Chemotherapy Induced Dental Changes in a Child with Medulloblastoma: A Case Report

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We describe the dental findings and therapeutic management of a child aged three years and eight months with medulloblastoma treated by surgical resection at age eight months followed by 20 months of chemotherapy. Thin and short roots of the primary molars were observed, as were microdontia and anodontia of the premolars. The boy suffered from severe early childhood caries (ECC). Dental treatment was carried out under general anesthesia. Follow-up examinations at three, six and twelve months after the initial dental treatment revealed healthy gingival tissue and no new caries. The boy passed away before the next scheduled follow-up dental examination.

Keywords: *Medulloblastoma, child, teeth.*

INTRODUCTION

Medulloblastoma is a primary brain tumor that develops in the cerebellum or posterior fossa, and is composed of primary neuroepithelial cells. This tumor is considered as being the most virulent among brain tumors because of its comparatively rapid spread and for sending metastases to distant parts of the body through the cerebrospinal fluid.[1-4] Medulloblastomas comprise 15%-20% of all brain tumors in children, and are therefore the second-most prevalent tumors after leukemia.[2] The common symptoms and signs in medulloblastoma are headache, vomiting, speaking disorders, drooling, hypotonia, and ataxia. There are sometimes difficulties in walking without support and even paralyses in extreme cases. One of the prevalent complications of this tumor is obstruction of the fourth ventricle, a complication that may lead to hydrocephalus with high intracranial pressure at an early stage.[3] The treatment of choice of medulloblastoma is surgical resection combined with chemotherapy and radiation.[4,5] Radiation therapy attempts to destroy tumor cells with minimal damage to normal tissue, however, any cells in the path of an external radiation beam or near implanted radioisotopes may be affected.[6]

Amelogenesis and dentinogenesis are affected by radiation directed at or near the mouth. Sufficiently high radiation doses cause ameloblast and odontoblast death regardless of their position in the cell cycle. Even non-proliferating odontogenic precursor cells (second and third molars in an infant) may be destroyed, resulting in complete tooth agenesis. The remaining development of partially formed teeth is halted, resulting in tooth and root agenesis. The common oral side effects of radiation consist of infections in the oral cavity, mucositis, bleeding, xerostomia, red and sore mouth, and difficulty in swallowing.

Radiation therapy for young children (under three years of age) may cause other long-term complications which affect their quality of life. These can include: short stature, low intelligence quotient, hormonal disturbances, auditory disturbances and cataract.[7] Because of the complications of radiation therapy, surgery in young children is usually followed only by chemotherapy,[8] which also attempts to destroy tumor cells with minimal toxicity to normal cells. Chemotherapy is selectively toxic to actively proliferating cells by interfering with DNA synthesis and replication, RNA transcription, and cytoplasmic transport mechanisms. Since tumors consist primarily of rapidly proliferating cells, they are more susceptible to chemotherapy.

Developing odontogenic cells that are remote from a tumor are also susceptible to chemotherapy-induced damage. Dental defects attributable to chemotherapy include arrested root development, inhibition of dentin formation, and enamel defects, while tooth eruption times appear to be unaffected.[6] Most reports deal with the effect of radiation therapy on the developing dentition, and there are very few published studies on the effects of chemotherapy alone on the teeth. Maguire et al. found that 60% of children who were treated with chemotherapy had missing teeth, small hypoplastic crowns, and thin roots, in addition to severe dental caries.[9] Purdell-Lewis et al. reported that teeth that were unerupted during the chemotherapy had severe caries after eruption.[10] These children are

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Figure 1. A frontal view of the anterior region before treatment. Note the severity of the caries in the incisors. The sinus tract is visible in the gingiva of the maxillary primary right lateral incisor.

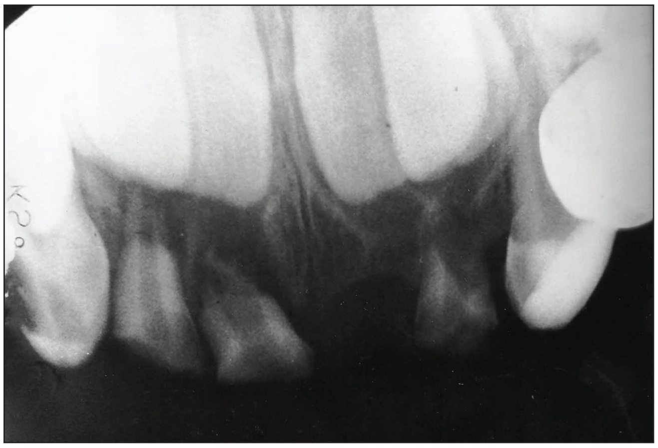

Figure 2. A periapical radiograph of the maxillary anterior region. The primary left incisor is missing. The roots of the other incisors seem resorbed, with periapical radiolucent lesions around them.

therefore considered to be at high risk to develop dental caries. A case of the oral and dental findings of a boy aged three years and eight months with medulloblastoma who was treated by surgery and chemotherapy without radiation is reported. His dental management is described.

Case report

The patient was a boy aged three years and eight months who was referred by his neurologist for consultation to the Department of Pediatric Dentistry, School of Dental Medicine at the Tel-Aviv University, because of severely decayed teeth, especially the maxillary incisors. The boy required a wheelchair and, according to the parents, his intellectual capability was diminished, he had difficulties in speaking, and he understood only simple orders. He had never attended a dental clinic before**.** Medical history revealed that the boy had developed normally until the age of eight months, when he was diagnosed with medulloblastoma of the posterior ventricle. The first expression of the tumor was weakness of the left leg. The tumor was partially resected, and paralysis of both legs developed shortly after that surgery. Metastases along the spinal cord were diagnosed and the boy underwent twenty months of chemotherapy with cytosine arabinoside, methotrexate, and hydrocortisone, once every three weeks. The three-week intervals allowed the stem cells of the bone marrow to divide quickly and compensate for the decreased blood counts. No radiation was performed. He had not been referred for dental treatment earlier.

His extraoral appearance was normal, and intraoral examination of the oral mucosa, hard and soft palate, tonsils, tongue, and mouth floor revealed no pathologic findings. Oral hygiene was extremely poor, and plaque and gingivitis were found around most of the teeth.

The dental examination revealed full primary dentition with the exception of a missing tooth 61 which was not visible on the radiograph. According to the parents, teeth had decayed and exfoliated. All the teeth were carious, and the maxillary incisors were decayed up to the gingiva. The mandibular primary incisors and canines had buccal caries. There were sinus tracts in the maxillary primary incisors (Figure 1).

Radiographic evaluation of the maxillary anterior area revealed root remnants of the three maxillary incisors (teeth 52, 51, 62), with external resorption and periapical lesions (Figure 2). Bite-wing radiographs could not be taken due to the child's lack of cooperation. A panoramic radiograph was also impossible to execute due to the boy's inability to stay still for the 14 seconds that are required by the panoramic machine to rotate.

The boy did not brush his teeth daily nor did he take fluoride supplements. His mother had been giving him a bottle of orange juice to help him sleep since he was one year old, and he arrived to the dental clinic clutching a bottle of orange juice. He was diagnosed as having severe early childhood caries (ECC). The goals of the dental treatment were to eliminate the etiological factors, to treat the lesions and to restore the function of the dentition, as well as to educate the parents on how to establish proper preventive measures.

The dental treatment was carried out with the child under general anesthesia because of lack of cooperation and the extent of required treatment. Bite-wing radiographs could then be taken, and they showed carious primary molars, especially the first primary molars. The second primary molars had thin and pointed roots. All the developing first premolars appeared smaller than normal. The bite-wing radiographs allowed the observation of the full length of the mandibular second primary molars. The tooth buds of the mandibular second premolars could not be clearly identified, however, possible signs of the beginning of their development could be seen (Figures 3, 4). Since the teeth which needed to be treated were fully visible on the available radiographs, it was decided to avoid taking any more at this stage. Treatment included amalgam restorations on the second primary molars, pulpotomy on tooth 64, stainless steel crowns on all first primary molars, esthetic restorations with compomer (Dyract AP, Dyract DeTrey, Dentsply, Konstanz, Germany) on all the canines and on the mandibular incisors, extraction of the three maxillary incisors, and topical application of fluoride varnish (Colgate® Duraphat® Varnish, Colgate Oral Pharmaceuticals, 300 Park Avenue, New York, NY 10022). Meticulous oral hygiene (brushing twice a day with fluoridated toothpaste) and dietary instructions (limiting sweets and sweet drinks, avoiding sweet liquids during the night) were given to the parents, as well as instructions for one-weekly use of fluoride gel (Elmex Gel, GABA International AG, Basel, Switzerland), which was supplied to the parents.

Figure 3. A bite-wing radiograph of the right side. Note the thin tapered roots of the mandibular primary second molar, and the small size of the mandibular first premolar. The mandibular second premolar is not visible. Severe caries is present on the maxillary and mandibular primary teeth.

Figure 4. A bite-wing radiograph of the left side. Note the thin tapered roots of the mandibular primary second molar, and the small size of the mandibular and maxillary first premolars. The mandibular second premolar is not visible. Severe caries is present on the maxillary and mandibular primary teeth.

Follow-up examination at three, six and twelve months after the initial dental treatment revealed healthy gingival tissue and no new caries. Figure 5 shows the anterior region at the 12-month follow-up examination. The gingival tissue appeared to be healthy and no new caries lesions were observed. The child had stopped drinking orange juice at night and now brushed his teeth regularly. Fluoride gel (2% sodium fluoride, Topex® Neutral pH ™, Sultan Healthcare Inc., Englewood, NJ, USA) was applied. Reinforcement of the oral hygiene and dietary instructions was given to the parents at each appointment. The boy passed away before the next scheduled dental follow-up.

DISCUSSION

In the present case, the treatment for a medulloblastoma consisted of surgical resection followed solely by chemotherapy between eight to twenty-eight months of age. Dental treatment was provided three years after the first course of chemotherapy. The pre-treatment radiographic findings had demonstrated that the roots of the primary second molars were thin and tapered, the developing first premolars were small, and the developing second premolars could not be clearly observed.

Normally, the enamel of most of the primary teeth, except for the second primary molars and canines, is usually completed at the age of eight months.[11] The roots of the primary teeth continue to develop until the age of three years. Crown formation of the permanent first molars is completed between the ages of twenty-four to thirty months. Thus, chemotherapy given during this period, as in the present case, may have altered the odontoblastic activity during initial root formation, resulting in thin, tapered roots. In addition, our patient's second premolars and second molars were not visible. Normally, hard tissue formation of premolars begins just before the age of 24 months, while the second molar's hard tissue formation begins between twenty-four to thirty months of age.

The prolonged course of chemotherapy given in the described case may have destroyed the precursor cells of the second premolars and the second molars, thus disrupting initial dentin and enamel matrices, and causing agenesis. The effect on the first and second permanent molars and on the second premolars demonstrates the severity of insult to any actively proliferating cells between the ages of two-three years. Other probable but not radiographically visible defects include local enamel hypoplasias on the incisors, the canines, and the first premolars in areas that are forming at that time. Since development of these teeth continued after chemotherapy in the present case, as expected, the later developing root morphology appeared normal.

Most reports on disturbed development of teeth during treatment for oncologic reasons included patients who received chemoradiation, and the disturbances were attributed to the radiation. Thus, given that no radiation therapy had been administered to the boy in the present case but rather chemotherapy alone, the insult to the developing teeth could be attributed to the tumor itself or to the chemotherapy. The effect of chemotherapy on the dental organ differs from the effect of high-dose radiation therapy: while chemotherapy affects cells in the proliferating stage, even non-proliferating dental cells may be destroyed during radiation. Furthermore, although

Figure 5. A frontal view of the anterior region at the 12-month follow-up examination. The gingival tissue appears to be healthy with no new caries.

radiation only affects cells in its path, the effect of chemotherapy is systemic. Therefore, developing odontogenic cells remote from the tumor are susceptible to chemotherapy-associated damage as well. Due to the short half-life of chemotherapeutic agents, dental defects are usually localized, resulting in transient changes in odontoblast function. Narrow pulp chambers and localized enamel defects may be present. Coronal size and shape are not affected, however, since crown morphology is determined before birth. Chemotherapy given to children with hematological malignancies was found not to interfere with the dental maturity or eruption of permanent teeth.[12] Thus, the eruption time of the permanent teeth in our case would not be expected to be delayed.

The child's unhealthy diet and his poor oral hygiene accounted for the severe ECC, however, it is also logical to assume that the enamel of the primary teeth was more susceptible and prone to caries. The decay had most likely started in his upper front teeth because of the habit of sleeping with a bottle of sweetened liquid. It then would have spread to the lower teeth and upper posterior teeth because of the drop in saliva secretion caused by the chemotherapy. It could be expected to worsen because of the lack of oral hygiene. We urged the parents to stop their child's habit of sleeping with a bottle of sweetened liquid, to improve his oral hygiene, as well as to give him fluoride supplements. Prognosis of the dental treatment in this setting largely depends on the cooperation of the parents and the child. It was therefore important that the child be under long-term, regular supervision by a dentist who could monitor the dental status and encourage appropriate preventive measures.

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