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Olgu Sunumu/ Case Report

MICRODONTIA ASSOCIATED WITH THE USE OF RADIOTHERAPY AND CHEMOTHERAPY OF A NON-HODGKIN LYMPHOMA: REPORT OF TWO CASES

NON-HODGKİN LENFOMADA RADYOTERAPİ VE KEMOTERAPİ SONUCU GÖRÜLEN MİKRODONTİ: 2 OLGU SUNUMU

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ABSTRACT

One of the childhood malignancies can be defined as non-Hodgkin lymphomas. These are known as the third most common malignancies in children and adolescents. Burkitt's lymphoma is a poorly differentiated rare and aggressive type of non-Hodgkin's lymphoma. Clinically, this disease occurs mostly in children. The incidence peaks between ages 3-8 years. It is well known that using chemotherapy and radiotherapy procedures could improve the survival rate of these malignant diseases. However, treatments may cause deleterious effects. Dentofacial abnormalities are known as the most common long-term side effects after the usage of chemotherapy and/or radiotherapy procedures in growing patients. These disturbances can be seen in different ways such as arrested root development, disturbances in enamel formation, discolorations, microdontia, anodontia, altered tooth eruption and mandibulary/maxillary hypoplasia. Mainly, several factors such as age, treatment time, radiation dose/ duration time of chemotherapy may effect the outcomes of these side effects. In such studies, dental disturbances have been shown in children who were treated before the ages of 5-6 years. This article reports the long-term alterations on dental development in two patients who had been treated with antineoplastic therapy at the age of 3-6 years. Chemotherapy and radiotherapy procedures were used together. Microdontia and arrested root development were detected in premolar teeth for both patients at follow up periods. These case reports indicated that children who had been exposed to the chemotherapy and/or radiotherapy procedures might have an increased risk of having developmental dental disturbances and should be carefully followed up during the developing dentition.

Key words: Chemotherapy, radiotherapy, pediatric dentistry

ÖZET

Çocukluk döneminde görülen malignensilerden birisi non-Hodgkin lemfoma olarak adlandırılabilir. Bunlar çocukluk ve ergenlik döneminde 3. en sık görülen malignensilerdir. Burkitt lemfoma zor teşhis edilen, nadir ve agresif bir non-Hodgkin lemfomadır. Klinik olarak, bu hastalık en çok çocuklarda görülür. İnsidansı 3-8 yaş arasında zirve yapar. Kemoterapi ve radyoterapi işlemlerinin bu malignant hastalıklarda sağ kalım oranını yükselttiği iyi bilinmektedir. Ancak, tedaviler zararlı etkiler de yapabilmektedir. Dentofasiyal anomaliler büyüme çağındaki hastalarda kemoterapi ve/veya radyoterapi kullanımı sonrası en çok görülen yan etki olarak bilinmektedir. Bu bozukluklar kök gelişiminin durması, mine oluşumunda bozukluk, renklenmeler, mikrodonti, anodonti, diş sürmesinde bozukluk ve mandibuler/maksiler hipoplazi gibi değişik şekillerde görülebilir. Aslında hastanın yaşı, tedavi zamanı, kemoterapinin ve radyasyonun dozu/süresi gibi birkaç faktör bu yan etkilerin sonuçlarını etkileyebilir. Bu tür çalışmalarda, 5-6 yaşından önce tedavi edilen çocuklarda dental bozukluklar gösterilmiştir. Bu makale 3-6 yaş arasında antineoplastik terapiyle (kemoterapi-radyoterapi) tedavi edilen 2 hastada dental gelişimdeki uzun dönem değişiklikler bildirilmektedir. Takip periyotlarında her iki hastada premolar dişlerinde mikrodonti ve kök gelişiminde durma tespit edilmiştir. Bu vaka raporları kemoterapi ve/veya radyoterapi işlemlerine maruz kalan hastaların gelişimsel diş bozuklukları yönünden artmış bir riske sahip olduklarını ve gelişim sırasında dentisyonun dikkatlice takip edilmesine işaret etmektedir.

Anahtar kelimeler: Kemoterapi, radyoterapi, pediatrik diş hekimliği

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INTRODUCTION

Non-Hodgkin lymphomas are the third most common malignancies in children and adolescents, accounting for 10–13% of newly diagnosed cancers in these age groups in most developed countries.[1] Burkitt's lymphoma is a highly aggressive non-Hodgkin lymphoma that has the highest cell proliferation rate among human neoplasms.[2] Clinically, this disease occurs mostly in children. The incidence peaks between ages 3 and 8 years, and males are affected about twice as frequently as females.[3,4]

The prognosis for childhood malignancies has improved, accomplished to a great extent by the combined use of radiotherapy and chemotherapy but chemotherapy and radiotherapy also have deleterious effects.[5] This essay illustrates the effects of chemotherapy and radiotherapy on dentition in children and adolescents.[6] These modalities alone or combination carry, however, the potential of causing organ-system morbidity.[7] One of the most basic problems is the lack of specificity of radiation therapy in respect to diffentiating between neoplastic cells and metabolically active normal cells. Since advances in the therapy of malignant diseases resulted in an improved life expectancy, attention is now increasingly focused on the long-term side effects and treatment-related complications. In growing individuals, the dental sequelae to chemotherapy and radiation are irreversible. Although the immediate effect of chemoradiotherapy to orodental structures is wellknown, limited information exists on the late effects of the treatment to oral health and developing structures.[8] Morphogenesis and calcification of teeth form a sequence of events that begins in utero and continues for 14–15 years**.** Abnormal events that occur during dental development have permanent sequelae that cannot be corrected later. Dental late effects of chemotherapy and/or radiotherapy in childhood may involve several kinds of developmental dental disturbances, including tooth agenesis, microdontia, enamel defects, discolorations, and disturbed root development.[9-13] The impact and severity of these side effects appear to depend on several determinants, e.g. age at the time of treatment, radiation dose or duration of chemotherapy.[14] In several studies, the most extensive dental disturbances (agenesis, microdontia, and root anomalies) have been reported in children who were treated before the ages of 5–6 years.[15] Although some investigations concerning this problem are reported in the literature there still exists no reliable data belonging to the specific long-term consequences of radiotherapy.[10] This article reports the long-term effects of chemotherapy and radiotherapy for treatment of non-Hodgkin lymphoma and Burkitt's lymphoma in two patients at the age of 3 and 6 years.

CASE REPORT

Case One: An eleven year old boy was referred to the Department of Pediatric Dentistry, Karadeniz Technical University from the office of a private dental practice, because of rapidly progressing caries and generalized gingivitis. At the age of three years an NHL had been treated by mantle-field radiotherapy. Chop chemotherapy (cyclophosphamide-doxorubicin-vincristine-prednisolone) between the ages 3 and 6 and 1950cGy radiotherapy to his cranium was applied in 150cGy*13 fractioned doses for one month. The medical history revealed that the patient was in excellent general condition. Dental caries on teeth 16,26,36,46,55,75,85 and mobility on tooth 64, microdontia on teeth 15, 25, 35, and 45 were observed during the radiographic examination. Tooth 64 was extracted and teeth 16,26,36,46,55,75,85 were restored. Teeth 15, 25, 35 and 45 are still being followed up (Figure 1).

Figure 1: Panoramic radiograph following restorations (one-year follow-up)

Case Two: A thirteen year old boy was referred to the Department of Pediatric Dentistry, Karadeniz Technical University from the office of a

private dental practice, because of caries and generalized gingivitis. At the age of four years a BL had been treated by mantle-field radiotherapy. Chop-r chemotherapy (cyclophosphamide-doxorubicin-vincristine prednisolone/rituximab) between ages 3 and 6 and total 4200cGy radiotherapy in 200cGy*21 fractioned dosages were applied for one month to the patient. The medical history revealed that the patient was in excellent general condition. Mobility in tooth 55 and microdontia in teeth 15, 25, 35 and 45 were detected during the radiographic examination. Tooth 55 was extracted and the patient was kept under observation (Figure 2). Three-year follow-up radiographs are presented (Figure 3,4,5,6).

Fluor protector VivAmpoule (Ivoclar vivadent AG, Schaan/Liechtenstein) was applied to all the remaining teeth following extractions in both cases. Oral hygiene recommendations, nutritional and dental health care information were presented to the parents. The patients were called for regular check-up in 6 month intervals. As is known, the growing of jaws and dentition period continues upon the adulthood period. Since the fixed prosthetic requirements were needed for the patients particularly for the teeth associated with microdontia, after considering the growing period, it was decided that waiting the appropriate prosthetic rehabilitation time could be considered as an acceptable way upon the completion of definitive treatment.

Figure 2. Initial radiograph of the affected tooth

Figure 3. Initial radiograph of the affected tooth (Three-year follow-up)

Figure 4. Initial radiograph of the affected tooth (Three-year follow-up)

Figure 5. Initial radiograph of the affected tooth (Three-year follow-up)

Figure 6. Initial radiograph of the affected tooth (Three-year follow-up)

HASTA İÇİN AYDINLATILMIŞ ONAM FORMU

Sizin çocuğunuza Karadeniz Teknik Üniversitesi Diş Hekimliği Fakültesi Pedodonti Anabilim Dalı'nda tedavi işlemleri yapılacaktır. Bölümümüzdeki tedaviniz süresince çocuğunuzun öncelikli olarak dişlerindeki tüm tedavi işlemleri tamamlanacaktır. Çocuğunuzun non hodgkin lenfoma hastalığından dolayı aldığı radyoterapi ve kemoterapinin dişler üzerindeki etkisi incelenmektedir.

Bu klinik vaka raporunda yer almayı kabul ediyorum. Konunun amacı ve sonuçları; karşılaşabileceğim olumlu ve olumsuz yönleri Dr. Özgül Baygın tarafından bana açıklanmıştır.

Katılımcı:

Adı soyadı, unvanı:
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Görüşme Tanığı :
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Katılımcı ile görüşen hekim:

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CONCLUSION

Irreversible dental sequelae due to chemotherapy and irradiation may be observed in growing individuals. Dental defects attributed to chemotherapy include arrested root development and disturbances in enamel formation. The timing of tooth eruption, however, seems to be unaffected by chemotherapy. The most severe and extensive disturbances have been reported in children treated with total body irradiation before 6 years of age.[10] Microdontia has also been reported after antineoplastic therapy, particularly in patients younger than 5 yr of age who received chemoradiotherapy. It might be speculated that the microdontia is caused by the chemotherapy. [15,17]

Like vincristine, cyclophosphamide also affects dental development leading to enamel and dentinal hypoplasia.[18,19] The chemotherapeutic agents, such as vincristine, vinblastin and cyclophosphamide that were commonly administrated to our patients. These agents have been shown to affect odontogenesis.[20] The severity of the effect on odontogenesis appears to be related to the dose injected and the stage in dental development. Short-term experiments show that in the rat incisor, cytotoxicity of a single dose of 40 mg/kg cyclophosphamide appears to be limited to undifferentiated odontogenic mesenchymal cells. As in Burkitt's lymphoma patients, mature odontoblasts and odontogenic epithelium, including ameloblasts, survive a therapeutic dose of cyclophosphamide. For reasons explained by injury to undifferentiated odontogenic mesenchyme arrests" development of basal enamel and dentine which is resumed' when odontogenic mesenchyme regenerates.[21] Thus the incidence 'of clinically' demonstrable dental abnormalities due to cyclophosphamide or a similarly acting anticancer agent would be greatest when it is used in a vigorous regimen early in childhood before the 'differentiation of coronal odontoblasts is completed. Arrested dental development or agenesis of teeth 'could conceivably result if odontogenic epithelium is also destroyed by the particular property of the anticancer agent employed, the intensity of therapy or the effects of the tumour. On the other hand, expansile abnormality of root form, apparently unrelated to chemotherapy, can commonly be demonstrated in sections of teeth from Burkitt's lymphoma patients with jaw lesions.[19]

The dental effects of radiation therapy are known well, although to our knowledge the minimum radiation dose that is harmful to developing teeth remains uncertain. Teeth exposed to a dose as low as 4 Gy have shown some abnormality in patients treated for soft tissue sarcomas of the head and neck.[22] The typical clinical consequences of irradiation on developing human teeth include microdontia, agenesis, and dwarfing of the roots.[23]

The dental consequences depend on the cell sensitivity and the radiation dose. Information regarding microdontia prevalence is scarce, and there are no solid diagnostic criteria for its assessment on panoramic radiographs.[24] Thus, radiographic microdontia assessments after pediatric anticancer treatment have been based on clinical judgment.[10,25] Microdontia, registered from panoramic radiographs is more frequent after pediatric anticancer therapy, ranging from 10%[10,15,16,25] after conventional chemotherapy for hematologic malignancies[16] to 78% after Stem Cell Transplantation in patients with neuroblastoma.[25] Nevertheless, the microdontia prevalence among Stem Cell Transplantation recipients clearly exceeded the microdontia prevalence of 1.9% among healthy Japanese school children as measured from dental casts.[26] Nasman et al.[16] reported a microdontia prevalence of 68% in SCT recipients (n =19 patients) who had a mean age of 6.5 years at diagnosis and 75% in 16 SCT recipients who had a mean age of 6.3 years at the start of treatment.[10] The subjective criteria for the microdontia assessment may explain the difference.

In conclusion the results of this case report show that all devoloping teeth are irreversibly affected by multiagent chemotherapy. The present case indicates that concerning pediatric chemotherapy and radiotherapy recipients emphasize the role of young age at chemotherapy and radiotherapy as a risk factor for late dental adverse effects, which we defined as tooth microdontia. Age seemed to be a stronger risk factor than total body irradiations, although total body irradiations caused additive impairment. Taking these facts into consideration, particular care in the supervision of dental development is recommended after successful treatment of paediatric malignant disease.

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