Case report: the Lesch-Nyhan syndrome

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ABSTRACT. Background The Lesch-Nyhan syndrome (LNS) is a rare x-linked excessive disorder of purine metabolism, caused by the congenital absence of hypoxanthine guanine phosphoribosyl transferase (HGPRT).

Case report In January 2000 a 2 year old boy was referred to a paediatric dental office in Landshut, Germany, because of severe and repeated lip chewing and aggressive tongue biting. A medical history revealed a normal pregnancy with no complications but a diagnosis of muscular hypotonia was made at four months of age. At 18 months a diagnosis of LNS was established through biochemical analysis and molecular examinations. The child displayed self-destructive behaviour, typical in children with LNS. Shortly thereafter the patient was supplied with arm cuffs for self-protection which were not tolerated and the self-mutilation continued. Eventually the extraction of all primary teeth was deemed necessary to prevent additional medical problems for this child.

Follow-up One year after the dental extractions the patient presented with no bite injuries but was now using his fingers to injure himself.

KEYWORDS: Lesch-Nyhan syndrome (LNS), Autocannibalism, Self-mutilation, Hypoxanthine guanine phosphoribosyl transferase (HGPRT).

Introduction

Lesch-Nyhan syndrome (LNS) was first recognized by Catel and Schmidt [1959] and later described by the physicians Lesch and Nyhan [1964] as an X-linked recessive metabolic disorder, caused by the complete absence of hypoxanthine guanine phosphoribosyl transferase (HGPRT) activity. The loss of enzyme function is caused by gene mutations on the long arm of the X-chromosome [Lee et al., 2002]. This enzyme catalyses the reaction of hypoxanthine or guanine with phosphoribosyl pyrophosphate to form inosinic and guanylic acids. The increased production of purine leads to an accumulation of uric acid [Evans et al., 1993] (Table 1) in the blood (hyperuricemia). Children with LNS may develop all clinical signs of gout such as uricosuria, urinary tract calculi, tophaceous gouty arthritis and nephrolithiasis [Budnick, 1969; Smith et al., 1994]. Usually these patients die in the second or third decade of life from infection or renal failure [Steadman et al., 1982; Evans et al., 1993; Smith et al., 1994; Cusumano et al., 2001]. Therefore genetic counselling is essential for appropriate prevention [Cusumano et al., 2001]. Prenatal diagnosis of LNS can be made by amniocentesis [Shoptaw and Reznik, 1978; Salman et al., 1987], hair root analysis [Steadman et al., 1982] or chorion biopsy [Cusumano et al., 2001] and ultramicroscale enzymology [Gibbs et al., 1984]. The incidence of Lesch-Nyhan syndrome is estimated to be approximately 1:100,000 live births [Steadman et al., 1982; Salman et al., 1987]. LNS is associated with moderate to severe mental retardation and a typical tendency toward self-mutilation [Lee et al., 2002]. However, it has not been established yet if patients with LNS are insensitive to pain or not [Sæmundsson and Roberts, 1997]. IQ values range from 25 to 101 [Scully, 1981; Steadman et al., 1982; Salman et al., 1987; Smith et al., 1994; Cusumano et al., 2001].

Major clinical manifestations occur usually in affected males and can be noticed first by 3 to 4 months of age [LaBanc and Epker, 1981]. The first clinical symptoms are typically poor motor development, abnormal hypertonic muscle tone or spasticity, often leading to a misdiagnosis of cerebral palsy.

Approaches to dental treatment to prevent the self-inflicted bite injuries have included placement of a soft mouth guard [Evans et al., 1993] or acrylic splint [Budnick, 1969; Sugahara et al., 1994; Chen and Liu, 1996]. While trying to maintain the dentition, Lee et al. [2002] reported on a child treated with vital pulpotomies and crown restorations. In severe cases extraction of all teeth [Smith et al., 1994; Rashid and...
Yusuf, 1997] has been suggested. Macpherson et al. [1992] described a child with LNS, who was treated with orthognatic surgery whereby an open bite was created, limiting the patient's ability to chew.

This paper describes the dental management of a child with LNS who inflicted severe injuries to himself through biting.

**Case report**

In January 2000 a 2 year old boy was referred to a paediatric dental office in Landshut, Germany, because of severe and repeated lip chewing and aggressive tongue biting. The mother reported a normal pregnancy and childbirth with no complications. The medical history revealed that the boy had been diagnosed with muscular hypotonia at 4 months of age. Physiotherapy was started at that time to improve head control and muscle tone. At 18 months of age the diagnosis of LNS was established through biochemical analysis and molecular examinations. Urine analysis revealed a significant increase of uric acid production. Upon physical examination his head control was still poor and the child had delayed motor skills and severe mental retardation and displayed the self-destructive behaviour typical in children with LNS.

In March 1999 the child had been placed on a purine-reduced diet and was taking Allopurinol® in an attempt to improve behaviour. The possibility of a bone marrow transplant had also been discussed with the parents to relive the clinical progression of the syndrome. Shortly thereafter the patient was supplied with arm cuffs for self-protection. However, the child was not able to tolerate these heavy arm cuffs and self-mutilation continued resulting in repeated and severe injuries. The medical team suggested the extraction of all his primary teeth to reduce the severity and incidence of bite injuries.

**Dental examination.** The child presented for the first oral evaluation at 27 months of age. He was unable to walk and speak. The parents’ chief complaint was their son’s frequent episodes of self-mutilation. These involved the destructive and repeated biting of his lips, tongue and hands. Although the biting had occurred before on several occasions the resulting injuries appeared to get worse in the previous month.

An extraoral examination of the boy revealed old scars and fresh wounds on the lower lip and on both hands. There were visible scratches and ulcerations on both hands presumably originating from his fingernails and teeth. The complete lower lip was scarred and the lip height was reduced to 3 mm from old biting episodes (Fig. 1). In addition, he presented with a partially healed wound on the left vermillion border, which was about 20 mm long. No lymphadenopathy or other pathology was noted. Radiographs could not be obtained due to the poor cooperation of the patient.

The intraoral examination revealed a normal complement of caries free primary teeth with all four second primary molars unerupted. The cheeks presented some small lacerations and deep wounds were present on the tongue. The parents reported that the child had bitten through his tongue three
days earlier, creating a 30 mm long laceration. Due to the severe injury to the tongue the parents sought medical care for their son at the local hospital, where the child was sedated. Blood analysis revealed a severe decrease of haemoglobin (5.5 g/dl). The child received a blood transfusion to bring the haemoglobin values back to 10 g/dl.

A paediatric dentist, an anaesthesiologist and a surgeon were consulted. A conservative approach using dental splints was considered, but due to the young age of the patient and the inability to tolerate such a splint this approach was rejected. The severity of the bite injuries and the resulting dramatic decrease of haemoglobin made urgent intervention necessary. The most effective dental approach in order to prevent further bite injuries and a possible medical problem was to extract all the child’s primary teeth. The parents consented to this type of treatment after all other alternatives had been discussed. The treatment was performed in the Children’s Hospital in Landshut, Germany. Under general anaesthesia the tongue was sutured by a paediatric surgeon and all primary teeth were extracted by a paediatric dentist. No postoperative complications occurred within 24 hours.

Follow-up care. On recall, after 20 days, healing of the extraction sites was proceeding normally. The parents were advised to maintain a 6 months recall schedule for their child. However, poor compliance of the parents caused a delay until one year post operatively (January 2001). Extraoral examination of the now 3 year old boy showed new lacerations of the lower lip and chin which were being caused by his own fingernails (Fig. 2). Enlargement of several lymph nodes in the perimandibular region could be palpated. Intraorally, the mucosa and gingiva were pink and firm with no new lacerations.

The mother reported that since she gave birth to a second healthy boy a few months earlier the self-mutilation tendency of her older son had increased. Although he was not biting himself anymore, he still showed self-destructive behaviour, injuring himself by pulling and poking with his fingers and fingernails. She was also under the impression that her elder son wanted to be restrained.

At the second recall appointment in April 2002, two years after the extraction of all primary teeth, the parents were informed about the future eruption of the first permanent molars and incisors. At this time there were no intraoral signs of tooth eruption but the parents were advised to keep a 6 months recall schedule. Six months later an extraoral examination showed continued healing of the lower lip, but with deformation due to scarring (Fig. 3). Still no permanent teeth were erupted. The patient seemed to be happy in his wheel chair and was wearing strong arm restraints. Periodic recalls were strongly suggested to the parents in order to monitor the eruption of the permanent dentition and decide on the best dental management for the child.

Discussion
The self-destructive behaviour of patients with LNS usually starts between the ages of 1.5 to 2 years [Shoptaw and Reznik, 1978; Salman et al., 1987;
Smith et al., 1994] or shortly after the primary teeth erupt [Sugahara et al., 1994; Cusumano et al., 2001]. The auto-aggressive behaviour is manifested as lip and tongue biting, scratching with the fingernails, head banging and aggression towards other people. Self-mutilation or self-injurious behaviour has been defined as a deliberate destruction or alteration of body tissue without conscious suicidal intent and occurs in conjunction with a variety of psychiatric disorders as well as various developmental disabilities and some syndromes [Finger and Duperon, 1991].

Dramatic and extremely rapid loss of tissue is a hallmark of LNS [Dicks, 1982]. Parents seek dental care and advice mainly due to the involuntary destruction of the lower lip or the tongue through biting.

Researchers have not yet been able to determine the cause of this aggressive behaviour which continues in spite of medical support (e.g. arm cuffs and medication). Tissue loss is severe and the most common dental management approach taken for these patients is the extraction of all teeth present [Dicks, 1982; Steadman et al., 1982; Salman et al., 1987; Evans et al., 1993; Smith et al., 1994; Rashid and Yusuf, 1997]. Some authors recommend manufacture and use of acrylic splints [Shoptaw and Reznik, 1978; Evans et al., 1993; Sugahara et al., 1994; Chen and Liu, 1996] retained by a head-gear or mouth guard as a conservative approach to prevent self-mutilation and at the same time maintaining the dentition. Short term findings showed that it was possible to reduce biting injuries.

However, complications in the use of splints have been reported. Some patients, wearing splints, have had problems with drooling and fungal infections that are frequent in patients wearing the splints for long periods of time. In some of these cases some authors have eventually resorted to the extraction of all teeth. The kind of treatment chosen strongly depends on the intensity of the auto-aggressive behaviour, which is related to the activity of HGPRT [Rashid and Yusuf, 1997]. Dicks [1982] divides clinical manifestations of the self-mutilation into three categories (no oral self-mutilation, some oral self-mutilation, and severe oral self-mutilation). Preventive and restorative treatment for each patient has to be based on clinical findings.

In the case reported here the young patient showed a very high incidence of aggressive biting episodes, which resulted in severe and repeated injuries with life-threatening complications (haemoglobin decrease below 5.5 g/dl). One year after the extractions, the patient was not biting himself anymore and had no bite wounds. The extraction of all teeth, although seemingly radical, was able to dramatically reduce the severity of oral tissue damage in this patient. Despite this improvement the patient did develop another way to hurt himself even more severely on his chin and lower lip by using his fingers. This phenomenon has also been described by Scully [1981]. Parents should be aware that extracting teeth may not prevent the patient to injure him or herself in the future. The additional use of physical restraints is therefore recommended to reduce the incidence of injuries [Sæmundsson and Roberts, 1997; Lee et al., 2002].

Children who suffer from LNS syndrome are usually relaxed and complacent when placed physical restraint. When the restraints are removed the patients become very agitated and often scream until restraint is replaced [Cusumano et al., 2001]. Our patient seemed to be content and calm with his hand bandages attached to his wheelchair. However, Scully [1981] describes more aggressive reactions and destructive behavioural patterns in patients with protective hand and forearm bandages. It remains to be seen if the development of new drugs can reduce the incidence and severity of self-mutilation in LNS patients.

Extractions of permanent teeth should be avoided if possible, especially considering the fact that the tendency towards self-mutilation decreases with age [Steadman et al., 1982]. The future dental

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**FIG. 4 – Photograph taken 2 and a half years after dental treatment showing the patient happily sitting in his wheelchair.**
management of our patient will depend on his psychological development and will be discussed with his parents and paediatrician. A re-evaluation of the treatment options will be necessary as the permanent dentition erupts. Any decision as to how to prevent biting episodes in LNS patients should be carefully thought out. Parents should be informed that children will find other ways to injure themselves. Therefore, extraction of teeth is recommended only for severe cases and if medical problems arise. The overall protection of the patient should always be the primary concern (Fig. 4).

**Conclusion**

Dental management of a child with LNS is dependent upon the severity and frequency of the biting episodes and the attitude of the parents towards the treatment plan. Conservative alternatives are available to maintain the dentition such as the use of acrylic splints or soft resin mouth-guards, while in severe cases, such as the one presented in this paper, the extraction of all teeth seemed to be necessary.

**References**


