

The effects of anti-leukemic therapy on the developing dentition: case report

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Abstract

The effects of radiation and chemotherapy on the developing dentition of a leukemic patient are described. Microdontia and bizarre morphology were observed in teeth developing in close proximity to the field of radiation. Teeth in more advanced stages of development were affected less severely. However, the deleterious effects of chemotherapy could not be excluded.

The effect of irradiation on human adult and developing teeth has been documented widely.¹⁻¹² However, the effect of chemotherapy is emerging only lately. Chemotherapy is a treatment modality that has been utilized more recently both as the sole treatment or in conjunction with radiotherapy. The effects of radiotherapy usually are confined to the radiation site, but the effects of chemotherapy may be more widespread because of its systemic distribution and structures and organs unrelated to the primary tumor may be affected. These manifestations may become apparent only after a number of years.¹² The present article reports the sequelae of the aforementioned treatments implemented in a leukemic child patient.

Case Report

A 9-year-old girl presented for dental treatment in the Unit for Handicapped Children of the Hadassah Faculty of Dental Medicine. Until the age of 2 years she had been a healthy child. The pregnancy and birth had been uneventful, and the birth weight was 3250 g. Development proceeded normally until age 2 years when she was diagnosed as suffering from acute lymphoblastic leukemia. At that time she was treated with combined chemotherapy and radiotherapy. The

chemotherapy included intrathecal injections of methotrexate which caused the rare complication of quadriplegic cerebral palsy. The cranial irradiation encompassed the field shown in Figure 1.

At age 5, the patient was already in complete hematological remission, when she had dental treatment under general anesthesia. Clinical and radiographic examination revealed the presence of hypoplasia in the primary dentition, indicating a prenatal or early postnatal disturbance, unaccounted for by the medical histories of either mother or child during that period. The right bite-wing radiograph clearly showed the development of the crown of the mandibular second permanent molar, which appeared to be of normal shape but of miniature dimensions (Fig

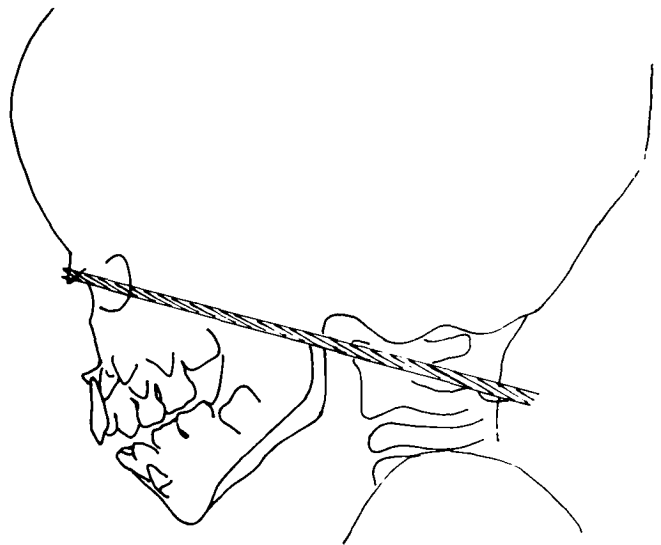


FIG 1. Tracing of lateral skull radiograph showing the field of irradiation (above the shaded line).

2a). The other mandibular teeth appeared to be developing normally. These radiographs, acquired when the patient was under general anesthesia, did not encompass the maxillary permanent tooth germs.

When the child presented at age 9, she was treated with the aid of local anesthesia and premedication. It was not feasible to obtain a panoramic radiograph due to the involuntary movements of the patient. However, lateral oblique and bite-wing films (Figs 2b, 3a & b) revealed that:

1. The mandibular second permanent molars had continued to develop proportionate roots, although the left appeared somewhat peg-shaped
2. The maxillary second permanent molars appeared to be developing in aberrant form and position
3. The roots of the first permanent molars appeared slender in comparison to their crowns

4. The maxillary left second premolar appeared to have a bizarre crown form.

Discussion

The effects that early irradiation can have on the development and eruption of teeth in humans have been listed by Pindborg.⁸ These effects are related to dosage, period of exposure, stage of tooth development, and the proximity of the teeth to the center of maximum dosage.⁹ The effects may include:

1. Complete absence of teeth
2. Arrested tooth formation
3. Microdontia
4. Altered morphology of the crown
5. Shortness and tapering of roots
6. Narrowing of the pulp canal
7. Widening of the periodontal membrane
8. Delayed tooth eruption.

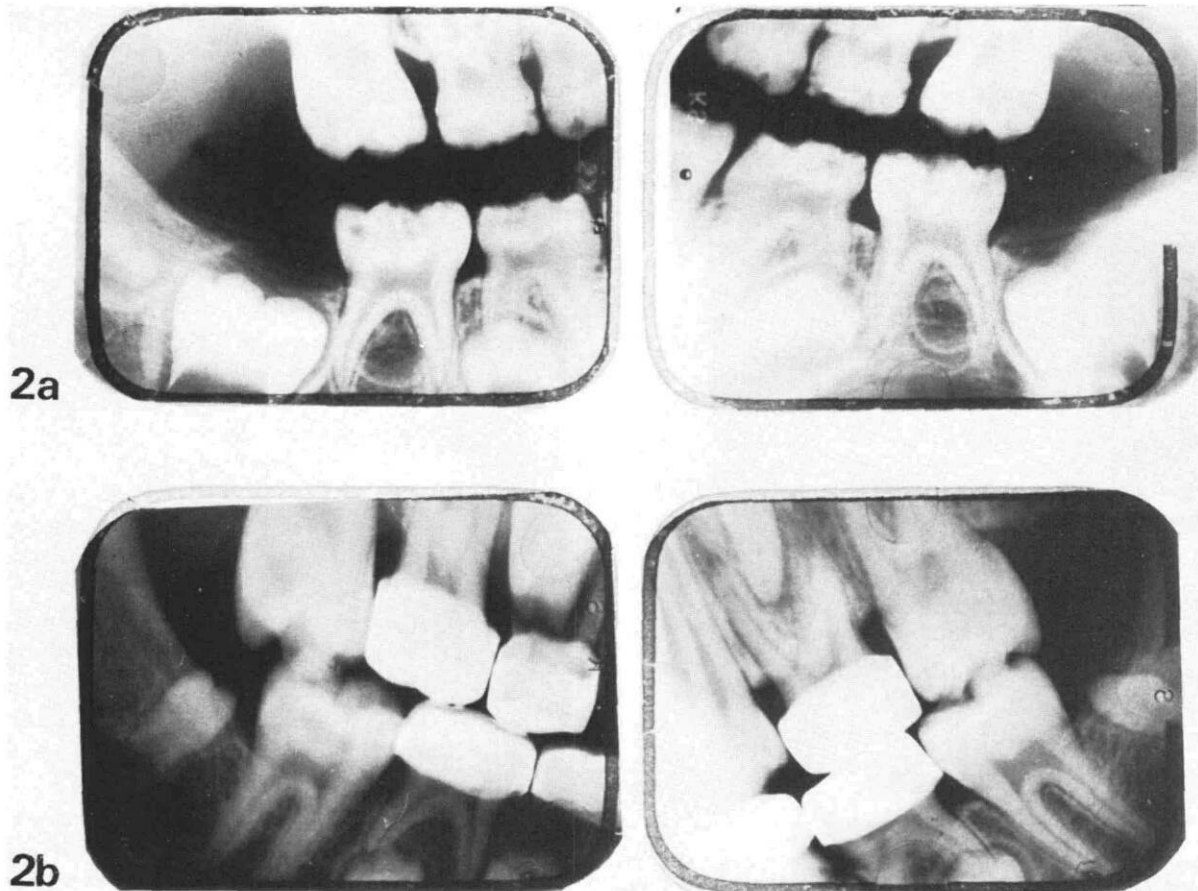


FIG 2a. (above) Right and left bite-wing radiographs taken at age 5. Note the hypoplastic areas in the primary crowns and the miniature bud of the right mandibular second permanent molar.

FIG 2b. (below) Right and left bite-wing radiographs taken at age 9. Note the continued development of the miniature right second permanent molar and its peg-shaped homologue; also note the aberrant morphology of the upper left second bicuspid.

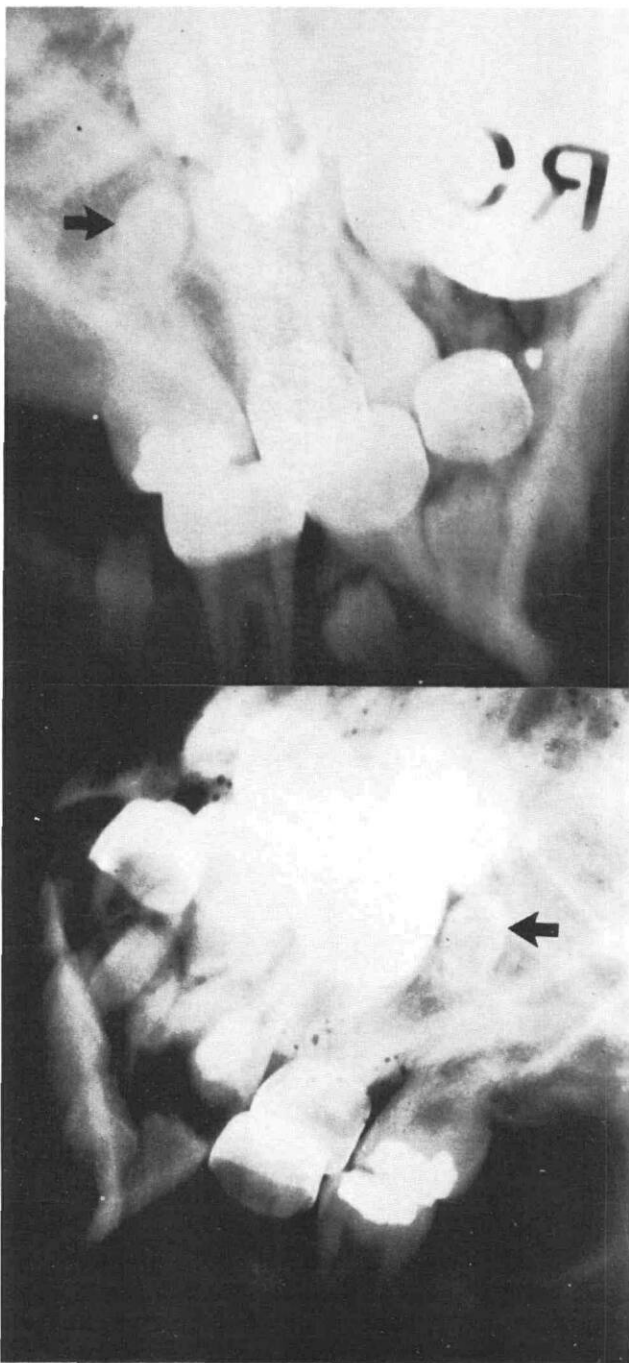


FIG 3. Right and left lateral oblique radiographs showing the slender roots of the lower first permanent molars and the inverted second permanent molars (arrows).

In addition, other authors have reported areas of hypocalcification and impaired dentinogenesis and amelogenesis, both in humans and laboratory animals.^{1,15}

It has been ascertained that when teeth are irradiated with therapeutic doses during their development their growth may be retarded severely. If the radiation precedes the stages of morphodifferentia-

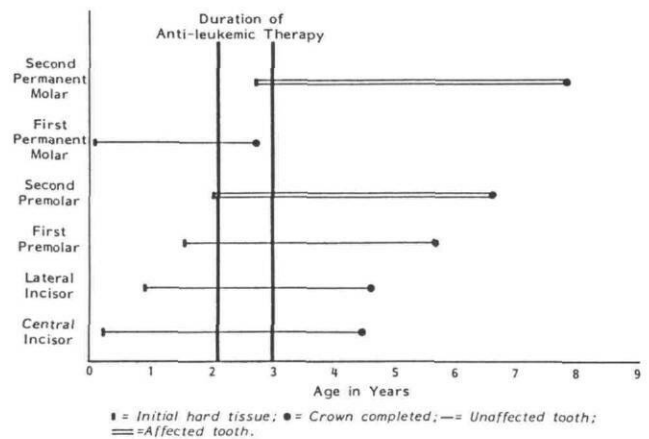


FIG 4. Representation of the relationship between the timing of the anti-leukemic therapy and the developmental disturbances affecting the dentition (based on the Table *Normal Chronologic Development of Secondary Dentition*).¹⁶

tion and calcification, the tooth bud may be destroyed. Irradiation at a later stage, after calcification has been initiated, may alter cellular differentiation, causing malformations or arrested growth.¹⁰ Deleterious effects on undeveloped and developing teeth are observed even when lower dosages are used. Animal studies suggest that the teeth are most vulnerable before histodifferentiation and that this susceptibility ceases once calcification is complete.^{13,14}

In the survey by Jaffe et al. 5 of 23 patients treated by chemotherapy alone manifested dental abnormalities including "acquired amelogenesis imperfecta, microdontia of the premolar teeth, and a tendency to thinning of roots with an enlarged pulp chamber." It was suggested further that potentiation of radiation with actinomycin-D may occur. Other contributory factors in the child oncology patient such as systemic disturbances and/or local factors cannot be excluded.¹²

As this patient received both chemotherapy and radiotherapy, it is not possible to separate the effects of these two treatment modalities. Examination of the field of irradiation, however, reveals that it borders closely on the site of the developing second permanent molars inferiorly and encompasses the site of the third permanent molars (Fig 1). However, since absence of third molars is a relatively common finding, missing third molars in this child could be the result of normal variation rather than inhibition of tooth bud formation due to early irradiation. Furthermore, the field and the attendant scatter rays were closer to the maxillary than the mandibular tooth germs, which might explain the more severe effects seen in the former. If chemotherapy alone had caused the abnormalities, it might be expected that all teeth

at the same stage of development might be affected similarly. In any event, there is a distinct correlation between the timing of the anti-leukemic treatment and the disturbances to the specific teeth affected. As previously mentioned, initial hard tissue formation appears to be the critical, susceptible phase in tooth development. Therefore, teeth which just had begun hard tissue formation were affected severely. Teeth which had begun hard tissue formation earlier — although they had not yet reached completion — appeared unaffected (Fig 4).

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Pioneers in pediatric/dentistry: Harold Kane Addelston

Dr. Addelston was born on May 29, 1908. He died April 19, 1971. He attended New York University and received the DDS degree in 1934. Following graduation his practice in New York City was limited to pediatric dentistry. He was chairman of the Department of Pedodontics at New York University for many years.

Dr. Addelston was a charter member of the American Academy of Pedodontics, and attended the organizational meeting of the Academy in Ann Arbor, Michigan February 14-15, 1947. He served the Academy as its tenth president, as treasurer, and as a member of the Board of Directors.

He was a Fellow of the American College of Dentists, member of the New York Academy of Pedodontics and the American Public Health Association. He was a Diplomate of the American Board of Pedodontics, and a past president of the New York State and American Society of Dentistry for Children. He was active in many community and philanthropic affairs.

