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Root Anomalies after Combined Chemotherapy Treatment for Acute Lymphoblastic Leukemia during Childhood: A Case Report

Talia Becker, Ella Lalum, Avi Levin, Joe Ben Itzhak, Idan Stiklaru, and Michael Solomonov

ABSTRACT

Dental abnormalities have been sporadically reported in patients treated as children for acute lymphoblastic leukemia (ALL) with multi-agent chemotherapy, with and without radiation. Reports included delayed dental development, microdontia, hypoplasia, agenesis, V-shaped roots, shortened roots, and cervical root resorption. These anomalies in pediatric patients require regular dental follow-up and sometimes highly complex treatment. We describe a well-documented case of a 19-year-old male who presented with such anomalies 12 years after treatment with several chemotherapy agents for ALL, and discuss the resultant disruption of normal tooth development that led to the ensuing abnormalities.

Keywords: Acute lymphoblastic leukemia, dental abnormalities, multi-agent chemotherapy, shortened roots, tooth development.

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I. Introduction

Chemotherapy and radiotherapy are widely used for the treatment of acute lymphoblastic leukemia (ALL). When one or both are administered during the period of tooth formation, they have the potential to affect critical stages of odontogenesis [1]-[8] with specific effects on the developing dentoalveolar complex dependent on the patient's age and treatment duration. Indeed, delayed dental development, microdontia, hypoplasia, agenesis, V-shaped roots, shortened roots, and cervical root resorption were all speculated to be related to chemotherapy during childhood [1], [2]. Histology studies showed that chemotherapy induces mainly qualitative disturbances in dentine and enamel, whereas total body irradiation induces both qualitative and quantitative changes [4].

We describe a well-documented case of a 19-year-old male who presented with dental abnormalities, most probably related to treatment as a 5-year-old child with combined chemotherapy for ALL.

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II. Report

This case report has been written according to Preferred Reporting Items for Case reports in Endodontics (PRICE) 2020 guidelines.

A 19-year-old male was referred to our endodontics clinic for consultation regarding their right lower first molar. Following a diagnosis of ALL at age 5, he was treated with a chemotherapy combination of mercaptopurine (6-MP), cyclophosphamide, cytarabine, daunorubicin, doxorubicin, L-asparaginase, vincristine, high-dose methotrexate (20,000 mg/m^2), and a high dose of corticosteroids. Radiotherapy was not part of the treatment protocol. Chemotherapy was administered for two years (Feb 2007 - Feb 2009), after which the patient was defined as in remission, and proceeded to lead a normal life.

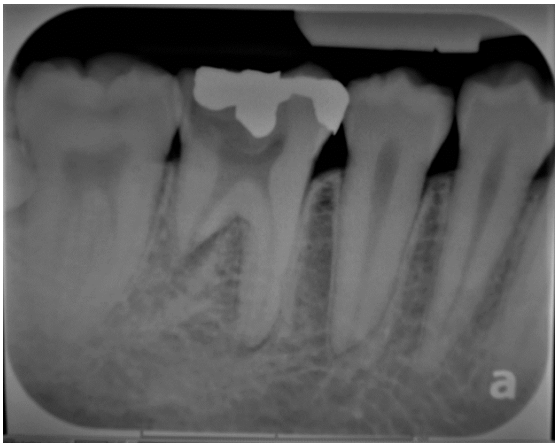

Fig. 1a. Pre-treatment radiographic image, right lower first molar. Shortened and tapered distal root and a radiolucent periapical area in the mesial root are evident.

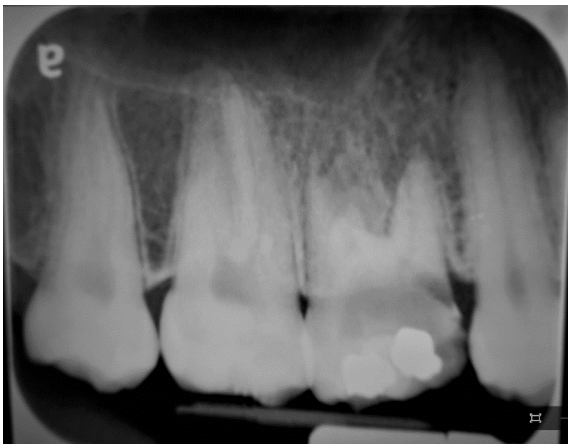

Fig. 1b: Radiographic image, right upper first molar. Shortened roots are evident.

The right lower first molar responded for more than 20 seconds to cold test (Endo-frost, Coltene /Whaledent AG, Altstätten, Switzerland), and positively to electric pulp testing (Digitest II, Parkell Inc., NY, USA). There was no sensitivity to percussion or palpation. Pocket depths were within normal limits and no swelling or sinus tract were evident. Radiographic examination (Fig. 1a) demonstrated significantly shortened and tapered distal root of the right lower first molar (less than half as compared to the lower second molar), and a radiolucent periapical area in the mesial root. The tooth was diagnosed with asymptomatic irreversible pulpitis and asymptomatic apical periodontitis with shortened tapered distal root. The right upper first molar (Fig. 1b) exhibited extensive crown caries and shortened tapered roots, with a radiolucent periapical lesion surrounding the apex of the mesiobuccal root. The left upper first molar (Fig. 1c) exhibited mildly shortened and tapered roots and no periapical radiolucency. The left lower first molar (Fig. 1d), which had been endodontically treated a few years earlier, exhibited mild shortening of both roots.

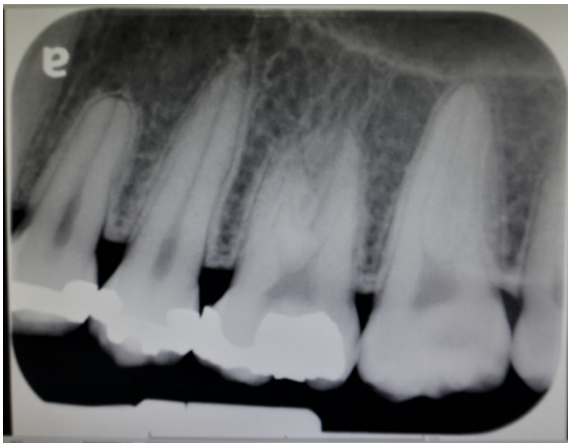

Fig. 1c: Radiographic image, left upper first molar. Incomplete roots are evident, with no apparent pathological apical lesion.

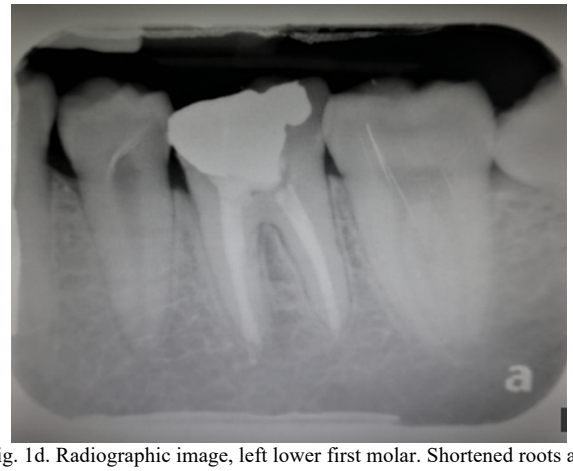

Fig. 1d. Radiographic image, left lower first molar. Shortened roots are evident, after sound root canal treatment a few years earlier, with no apparent pathological apical lesion.

The treatment plan was extraction of the right upper first molar, endodontic treatment of the right lower first molar, and regular follow-up on the left lower and left upper first molars.

Following signed consent from the patient, local anesthesia was applied via local infiltration with one 1.8 mL cartridge of 4% articaine with 1:100,000 epinephrine (Septocaine, Septodont Inc., Louisville, CO, USA). The rubber dam was applied with clamp on the right lower first molar. After access cavity preparation, working lengths (WLs) were obtained with an electronic apex locator (EAL) (Apit 11, Osada Electronic Co., Tokyo, Japan) and a periapical radiograph in mesial canals. Because the EAL was unstable in the distal canal [9], WL was determined by direct operating microscope observation and periapical radiograph into the open apex (Fig. 2a). The distal root canal contained necrotic pulp tissue, and mesial canals contained

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vital pulp-conditions indicative of pulp necrobiosis [10]. The medial canals were widened to ISO size 15# using stainless steel files (K-Files, Kerr dental, CA, USA). Further chemo-mechanical preparation of the root canals was performed according to the DC Taper NiTi Rotary File System (SS White Dental, NJ, USA), up to size 30/06, followed by the XP-endo Finisher (FKG Dentaire, La Chaux-de-Fonds, Switzerland). The distal canal was prepared with XP-endo Finisher R (FKG Dentaire, La Chaux-de-Fonds, Switzerland), irrigated with sodium hypochlorite 3% (NaOCL), and final irrigation was with ethylenediaminetetraacetic acid 17% (EDTA). A calcium hydroxide dressing was applied and remained in place for 4 weeks. The access cavity was double sealed with Cavit (3M ESPE) and IRM (Dentsply Caulk, Milford, DE, USA). At a second appointment, the calcium hydroxide dressing was removed using the XP-endo finisher with NaOCL 3%, followed by EDTA 17% rinses. EndoSequence BC RRM putty (Brasseler USA, Savannah, GA, USA) provided an artificial plug in the apical 4 mm of the distal canal (Fig. 2b). SuperEndo-Beta (B&L BioTech) and EndoSequence BC sealer (Brasseler, Savannah, GA, USA) were used to obturate the middle and coronal parts of the distal canal, and the mesial canals were obturated by EndoSequence BC sealer (Brasseler, Savannah, GA, USA) with gutta percha.

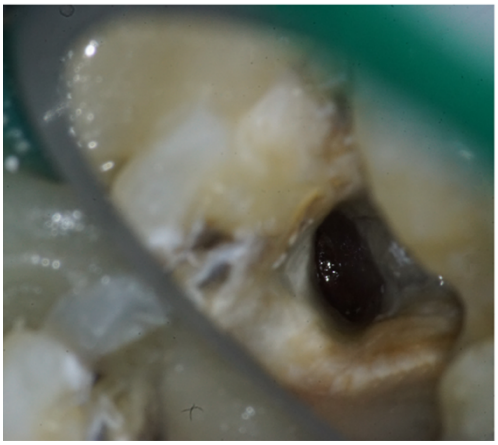

Fig. 2a. The open apex of the distal root of right lower first molar. Clinical image through the operating microscope during endodontic treatment.

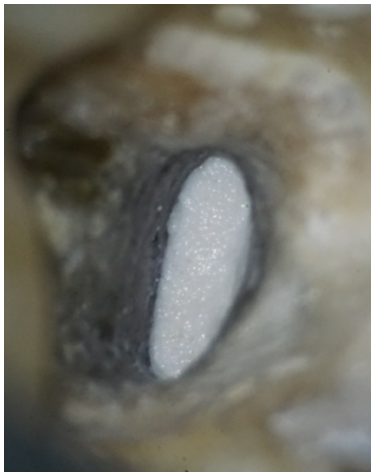

Fig. 2b. Right mandibular first molar. Clinical image through the operating microscope during endodontic treatment after apical plug of the distal root canal.

At 6-month follow-up (Fig. 3), the right lower first molar was clinically asymptomatic, with no evidence of swelling or sinus tract. There was no sensitivity to percussion or palpation, no periodontal pockets upon probing, and mobility was normal.

Signed informed, valid consent was given by the patient for publication of the case in the scientific literature.

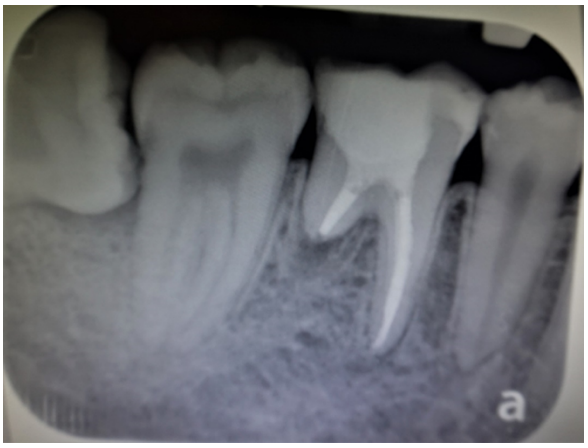

Fig. 3. Post treatment radiographic image, right lower first molar.

III. Discussion

The final diagnosis in our case was pulp necrobiosis. A tooth with necrobiosis has both inflamed and necrotic (usually infected) pulp tissue. Many dentists use the term “partial necrosis” for this stage of the disease process but the suggestion of [11] of “necrobiosis” more accurately describes the condition, in which the key factor in its spread is the presence of bacteria within the necrotic part of the pulp and not the necrosis of part of the pulp. The necrotic tissue may be in the coronal portion of the pulp with the inflamed tissue located apically, or the different tissue states may exist in different canals of a multi-canal tooth [10].

Data on the long-term effects of cancer therapy on dental growth in pediatric patients are limited. It is well established; however, that chemotherapy interferes with cell cycle and intracellular metabolism and may thereby cause retarded dental development, microdontia, enlarged pulp chambers, and root stunting [1]. A number of factors contribute to the development of these and other dental abnormalities, including the type of treatment administered (chemotherapy, which agents, with and without radiation), and the age at which the child received the treatment.

Calcification begins within 1 year of birth for permanent incisors and first molars, and 1-3 years of age for premolars and second molars. The crowns are completed at 2-8 years of age and the roots are completed by the age of 16. Thus, it is likely that children undergoing chemotherapy below 8 years of age are at risk for tooth agenesis or microdontia, and between 8 and 16 years for short-rooted teeth [12]. Our patient received chemotherapy at 5-7 years of age, but the effect on his dentition was limited to shortened roots of the first molars, with no apparent tooth agenesis or microdontia. Discrepancy between chronological and dental age can explain our findings.

In a study by [12] short-rooted teeth occurred in subjects

who had undergone chemotherapy at ages younger than 11.8 years. There were more incidences of tooth agenesis, microdontia, and short-rooted teeth, as well as higher tooth formation anomaly scores, in the high-dose chemotherapy (HDC) groups as compared to conventional chemotherapy groups.

Research has demonstrated developmental disturbances in both enamel and dentin after courses of chemotherapy [4]. The distribution of incremental lines in the enamel were found to correspond to periods of treatment with vincristine, doxorubicin, and methotrexate combined with arsparginase, mercaptopurin, and cyclophosphamide [4]. The enamel and dentin in areas developed after chemotherapy were mostly normal in size, indicating that cytotoxic drugs induce mainly qualitative abnormalities during tooth formation. However, disturbances in root development, such as short, tapered roots, have also been reported in patients treated solely with high dose chemotherapy. Studies have also reported more enamel opacities in patients receiving combination chemotherapy as compared to controls [13]-[15].

The protocol of the chemotherapy, with and without radiotherapy, also has a strong effect on later tooth development. In a study of children treated for ALL with and without radiotherapy, [16] observed dental abnormalities in 50% of the patients who received both chemotherapy and radiotherapy as compared to only 25% of the chemotherapy alone group. These abnormalities included root stunting, microdontia, hypodontia, enlarged pulp chamber, and over-retention of primary teeth. Reference [1] studied three groups of patients with different treatment protocols: Group I - high-dose chemotherapy and cranial radiotherapy; Group II - low-intensive chemotherapy with no cranial radiotherapy; and Group III - high doses of methotrexate with no radiotherapy during induction and re-induction. The dental abnormalities differed according to the protocols used. Hypoplasia and shortened roots were more common in Group I while higher incidence of microdontia and delayed dental development were seen in Groups II and III.

Other findings reported in the literature include root agenesis following repetitive high doses of some chemotherapeutic agents; 4 tooth agenesis following intensive, repetitive chemotherapy at the time of initial hard tissue formation;4 and shortened, thinned, and blunted roots resulting from altered odontoblastic activity [1], [17].

Conflicting results have been reported on the caries' profiles of children treated for malignant disease. A number of studies reported an increased rate of dental caries [6], [13] [18], while another study [19] found no significant difference in dental caries status between children who received chemotherapy and their healthy siblings. Our patient had several untreated caries' lesions.

Our patient exhibited the shortest roots in the right lower first molar as compared to the other molars. One possible explanation is a combination of shortened roots after chemotherapy combined with the burden of apical inflammatory root resorption, which can also account for the open apex in this patient. Apical inflammatory resorption was detected in 81% of cases with apical periodontitis, in a study on the diagnosis of inflammatory apical root [20]. Shortened roots may direct oral health practitioners to diagnoses related to parafunctions, orthodontics, and other possible triggers of root resorption, resulting in unnecessary examinations and treatments.

IV. Conclusions

Dental abnormalities are documented in pediatric patients treated with chemotherapy for ALL as well as other cancer types that require regular dental follow-up and, sometimes as in our case, complex endodontic treatment. Shortened roots combined with endodontic pathology and apical root resorption may lead to tooth loss. The importance of regular follow-up by a dental practitioner, and the possibility of dental complications that are yet to be found, should be emphasized following treatment. Awareness of dental practitioners to the possible dental consequences of chemotherapy and/or radiation carried out in childhood should be among their first investigations as they search for the etiology of dental abnormalities in these cases.

Conflict of Interest

Authors declare that they do not have any conflict of interest.

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