections. Dreizen et al. noted that gingival enlargement was encountered up to 4-5% on a sample of 1076 patients with acute leukemia (9). In most cases, the gingival enlargement disappear totally or partially after chemotherapy administration (10). These oral manifestations were reported for acute lymphoblastic leukemia (8), acute myeloblastic leukemia (11), acute myelomonocytic leukemia (12), acute myeloid leukemia (13, 14), and acute lymphoblastic leukemia (14). The specific/local treatment methods of oral lesions include: oral hygiene, topical solutions, gingivectomy, etc. Dental physicians often resort to interdisciplinary consults, to

In the above figures there are presented oral manifestations encountered in a 47 years old patient with acute myeloblastic leukemia, consisting in generalized gingival enlargement, ulcerations covered by fibrinous deposits, spontaneous and induced bleedings.
complete his oral diagnosis and treatment with specific procedures (as described above) that could highlight/contribute to diagnosis of a possible coexisting systemic disease, such as leukemia. In our practice the most required were hematologic evaluations/ consults, but we had also cases who developed depressive symptoms (that required psychological/ psychiatric support) when were informed about possibility that a severe systemic disease could coexist (15).

**Conclusions**

As a conclusion, dentists should be advised not only to recognize and treat the oral lesions which are encountered, but also to refer the patient to specialized professionals for additional tests/ investigations when suspect that a systemic disease would be the cause of the respective oral manifestations (16).

In respect to oral lesions due to acute leukemia, the gingival enlargement (the most frequent encountered) disappeared totally or partially after administration of chemotherapy and topical/ oral solutions. Such cases require in our opinion an interdisciplinary approach for a complete diagnosis and therapeutic management, including but not necessarily limited to: dental physicians, haematologists, psychologists and internists (for coexisting affections- heart, lung, etc.) (17).
Disclosure

No authors involved in the production of this article have any commercial associations that might pose or create a conflict of interest with information presented herein.

References


