CASE REPORT

DOI: 10.5336/caserep.2022-93352

Molar-Incisor Malformation in a Pediatric Patient on Chemotherapy Treatment

Büşra Seda İMAMOĞLU[a], Şeniz KARAÇAY[a], Ersin YILDIRIM[a], Barış KARABULUT[b]

[a]Department of Orthodontics, University of Health Sciences Hamidiye Faculty of Dentistry, İstanbul, Türkiye
[b]Department of Pediatric Dentistry, University of Health Sciences Hamidiye Faculty of Dentistry, İstanbul, Türkiye

This case report was presented as a poster at the 26th Turkish Dental Association International Dental Congress, September 8-11, 2022, İstanbul, Türkiye

ABSTRACT Certain chemotherapeutic agents used for malignancies in early childhood may cause abnormal tooth and root development. The panoramic examination of a patient who received chemotherapy for hepatoblastoma at the age of 18 months showed maxillary and mandibular first molars with clinically normal-looking crowns and insufficient root development, which were diagnosed with molar-incisor malformation (MIM). The review of the patient's medical file revealed that the chemotherapeutic agents causing the root anomaly were the combination of doxorubicin and cisplatin. The aim of this case report is to evaluate the relationship between MIM, and multiple chemotherapeutic agents used in early childhood.

Keywords: Cisplatin; doxorubicin

Chemotherapeutic agents used for the treatment of children with cancer can lead to various complications affecting the oral cavity. These drugs used in the oncological treatment of pediatric patients are not selective because they have a low therapeutic index and also damage healthy cells. In order to minimize drug-related complications, chemotherapeutic agents with different mechanisms can be used together during treatment.[1]

During chemotherapeutic treatment, an interaction occurs between the physiological cycle of cells with special functions in the formation and mineralization of tooth structures and cytostatic agents. Cytostatic drugs are agents that halt the proliferation of cancer cells without killing cancer cells. Although these agents can prevent the development of metastases by stopping the growth of tumors, dental anomalies may occur depending on the child age at treatment initiation, the type, dose and frequency of the cytostatic drug.[2,3]

Due to the proliferation of dental stem cells before the age of 5 years, children receiving chemotherapeutic treatment during this period are at greater risk for odontogenic developmental anomalies.[4,5] Although it has been reported that odontogenic toxicities caused by chemotherapy agents cannot be fully predicted, it is important for the patient's oral and dental health to seek consultation from a dentist before chemotherapy, to evaluate dental anomalies by performing a radiographic dental examination, and to plan the treatment approach accordingly.[2]

CASE REPORT

The oral examination of a 12-year-old female patient who presented to our department with crowded teeth revealed Class I malocclusion, increased overbite, crowding in the mandibular anterior region, and crossbite of the maxillary lateral teeth. The panoramic examination showed that the permanent second premolar was impacted due to the persistence of the primary tooth 85, with root anomaly in all permanent first molars (Figure 1A, 1B). The anomaly was diagnosed with molar-incisor malformation (MIM) since the stunted and insufficient root

Correspondence: Büşra Seda İMAMOĞLU
Department of Orthodontics, University of Health Sciences Hamidiye Faculty of Dentistry, İstanbul, Türkiye
E-mail: dt.busraimamoglu@gmail.com

Peer review under responsibility of Turkiye Klinikleri Journal of Case Reports.

Received: 12 Oct 2022 ***Received in revised form:*** 10 Jan 2023 ***Accepted:*** 11 Jan 2023 ***Available online:*** 23 Jan 2023

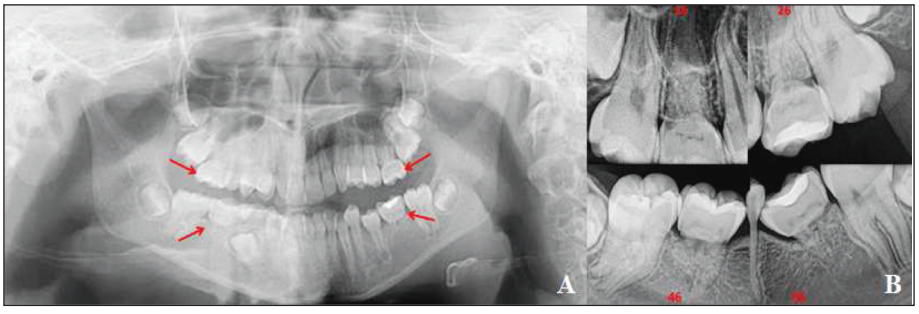

FIGURE 1: Panoramic radiograph before orthodontic treatment **(1A)**. Periapical radiographs of teeth 16, 26, 36 and 46 **(1B)**. The anomaly was diagnosed with molar-incisor malformation since the stunted and insufficient root development of the permanent first molar teeth was accompanied by a clinically normal-appearing crown and abnormal pulp chamber.

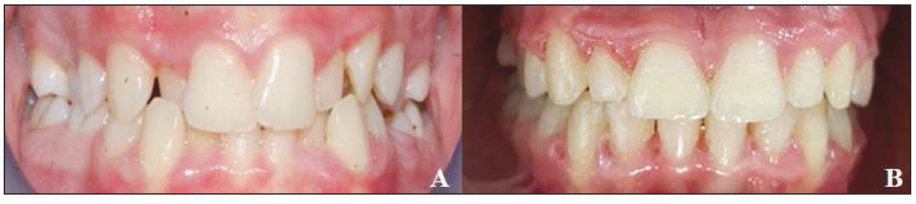

FIGURE 2: Intraoral photographs of the patient before **(2A)** and after **(2B)** orthodontic treatment.

development of the permanent first molar teeth was accompanied by a clinically normal-appearing crown.

Informed consent was obtained from the parents of the patient before treatment. After obtaining permission from the parents to determine the cause of the root anomaly in the first molars, the patient's medical file was reviewed and it was learned that she was diagnosed with hepatoblastoma at the age of 18 months; the needle biopsy revealed a tumor of fetal epithelial type. It was found that our patient was given chemotherapy with doxorubicin and cisplatin after the diagnosis and the right lobe of the liver was operated on 6 months after the oncological treatment started. Following her treatment, which lasted for 8 months in total, our patient oncologically recovered.

The Hays-Nance model analysis results of our patient revealed 3.5 mm maxillary crowding and 4.5 mm mandibular crowding, and non-extraction orthodontic treatment was planned. It was considered appropriate to leave permanent first molar teeth in the patient's mouth as they were non-mobilized, periodontally healthy, asymptomatic, and had clinically normal-appearing crowns. After 24 months of fixed orthodontic treatment, anterior crowding, cross-bite and increased overbite of the maxillary lateral teeth were corrected (Figure 2A, 2B). After the completion of the fixed orthodontic treatment, the patient was initiated on reinforcement treatment with clear aligners and invited for follow-ups every 6 months.

DISCUSSION

MIM was first described in 2014 as an anomaly that radiographically resembles dentin dysplasia Type 1b.[6] MIM, also known as a molar root-incisor malformation, typically involves normal crowns with short and underdeveloped roots, and is mostly seen in permanent first molars.[7,8]

Although the etiology of MIM remains unknown, it is thought to be caused by an environmental factor that is not genetic and may be related to medical history as root malformations are limited to isolated teeth. The most important finding of systemic disorders associated with MIM has been reported to be central nervous system disorders seen at the age of 1-2 years.[7] A significant portion of patients affected by MIM has a history of neurological sys-

temic diseases such as meningitis, or idiopathic brain diseases. Another less frequently defined condition is preterm birth.[7,8] Kim et al. stated that intensive antibiotic use during critical periods of tooth development may be one of the factors causing MIM.[9]

In the presented case report, it is believed that MIM occurred due to combination of doxorubicin and cisplatin. MIM was not noted in any other family member. Animal studies have shown that chemotherapy, with its detrimental effect on mitotic activity in preodontoblasts, disrupts the development of the Hertwig epithelial root sheath, causing abnormal and stunted roots, and it is thought that the reason for the closure of the apexes is the formation of osteodentin in this region.[10,11] As a result of micro-computed tomography examination of 5 permanent first molars diagnosed with MIM, abnormal osteodentin-like hard tissue was detected.[12]

In our patient, mandibular first molars were affected by the anomaly more than maxillary molars. In all reported cases, permanent mandibular first molars were affected, and in the vast majority of individuals, all four first molars were affected by this anomaly. This can be explained by the increased susceptibility of mandibular first molars to MIM and earlier onset of their root development compared to maxillary first molars.[13]

Since MIM is a relatively new anomaly, there is no definitive treatment method in the literature yet. According to the current situation of the case, the doctor, patient and family should decide on the treatment method jointly. While making the decision to extract these teeth; factors such as the presence of caries, apical lesions, periodontal damage, mobility, and third molars, the amount of crowding in the dental arch, sagittal molar relationship, malocclusion and skeletal profile of the patient should be evaluated. If bone loss or endodontic lesions have developed in these teeth, the patient has an open bite, hyperdivergent skeletal pattern, severe crowding, and the third molars are not missing, extraction of the teeth affected by MIM is considered appropriate. In this case, since the amount of crowding in the dental arch did not require tooth extraction, the patient had Class I malocclusion and these teeth were asymptomatic, so we planned orthodontic treatment non-extraction and continued the patient's routine follow-up.[14]

Recommend the use of appliances that minimize the risk of root resorption, the application of lighter forces, and the choice of the simplest treatment option and terminating the treatment earlier than normal to reduce the complications that may develop secondary to orthodontic treatment in patients who have received chemotherapy.[15] During our patient's orthodontic treatment, care was exerted to work with minimum forces to prevent possible root resorption and first molars were not included in the fixed treatment due to insufficient root support.

Following oncological treatments, the dental treatment approach of children should be multidisciplinary, and if necessary, should be consulted by pediatric oncology doctors before treatment, dental treatment planning should be shaped after taking a detailed medical history and reviewing the medical file. It should be taken into account that early cancer treatments may cause root anomalies as well as anomalies in the shape and number of teeth, and a detailed radiological assessment should be carried out before orthodontic treatment planning.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Büşra Seda İmamoğlu, Şeniz Karaçay;* ***Design:*** *Büşra Seda İmamoğlu;* ***Control/Supervision:*** *Şeniz Karaçay;* ***Data Collection and/or Processing:*** *Büşra Seda İmamoğlu;* ***Analysis and/or Interpretation:*** *Ersin Yıldırım, Barış Karabulut;* ***Literature Review:*** *Büşra Seda İmamoğlu;* ***Writing the Article:*** *Büşra Seda İmamoğlu;* ***Critical Review:*** *Şeniz Karaçay.*

REFERENCES

1. Krasuska-Sławińska E, Brożyna A, Dembowska-Bagińska B, Olczak-Kowalczyk D. Antineoplastic chemotherapy and congenital tooth abnormalities in children and adolescents. Contemp Oncol (Pozn). 2016;20(5):394-401. [Crossref] [PubMed] [PMC]
2. Kaste SC, Goodman P, Leisenring W, Stovall M, Hayashi RJ, Yeazel M, et al. Impact of radiation and chemotherapy on risk of dental abnormalities: a report from the Childhood Cancer Survivor Study. Cancer. 2009;115(24):5817-27. [Crossref] [PubMed] [PMC]
3. Rixe O, Fojo T. Is cell death a critical end point for anticancer therapies or is cytostasis sufficient? Clin Cancer Res. 2007;13(24):7280-7. [Crossref] [PubMed]
4. Ubios AM, Piloni MJ, Cabrini RL. Mandibular growth and tooth eruption after localized x-radiation. J Oral Maxillofac Surg. 1992;50(2):153-6. [Crossref] [PubMed]
5. Sonis AL, Tarbell N, Valachovic RW, Gelber R, Schwenn M, Sallan S. Dentofacial development in long-term survivors of acute lymphoblastic leukemia. A comparison of three treatment modalities. Cancer. 1990;66(12):2645-52. [Crossref] [PubMed]
6. Witt CV, Hirt T, Rutz G, Luder HU. Root malformation associated with a cervical mineralized diaphragm--a distinct form of tooth abnormality? Oral Surg Oral Med Oral Pathol Oral Radiol. 2014;117(4):e311-9. [Crossref] [PubMed]
7. Lee HS, Kim SH, Kim SO, Lee JH, Choi HJ, Jung HS, et al. A new type of dental anomaly: molar-incisor malformation (MIM). Oral Surg Oral Med Oral Pathol Oral Radiol. 2014;118(1):101-9.e3. [Crossref] [PubMed]
8. Wright JT, Curran A, Kim KJ, Yang YM, Nam SH, Shin TJ, et al. Molar root-incisor malformation: considerations of diverse developmental and etiologic factors. Oral Surg Oral Med Oral Pathol Oral Radiol. 2016;121(2):164-72. [Crossref] [PubMed]
9. Kim JE, Hong JK, Yi WJ, Heo MS, Lee SS, Choi SC, et al. Clinico-radiologic features of molar-incisor malformation in a case series of 38 patients: A retrospective observational study. Medicine (Baltimore). 2019;98(40):e17356. [Crossref] [PubMed] [PMC]
10. Näsman M, Hammarström L. Influence of the antineoplastic agent cyclophosphamide on dental development in rat molars. Acta Odontol Scand. 1996;54(5):287-94. [Crossref] [PubMed]
11. Itoiz ME, Lafranchi HE, Cabrini RL. Ultrastructural study of osteodentin formation induced by irradiation. J Biol Buccale. 1983;11(2):109-17. [PubMed]
12. Charisi C, Kodonas K, Keklikoglou K, Arhakis A, Arapostathis KA, Kotsanos N. Morphological, histological, and chemical analysis of first permanent molars with molar incisor malformation. Eur Arch Paediatr Dent. 2022;23(4):601-8. [Crossref] [PubMed]
13. Neo HL, Watt EN, Acharya P. Molar-incisor malformation: a case report and clinical considerations. J Orthod. 2019;46(4):343-8. [Crossref] [PubMed]
14. Korte A, Angelopoulou MV, Yfanti K. Guidance for permanent first molar extraction in molar-incisor malformation: report of two cases. J Dent Child (Chic). 2022;89(1):29-35. [PubMed]
15. Dahllöf G, Jönsson A, Ulmner M, Huggare J. Orthodontic treatment in long-term survivors after pediatric bone marrow transplantation. Am J Orthod Dentofacial Orthop. 2001;120(5):459-65. [Crossref] [PubMed]