The Teeth in Patients with Laron Syndrome

23

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Core Message

› Laron syndrome patients have delayed tooth eruption, crowding, many caries and a tendency to break. Histological examination revealed defects in enamel formation.

23.1 Introduction

Knowledge on direct effects of hGH or IGF-I on dental development and structure is scant (Hamori et al. 1974; Kosowicz and Rzymski 1977); so is experimental literature. IGF-I has been shown to act on periodontal fibroblasts (Blom et al. 1992; Palioto et al. 2004), and mouse molar dentin size and shape is dependent on growth hormone (Smid et al. 2007). Laron syndrome (LS) with congenital absence of hGH and IGF-I activity is an ideal model to further our understanding on the action of these hormones on the dental structure. Forthwith our studies and findings.

23.2 Clinical Aspects

In untreated children with LS, the eruption of the primary and permanent teeth is delayed (Laron 2004). Already in infancy and prepuberty, teeth are defective with many caries (Figs. 23.1 and 23.2), probably an interplay between the IGF-I deficiency and frequent sweet food offered due to hypoglycemia in early age. Due to the underdevelopment of the facial bones (Chap. 9) (Scharf and Laron 1972; Konfino et al. 1975), there is crowding (Fig. 23.3), which again promotes caries and breakage of teeth (Fig. 23.4). Around the age of 40 years,

Fig. 23.1 Defective and spaced teeth and caries in a boy with Laron syndrome (LS) aged $5^{6/12}$

Fig. 23.2 Delayed eruption of permanent teeth and defective, spaced teeth and caries in a boy with LS aged $9^{3/12}$ years

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Fig. 23.3 Crowding of teeth in a $13^{8/12}$ year-old boy with LS

Fig. 23.4 Crowding and broken tooth in a $16^{7/12}$ year-old girl with LS

Fig. 23.5 Loss of teeth in a 42-year-old female with LS

many of the patients lose or break their teeth (Fig. 23.5) and therefore require a prosthesis at a younger age than the aging general population (Laron 1984, 2004).

23.2.1 Patient Investigations

23.2.1.1 Subjects and Methods

Detailed dental examination, accompanied by casts of the dentitions and panoramic radiographs, was performed in 13 untreated LS patients (seven males and five females). The age of six patients ranged between 2 and 18 years, and seven were adults, ages ranging from 19 to 48 years (Sarnat et al. 1988). Measurements of the arch length, arch circumference, and mesiodistal tooth dimensions were made on the plaster casts according to the methods described by Moorrees (1959) and Moyers (1973).

The dimensions for the maxilla and the mandible were analyzed separately. Panoramic radiographs were used to determine dental age and to record missing teeth, supernumerary teeth, and impacted teeth. The data were compared with 19 patients with congenital IGHD treated with hGH and healthy school children (Sarnat et al. 1988), as well as established norms (Moorrees 1959).

23.2.2 Results

The main findings were:

(a) The retardation of dental age in the untreated children with LS was less than that of the skeletal age.
(b) In the untreated LS group, 92% were without third molars compared with 37% in the treated IGHD group. All four molars were missing in 75% of the LS patients.
(c) There was a high prevalence of hypodontia in the LS patients as compared with the normal population . The high prevalence of hypodontia found only in the permanent dentition might be due to the retarded postnatal development of the maxilla and mandible.
(d) In two LS patients, a small groove-like enamel defect in the upper incisors was found.

23.2.2.1 Arch Length

Except for one male and one female LS patient, all measurements fell below the normal mean. No differences were found between the IGHD and LS groups in the maxillary arch length, but the arch length of the mandible was significantly smaller ($p<0.05$) in the untreated LS patients than in the treated IGHD patients.

23.2.2.2 Arch Circumference

According to Moorrees (1959), arch circumferences change little with age; however, the arch circumference of the mandible in patients with LS was significantly smaller than in normal subjects. These measurements complement those made by Konfino et al. (1975) (Chap. 9).

23.2.2.3 Tooth Width

Eighty percent of the LS males had a reduction in the mesiodistal width of the primary teeth; 40% of them were below 2 SD of the norm compared to 24% of female patients. The permanent teeth of 70% of the males were 2 SDs below the normal width compared to 60% of the female patients. Similar measurements are planned in IGF-I treated children.

23.3 Morphological and Histological Studies

A study on dental morphology and histology on 13 exfoliated or extracted dry primary teeth of our LS patients aged 4–13 years was performed in collaboration with the School of Dentistry of North Carolina (Wright et al. 2008).

23.3.1 Methods

Thirteen exfoliated or extracted, dry primary teeth from LS patients (aged 4–13 years) were evaluated by photography, morphometry of whole teeth, and histology using light microscopy. The findings were compared to healthy controls matched for age and sex.

23.3.2 Results

The teeth appeared grossly normal with normal crown morphology and lacking visible enamel hypoplasia or enamel discoloration suggestive of gross mineralization defects. The teeth showed a normal architecture and morphology, but reduced facial-lingual enamel thickness when compared to the total tooth width ($p<0.05$) (Table 23.1). This indicates that the enamel is significantly thinner than normal in teeth of LS patients. The facial-lingual width of some teeth was also reduced. The enamel thickness to tooth width ratios in the teeth of LS patients is significantly thinner than normal.

Table 23.1 Ratio of tooth width to enamel thickness in teeth from LS patients compared to normal controls

Tooth type	Laron syndrome	Normal controls
Primary maxillary canine	0.11	0.27
Primary mandibular second molar	0.14	0.26
Primary mandibular lat incisor	0.1	0.22
Primary mandibular central incisor	0.13	0.24
Primary mandibular first molar	0.17	0.24
Permanent mandibular central incisor	0.17	0.23

Histological evaluation showed several changes seen in some but not all teeth. The dentin in some cases showed increased interglobular dentin, while in others, there was a normal appearance of the dentinal tubules (Figs. 23.6 and 23.7). The histological examination revealed that despite a normal prismatic structure of the enamel, some patients had an accentuated neonatal line and Striae of Retzius (Fig. 23.8). The presence of interglobular dentin and accentuated Striae of Retzius are both indicative of stress on the cells responsible for mineralization of dentin and enamel respectively.

23.4 Periodontal Tissues

IGF-I deficiency affects not only the teeth but also the periodontal tissues. IGF-I is a potent modulator of periodontal regeneration stimulating cell proliferation, differentiation, and synthesis of Type I collagen and noncollagenous proteins (Blom et al. 1992). Furthermore, IGF-I and enamel matrix derivative stimulate periodontal ligament fibroblasts (Palioto et al. 2004). Thus, the IGF-I deprivation affecting the facial bones and periodontal tissues may be a contributory factor to the early loss of teeth in LS patients.

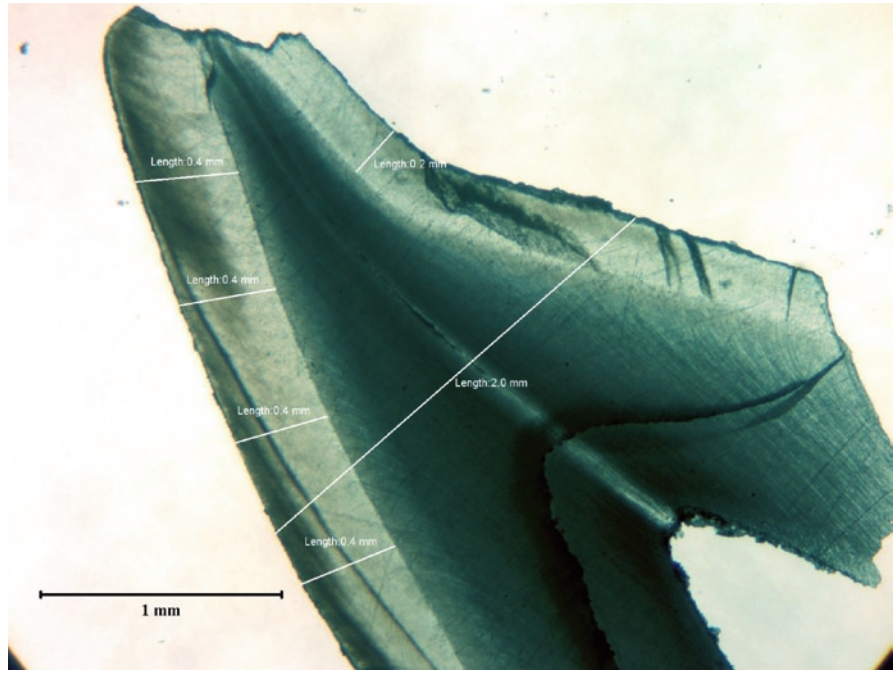

Fig. 23.6 This thin section of a primary tooth illustrates the normal tubular architecture with no evidence of mineralization defects. Many teeth showed a pronounced neonatal line

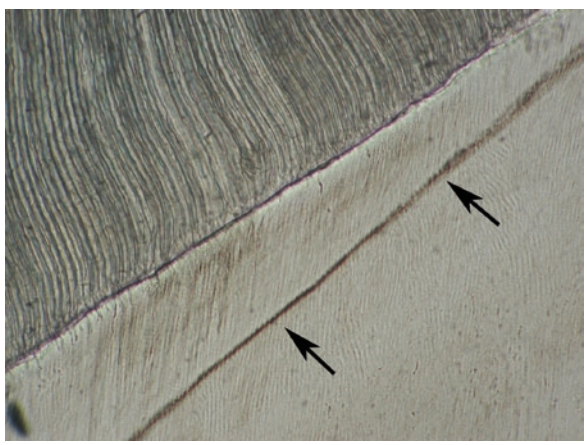

Fig. 23.7 The dentin had a normal tubular architecture with no evidence of mineralization defects. Many of the teeth showed a pronounced neonatal line (see also Fig. 23.8). The enamel prisms appeared normal in structure and course as observed in this thin section Laron syndrome

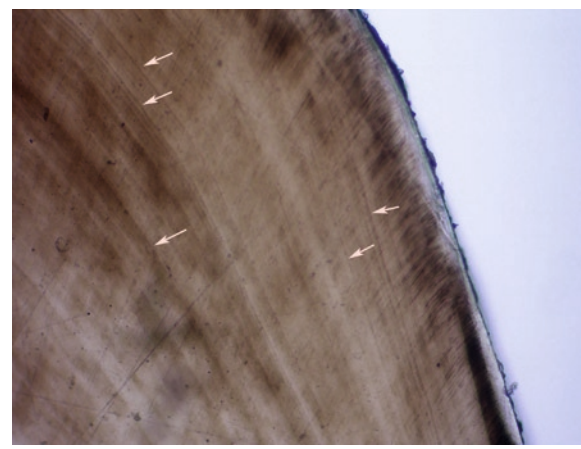

Fig. 23.8 In addition to a pronounced neonatal line, some Laron teeth had numerous pronounced Striae of Retzius (*arrows*) as seen in this thin section of enamel viewed with light microscopy. The multiple accentuated Striae of Retzius suggest a continued (albeit mild) disturbance of the enamel formation process

23.5 Conclusion

Long-term congenital IGF-I deficiency in LS patients, starting in utero, affects tooth development, size, morphology, and composition including the enamel, as well as the periodontal tissues. The defects may be due to both direct effects on the teeth as GH receptors are present during tooth bud formation (Zhang et al. 1997) and IGF-I deficiency in combination with pathological changes in the surrounding tissues. Pathological dentogenesis was also reported by Smid et al. (2007) in GH-R KO mice.

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