Remarks on Odontogenesis in Children After Chemo-radiation Therapy

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Introduction: Leukemias are the most frequent forms of neoplasias in children. The oral complications that occur in time, after the specific treatment through chemotherapy or radiotherapy, are represented by the occurrence of multiple carious lesions, disorders of dental eruptions, the premature loss of the primary teeth, anomalies in the development of teeth.
Material and method: Through the clinical examination of the oral cavity and through radiological examination, with the help of the orthopantomogram, we revealed the disorders of dental development consecutive to the cytostatic therapy and radiotherapy in the acute lymphoblastic leukemia.
Results: The specific treatment through chemotherapy and radiotherapy overlapped with important stages of the physiological process of odontogenesis. We noted ageneses, microdontias, precocious eruptions and disorders of the eruption order.
Conclusions: The cytostatic medication and radiotherapy can be followed by anomalies in the development and eruption of the dental buds. The severity of these secondary effects varies according to the patient's age at the moment of the start of the specific therapy, the stage of dental development, the type of cytostatic medication and the dose and frequency of treatment cycles.

Keywords: leukemia, chemotherapy, radiotherapy, dental development

Introduction

Malignant tumors represent the main cause of mortality in children aged 0–14 years, reaching a large incidence in the first years of life. Leukaemias are the most frequent forms of neoplasias in children, accounting for 40% of the malignant affections in children under the age of 16 [1].

The occurrences at the level of the oral cavity are clear. They are determined both by the leukaemia affection in an indirect way, being secondary to thrombocytopenia, anaemia and neutropenia, as well as the specific chemotherapeutical treatment, representing the precocious, drug specific complications. The complications occurring at the level of the oral cavity during chemotherapy and radiotherapy are very frequent and are represented by toxic mucositis or gingivostomatitis, dentine sensitivity, hyperplasias and gingival bleedings, ulcers, bacterial, fungic and viral infections [2]. The complications that occur in time refer to the explosion of carious lesions, disorders of dental eruptions, dental mobility, premature loss of primary teeth, anomalies of dental development [3].

The aim of this paper is to evaluate dentition and to reveal the dental development disorders in a clinical case with acute lymphoblastic leukaemia. This case presents a peculiar interest because the specific protocols of chemotherapy and radiotherapy interfered with the physiological process of odontogenesis over a very lengthy period, when the formation and mineralization of an important number of dental buds took place.

Material and method

The disorders of dental development in a 10.5 year old child have been revealed. The child was investigated at the age of 2 years and 4 months, the patient being admitted for joint and bone pains that started 2 months before, fever which started 2 weeks before, and adynamia. Based on the hematological picture and on the examination of the peripheral smear, the examination of bone marrow and the immunophenotypical examination through flow cytometry, the patient was diagnosed with acute lymphoblastic leukaemia with pre B cells. Figure 1 presents the immunophenotypical profile of the lymphoblasts, and Table I contains the patient's laboratory examinations.

Protocol of oncological treatment and evolution: cytostatic treatment according to protocol ALL-BFM-95 followed by the maintenance treatment, but under this medication the patient presented the first isolated relapse in the

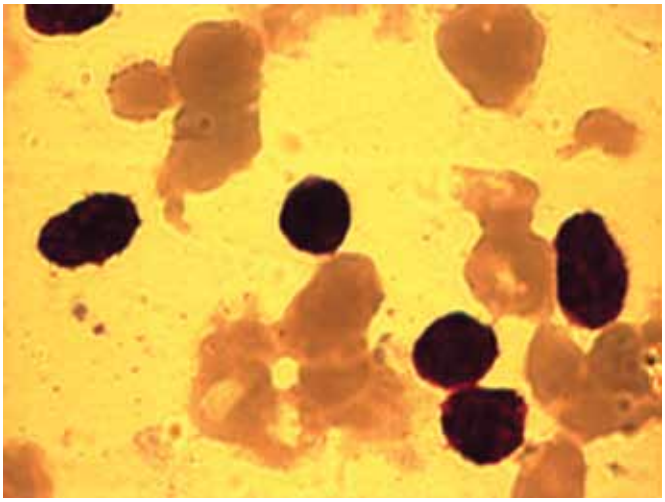

Fig. 1. Bone marrow infiltrated with pre B lymphoblasts

Table I. Laboratory data

Examination of bone marrow:	Hgb 7.5 g/dl
74% cells with aspect of lymphoblasts	Htc 22.5%
	Leucocytes 4500/mm³
Peripheral smear:	Neutrofiles 400/mm³
Atypical lymphocytes 9%	Trombocytes 120000/mm³
	VSH 60 / I h PCR positive
	LDH 527 U/ l

Table II. The clinical and radiological examination of the mouth

Clinical examination of the mouth	Radiological examination
Mixed dentition with replacement of the teeth in the support areas	Agenesis 15, 35
Deciduous molars present: 54, 64, 65, 75, 84, 85	Microdontia 14, 24, 34, 44
Mobility: 54, 64	Gracile roots 36, 46
Canines 33, 43 erupted; 13, 23 eruption in progress	
Precocious eruptions 13, 23	
Eruption order 13 → 14 and 23 → 24, 25	

CNS; treatment according to protocol ALL-REZ-95 and therapeutic cranial radiation; after a period of 2.5 years we noticed the second systemic relapse, treated according to the specific protocol for relapse; after another 3 months the patients presented the third CNS relapse; at the moment the patient receives palliative treatment.

Results

The examination of the oral cavity revealed a status with mixed dentition in the replacement phase of the side teeth, the persistence of some deciduous molars (Figure 2), physiological mobility of the first upper primary molars, the eruption of permanent lower canines and the start of the eruption of upper canines, the microdontia of the left lower first premolar, unfavourable sequences of eruption with the emergence of the right upper canine before the first premolar and the left upper canine before both premolars, precocious eruptions of the upper canines, coronary destruction of the left side upper secondary incisor. The radiological examination indicated the agenesis of the right upper secondary and left lower premolar, microdontias at the level of the first premolars, the gracile roots of the first permanent molars (Table II).

The complex dental diagnosis consists in simple and complicated multiple untreated caries, orders of unfavorable eruptions, precocious eruptions, ageneses, microdontias; the incriminated etiological factors are represented by the deficient oral hygiene, chemotherapy and radiotherapy. The dental therapy: the patient benefited from the treatment of carious lesions, endodontic treatment followed by the radicular obturation and physionomical restoration of the side incisive, training regarding the hygiene of the mouth and professional brushing.

Discussion

The physiological process of odontogenesis starts in the first weeks of intrauterine life and continues until the age of 14–15 years. The effective curative treatment of acute lymphoblastic leukaemia in children, through chemotherapy and radiotherapy, overlaps with the important stages in odontogenesis [4]. Dental maturation represents a complex process that takes place over a long period of time and includes a series of important stages that each dental bud experiences in its evolution. Vasconcelos et al. [5] indica-ted the fact that there would be 8 distinct development stages and they appreciated the degree of dental maturation on a cohort of 92 children with acute lymphoblastic leukaemia, who followed a curative treatment according to protocol ALL-BFM-95, through comparing the chronological age of the children included in the study with the dental age, appreciated according to the stage of teeth development. The authors noticed that there are significant inconsistencies between the chronological ages and the dental ages as indicators of dental maturation, in children who followed the cytostatic medication and radiotherapy. The presentation of our clinical case revealed the fact that the child's chronological age does not coincide with his dental age, as there are severe problems of eruption order as well as the precocious eruption. The cytostatic treatment and the therapeutical cranial irradiation interfered with the processes of radicular building of the primary teeth from the support areas (canines, first and second deciduous molars), so that the roots of these teeth presented stressed resorption, before the physiological age. The consequences consisted in premature losses of these teeth and precocious eruption of the permanent replacement teeth.

Minicucci et al. appreciated the frequency of dental anomalies on a cohort of 76 children with acute lymphoblastic leukaemia who followed specific chemotherapy with or without cranial radiotherapy [6]. Of all the 76 children, 13 did not present any anomaly of dental development, but 8 of them were only at the formation age of dental germs; the rest of 82.9 % presented at least one dental anomaly. The patient described by us presented microdontion in all the four first premolars and stressed eruption of the permanent teeth due to the premature loss of deciduous teeth. The radiosensitivity of teeth in formation was also proved by other authors [7,8,9] who showed that the nature and effects of the potential negative effects of therapeutical irradiation upon dental development varies according to the child's age at the moment of diagnosis with acute leukaemia and start of the spe-

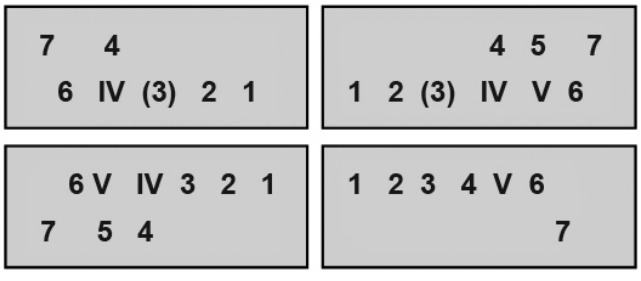

Fig. 2. Dental formula at age 10.5 years old

cific therapy, the stage of tooth development, the treatment protocol and the irradiated anatomical region. The adverse effects of radiotherapy upon the dental buds in formation are represented by the destruction of the dental bud, the block of the eruption potential of the tooth, troubles of mineralisations, insufficient coronary or radicular development, radicular agenesis, the occurrence of well built and dull [10]. In the present case, the formation of the first and second premolars started around the age of 2, life stage that coincided with the diagnosis of the acute lymphoblastic leukaemia pre B and with the establishment of the cytostatic treatment according to protocol ALL-BFM-95. Practically the whole process of mineralisation and development of first and second premolars interfered with the cytostatic medication and the therapeutical cranial irradiation. The influence of the cytostatic treatment and radiotherapy upon odontogenesis manifested through the insufficient development of all the first premolars as well as the lack of development of the second premolar buds 15 and 35.

Conclusions

The clinical case presents a particular interest because the curative cytostatic treatment and the cranial irradiation extended on a long time span, while the stages of odontogenesis were fulfilled in the child's life.

From the pediatric dentist's point of view, this case proves on one hand the need to monitor children with leukemic conditions under cytostatic treatment and radiotherapy with the aim to improve the state of orodental health, and on the other hand, it reveals the impact of the curative treatment upon the processes of dental development and mineralisation.

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