DOI: 10.1111/j.1365-263X.2006.00763.x

Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency with inadvertent caries in infants

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International Journal of Paediatric Dentistry 2007; 17: 72–74

Background. Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency (LCHADD) is a rare systemic disease that is associated with early tooth decay.
Case report. This report describes the case of a 3-year-old boy suffering from LCHADD. At the time of referral, extensive carious lesions of the subject's maxillary dentition necessitated the surgical removal of eight teeth. Preventive treatment for LCHADD involves a regular oral intake of glucose that is vital for the survival of the affected individual. In young infants, the glucose solution needs to be administered as often as every 3 h in order to prevent hypoglycaemia, leading to a local environment similar to that experienced in nursing bottle syndrome. While nursing bottle syndrome can be resolved by eliminating the sugar substrate and curtailing the feeding sessions, these alternatives are not available in cases of LCHADD.
Conclusion. This report highlights this rare disease and emphasizes its dire consequences for the dentition. Prophylactic recommendations for high-risk children are reviewed. Familiarity with LCHADD allows this high-risk group of patients to be identified, and thus, ensures diligent prophylactic action.

Introduction

Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency (LCHADD; OMIM #609016) is a rare, recessively inherited genetic syndrome (1:50,000 births)[1,2] that is caused by an enzyme defect in the beta-oxidation cycle. The impaired enzyme is long-chain 3-hydroxyacyl-CoA dehydrogenase, which catalyses the third step of the mitochondrial oxidation of long fatty acids, being part of the mitochondrial trifunctional protein. The most prominent clinical sign of LCHADD is hypoketotic hypoglycaemia, but additional features including cardiomyopathy, severe liver disease, pigmentary retinopathy and peripheral neuropathy may be observed[3,4]. The prevention of hypoketotic hypoglycaemia involves a stringent low-fat, high-carbohydrate diet[3,5,6] administered at least every 3–4 h[1,7]. After it was first described in 1990, hypoketotic hypoglycaemia was originally treated with the mandatory administration of glucose, either intravenously or via a gastric tube[7]. Various dietary regimes are now available which allow oral ingestion of the required nutrients. Treatment for LCHADD means that the primary and then the permanent teeth are exposed to sugar solutions at regular intervals, mimicking the situation observed in nursing bottle syndrome[8]. Because of the severity of this disease, which has a mortality rate of up to 38% within 3 months of diagnosis[3], the development of dental caries in the primary teeth seems circumstantial in comparison with the other possible side-effects, and this often leads to late referral for dental consultation.

Case report

A 3-year-old boy was referred to the Department of Oral and Maxillofacial Surgery, University Hospital Hamburg-Eppendorf, Hamburg, Germany, by the paediatrician treating the subject, who noticed severe decay of the child's primary dentition. The subject's medical history revealed that his birth and early development were normal. Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency was first diagnosed at the age of 6 months. The boy suffered from vomiting and a lack of appetite, along with a

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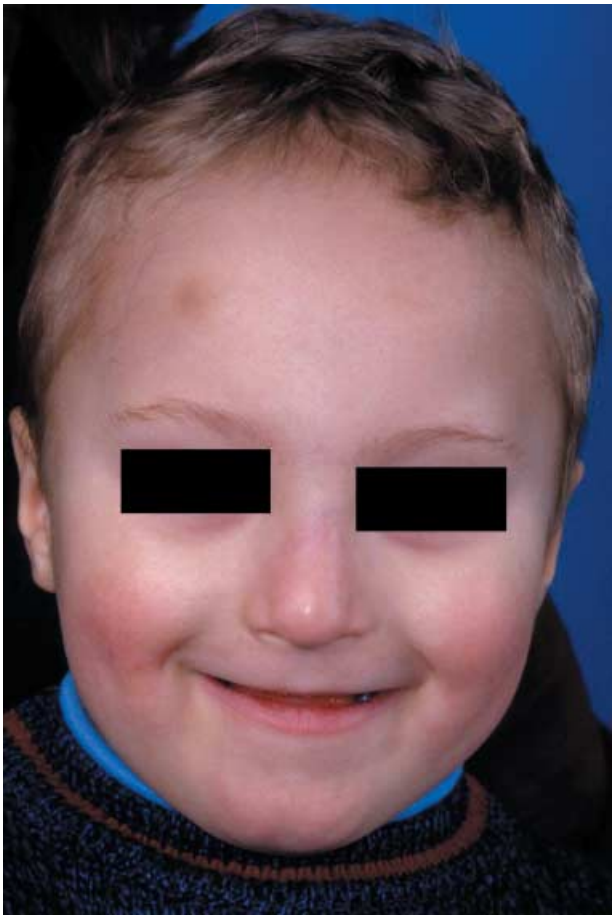

Fig. 1. Clinical appearance of a 3-year-old patient with long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency.

fever and diarrhoea, and the primary diagnosis was that he had a gastrointestinal infection. The subject's status did not improve and the clinical signs persisted. Routine serological examinations revealed a low glucose level of < 50 mg dL^{-1}. This prompted further examination and the presence of LCHADD was finally revealed. After this, the boy was referred to a university clinic for counselling. According to his mother, no signs of enamel hypoplasia were evident following the eruption of the subject's primary teeth. At this time, the boy's diet was supplemented with glucose solution every 3 h to prevent hypoglycaemia. His mother reported that she avoided long feeding times, but that close attention was paid to adhering to the schedule. At presentation, the subject appeared to be a healthy young boy (Fig. 1).

Intraoral examination revealed extensive decay in the maxilla from teeth 54 to 64 (Fig. 2).

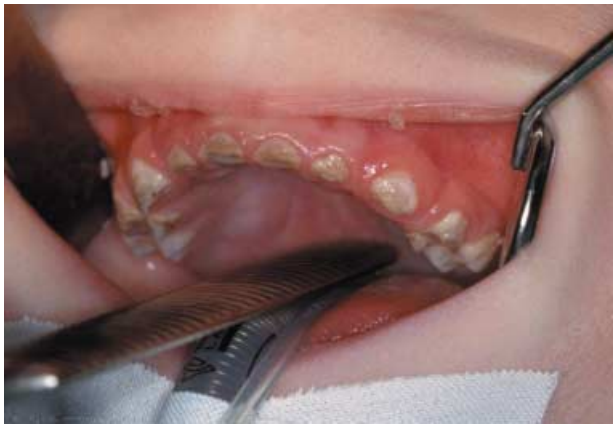

Fig. 2. Intraoperative view of the damaged primary dentition of the upper jaw. All the visible teeth are covered by a thick layer of plaque.

Radiographic imaging was not possible because the boy refused to cooperate. The child was treated under general anaesthesia. This involved the extraction of primary teeth 54–64. Close examination of the remaining dentition revealed only minor demineralization of the enamel of the molars. The postoperative healing was uneventful, and the 6-week follow-up showed perfectly healed gums. At this point, the subject was referred to the Department of Prosthetic Dentistry, University Medical Center Hamburg-Eppendorf, for the adaptation and incorporation of dentures to facilitate mastication, phonation and social integration. The boy's mother was also referred to a paediatric dentist for further prophylactic instructions and a recall system to ensure biannual fluoride varnish application.

Discussion

Patients with LCHADD are at risk of developing dental caries. This condition is a rare systemic inherited disorder, but dentists should be familiar with LCHADD nonetheless, because it has serious implications for dental health and early intervention can prevent the development of early childhood caries (ECC). Because LCHADD is an autosomal recessively inherited disease[6], the heterozygous parent shows no signs of this condition under normal circumstances, but the likelihood of having offspring suffering from this disease increases.

Regular and effective plaque control, and the use of fluoride toothpaste at least twice a

day are important parts of the successful treatment of patients suffering form LCHADD. Microbiological risk factors which promote the development of dental caries also have to be considered since an early colonization of the oral cavity with *Streptococcus mutans* facilitates the development of ECC[8].

Fluoride therapy is generally considered to be the most important preventive measure for this disease[9–11] and it should play a central role in prophylactic measures for children suffering from LCHADD. These fluoride measures should primarily consist of the topical application of fluoride varnish since systemic application via ingestion of fluorides during tooth development seems to be less effective than the frequent local availability of fluoride following the eruption of the teeth[12,13]. In accordance with the guidelines of the German Society of Dental Health, the present authors recommend fluoride varnish application (e.g. Duraphat, NaF 5%) as being the most efficient topical fluoride application[12,14]. This should be applied at least biannually, and only under the supervision of a dentist or oral hygienist.

Children with LCHADD should be introduced to the environment of the dental practice to ensure that they become familiar with the nature of the dental check-up and look forward to their next visit. Furthermore, parents should be instructed to:

1 teach their children to brush their teeth effectively with a fluoride-containing toothpaste;

2 prevent or postpone mother-to-child transmission of *Streptococcus mutans*; and

3 take their children for regular dental check-ups, with the frequency of visits being determined by the dentist.

What this paper adds

- Long-Chain 3-hydroxyacyl-CoA dehydragenase deficiency (LCHADD) is a systemic disease with dire consequences for the deciduous dentition, if the necessary precautions are not met.

Why this paper is important to paediartric dentists

- The inconspicuous clinical appearance of these children does not enable a first glance diagnosis.
- This article familiarises the paediatric dentist with this rare disorder and provides a therapy scheme for the proficient treatment of these patients, highlighting the currently applicable prophylactic recommendations.

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