



Dental findings in Lowe syndrome

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Abstract

This paper presents the dental findings of a child with the oculocerebrorenal syndrome of Lowe. The genetic abnormality in this condition results in an inborn error of inositol phosphate metabolism. Renal tubular dysfunction leads to metabolic acidosis and phosphaturia. At 4 years, generalised mobility of all primary teeth was noted. It is postulated that a defective inositol phosphate metabolism was responsible for the periodontal pathology found in this case. This is in direct contrast with previous reports of prolonged retention of primary teeth in children with this condition. Histology of extracted primary incisors demonstrated enlarged pulp chambers and mildly dysplastic dentin formation. This is consistent with a chronic subrachitic state, a known feature of Lowe syndrome, but no prominent interglobular dentin was present. (Pediatr Dent 21:425-428, 1999)

Lowe syndrome, also known as oculocerebrorenal syndrome, is a rare X-linked recessive disorder characterized by congenital cataracts, mental retardation, stunted growth, hypotonia, renal tubular dysfunction, and moderate to severe metabolic bone disease.¹⁻⁴ Less consistent findings are hyperactivity⁵ and seizures.⁶ The genetic abnormality maps to Xq24-26, the site of translocation in occasional spontaneous cases, and may code for a Golgi apparatus protein⁷ resulting in an inborn error of inositol phosphate metabolism.^{8,9} World-wide incidence is difficult to estimate; around 150 cases are known to the Lowe Syndrome Association in the United States.

The condition manifests itself in three stages.¹ Cataracts develop in the neonatal period and are frequently associated with glaucoma, resulting in impaired vision or blindness. Mental retardation is also evident. The second stage is marked by metabolic abnormalities during early childhood. Renal tubular dysfunction causes metabolic acidosis, reduced ammonia production, phosphaturia, proteinuria, and aminoaciduria. Moderate to severe rickets and skeletal demineralization may develop as a result of metabolic acidosis and hypophosphatemia, leading to fractures, pain, and reduced motor development. In the final stage, metabolic disturbances may continue or resolve, but chronic renal failure ensues.

Treatment is mainly supportive. Phosphate and sodium-potassium citrate are administered for renal tubular acidosis and rickets. Vitamin D supplements may also be beneficial. Patients

may survive to the third decade, but usually succumb to renal failure, infections, or dehydration.¹

There are few reports of oral findings in Lowe syndrome. Dental crowding, delayed eruption of the permanent dentition, over-retained primary teeth with ectopic eruption of the permanent teeth, and taurodontism have been described.¹⁰ One report described enlarged dental follicles and enamel hypoplasia.¹¹ In a questionnaire survey of 96 patients with Lowe syndrome, 26% of respondents reported a "double row of primary teeth," resulting in a high frequency of dental extractions.⁶ Other dento-facial signs include constricted palate, dental cysts, and frontal bossing due to rickets.⁴

This report describes the dental clinical and histological findings in a child with Lowe syndrome, postulates a periodontal manifestation of the defective inositol phosphate metabolism and discusses the differences from dental findings in other rickets-like conditions.

Case report

Clinical history and examination

A four year-old male with Lowe syndrome was referred by his general medical practitioner for investigation of facial or dental pain. He had recently started chewing his fingers constantly, always on the right side of his mouth. A preliminary diagnosis had been made of right-sided otalgia and antibiotics prescribed. The symptoms persisted, initiating the dental referral.

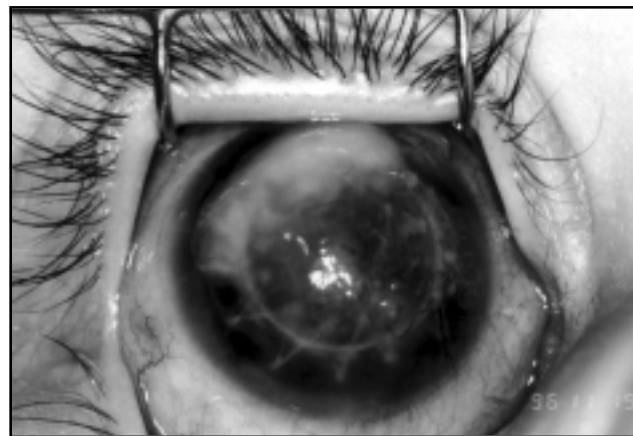


Fig 1. Corneal graft and recurrent cataract.

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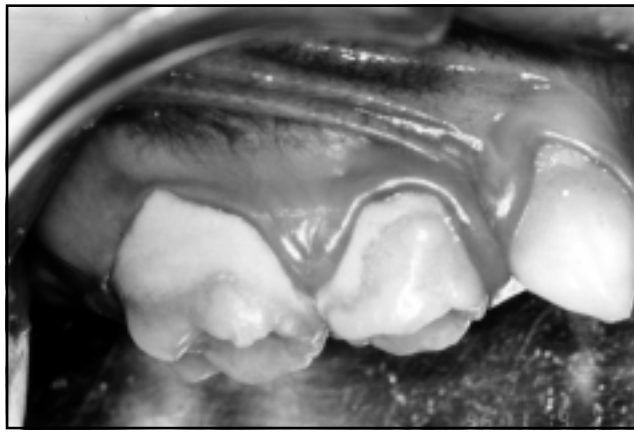


Fig 2. Calculus deposits on primary maxillary molars.

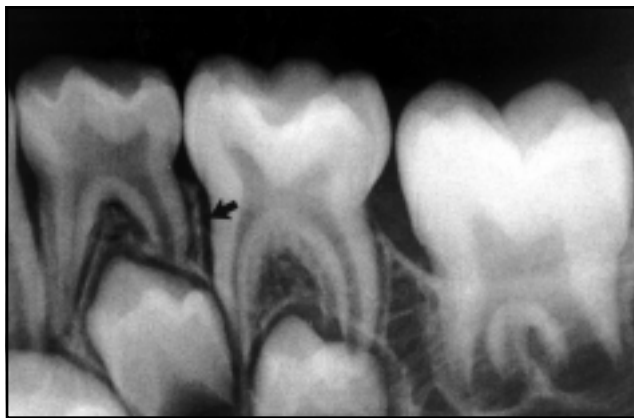


Fig 3. Radiograph taken age six years demonstrating widened periodontal ligament on primary molars (arrowed).

Cataracts had been noted at birth, for which he had undergone bilateral lens removal and corneal grafting (Fig 1). Metabolic acidosis was corrected with daily sodium bicarbonate supplements, but progressive phosphaturia resulted in hypophosphatemia in his second year of life. Daily supplements of 1-a-hydroxycholecalciferol and neutral sodium phosphate were provided. Plasma calcium and alkaline phosphatase levels were tested at four month intervals from the neonatal period to infancy, remaining always within normal limits, indicating apparently successful rickets prophylaxis. Plasma urea level remained low. An early endocrine screen indicated no abnormalities. Convulsions were controlled with carbamazepine.

Examination at age four revealed generalised hypotonia and limited awareness of his environment. He repeatedly gnawed his fingers and pulled his tongue throughout the consultation. The swallow pattern was normal, with no other parafunctional habits noted. Marked frontal bossing was present. Intra-oral examination showed chronic hyperplastic marginal gingivitis, an intact primary dentition, generalized mobility of all teeth (including primary molars), with grade 3 mobility of lower primary central incisors. Extensive deposits of calculus were noted on the lingual aspects of the lower labial segment and the buccal aspects of the upper molars (Fig 2). No source of oral pain was clinically evident, although examination was difficult. Radiographic examination was impossible due to poor cooperation. A provisional diagnosis was made of

myofunctional pain, simulating otitis, secondary to the finger gnawing habit, but pain of dental origin could not be ruled out without closer examination and radiographs.

Examination was performed under general anesthesia. Despite the mobility of all teeth, no true or false gingival pocketing or attachment loss was found. Clinically, no caries was detected, which was confirmed by extraoral films of the buccal segments. Stage of dental development was noted to be normal for the child's age. Thorough scaling was performed, and, in view of their marked mobility, the primary lower central incisors were extracted. It is unfortunate that no radiograph was taken of these teeth prior to extraction, but it was remarkable that despite their mobility there was minimal apical root resorption. No cause for the facial pain could be found and recovery was uneventful, but the hand-chewing habit persisted.

A program of professional oral hygiene care was commenced to improve the gingival health, but although the gingival inflammation was reduced, no change was found in the dental mobility. Continued difficult management required a second general anesthetic for repeat scaling at six years of age. At this time intraoral radiographs were taken of the primary molars, demonstrating a widened periodontal ligament space (Fig 3). On review at seven years of age, the child appeared generally well, the remaining primary incisors had exfoliated naturally, and the permanent incisors and first permanent molars all exhibited grade 2 mobility with no gingival pockets greater than 3mm.

Histological examination

Macroscopically, the primary incisors were of normal external morphology but with only a small amount of a physiological pattern of apical resorption. Their histological appearances were similar. Ground sections viewed under transmitted and polarized light revealed well-formed but slightly thin enamel with a normal prism structure.

In decalcified sections the pulp chamber was seen to extend incisally, but as a result of uniform enlargement rather than formation of an elongated pulp horn typical of rickets (Fig 4). A prominent incremental line, consistent in position with the neonatal line, was evident in the dentin dividing normal and evenly formed prenatal dentin from postnatal dysplastic dentin. Defects in the dysplastic dentin were mild. The predominant feature was small, round, well-demarcated defects suggesting tiny pulpal inclusions which had subsequently calcified. Each comprised a zone of amorphous mineralization, often with hematophilic incremental rings within it lying in a small zone in which tubules were sparse. Disturbed mineralization was most prominent in the mantle dentin close to the tooth surface on one side of the root (Fig 5). The predentin layer and mineralizing front in dentin were normal. No excessive interglobular dentin to suggest rickets was present on routine staining or microradiography. Cementum was quantitatively and qualitatively normal. A few fragments of periodontal ligament adhered to the root. These were insufficiently large to shed light on the abnormal mobility.

Discussion

Dental care for a young individual with Lowe syndrome is complicated by their limited communication skills and reduced ability to cooperate with even simple investigative procedures.



Fig 4. Longitudinal ground section of the primary incisor showing a slightly thin enamel layer and an evenly enlarged pulp chamber (bar=1mm).

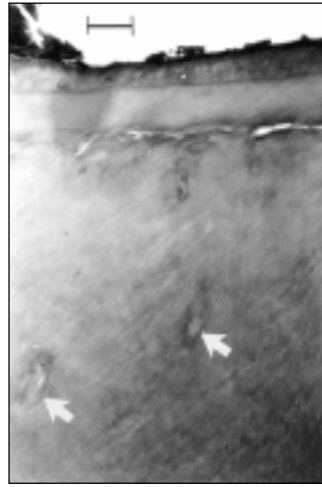


Fig 5. Dysplastic dentin below the root surface showing mineralized remnants of pulpal inclusions (arrowed) and a linear band of dysplastic dentin parallel to the surface (bar=0.1mm).

Irritability, obsessions, and complex repetitive behaviors (stereotypy) have been described as part of a distinct behavioral phenotype in Lowe syndrome.¹² This may account for the repeated finger-chewing in this case, in the absence of any oral source of pain.

The cause of the marked mobility of the primary dentition was unclear. No pathological pocketing was detected on probing, and radiographs revealed a widened periodontal ligament. The small fragments of periodontium adhering to the extracted teeth were insufficient to allow proper histological interpretation. In this case the clinical picture did not match any known cause of pathological dental mobility, such as prepubertal periodontitis, nor was there evidence of endocrinopathy or neutropenia at any time. The known metabolic defect in Lowe syndrome may account for the periodontal pathology in this case. Inositol phosphate hydrolysis occurs during the formation and regeneration of periodontal connective tissues, along with calcium ion mobilization and activation of phosphokinase C. These mitogenic events are thought to be regulated by a variety of polypeptides, including cementum-derived growth factor.^{13,14} Disturbances in periodontal tissue formation and maintenance may lead to clinically detectable changes in tooth mobility in the absence of periodontal disease.

The mild dysplasia of dentin seen histologically is presumed to result from both the metabolic disturbances associated with Lowe syndrome and its treatment. However, the signs are different from those in other forms of vitamin D-resistant rickets (VDRR) due to defects in 1-(25OH) vitamin D hydroxylase (VDRR type I), end-organ resistance to vitamin D (VDRR type II), other renal defects such as renal tubular acidosis, Fanconi syndrome, or the other rare types of X-linked hypophosphatemia.¹⁵⁻²¹ The most striking differences are the complete absence of interglobular dentin and large calcospherites and lack of a wide predentin band.

Clinical rickets is present in 60% of Lowe syndrome cases before one year of age²² and sub-clinical rickets is considered universal on radiographic or biochemical examination.⁴ Dentin structure is a sensitive indicator of rickets and it is surprising that these features were not seen in the current case, despite

that fact that rickets was relatively mild. Treatment of rickets in this case cannot explain the lack of dentin changes; it does not affect interglobular mineralization in VDRR type I²³ and, in addition, no layer of interglobular dentin was present in the dentin formed before diagnosis. The abnormally large pulp chambers and normal mantle dentin resemble other forms of VDRR but the pattern of dysplastic dentin is not a feature of VDRR.¹³

Summary

This report outlines the dental findings in a child with Lowe syndrome. There was gross calculus formation, probably the result of a combination of difficult home oral hygiene control practices and hyperphosphatemia secondary to daily oral phosphate supplementation. The histological findings of enlarged pulp chambers and mildly dysplastic dentin formation are consistent with a chronic subrachitic state, a known feature of Lowe syndrome, but no prominent interglobular dentin was present. The pathological mobility of the primary dentition with generalized widening of the periodontal ligament contrasts with previous reports of delayed exfoliation. On review, the erupting permanent dentition also demonstrated an abnormal degree of mobility. It is postulated that an inborn error of inositol phosphate metabolism may directly account for the development of abnormal periodontal connective tissues. Further reports of the dental findings are required to establish whether these findings are isolated or representative of some patients with Lowe syndrome.

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