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CLINICAL CASE

Oral self-mutilation in Lesch-Nyhan Syndrome. Case Report

Síndrome de Lesch-Nyhan y automutilación oral. Reporte de un caso

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Abstract

Introduction: Lesch-Nyhan syndrome (LNS) is an inherited recessive X-related disorder caused by the deficiency of the enzyme hypoxanthin-guanine phosphorribosyl transferase (HPRT). Compulsive self-mutilation and dystonia occurs before the first year of age and is expressed by persistent bites on the oral mucosa, lips, tongue, fingers, and shoulders. The dental intervention performed on most of these patients is multiple tooth extraction to prevent serious secondary lesions. **Objective**: To present a clinical case of LNS and describe pediatric dentistry management in patients with self-mutilating behavior. **Clinical case:** Male patient, 7 years old, LNS carrier. He was referred to the Dental Unit from the Department of Pediatric Neurology for evaluation and management of self-inflicted wounds on fingers, lips and cheeks associated with weight loss and decreased food intake. The surgical procedure consisted of multiple extractions, surgical remodeling of the residual alveolar ridges under general anesthesia. In the second postoperative month, the patient was discharged definitively, with an adequate nutritional status and no signs of self-mutilation in hands or oral cavity. **Conclusions**: Although LNS is rare, it is essential to know how to proceed in order to provide the best quality of life for patients and their families. Early tooth extractions, as an initial phase in severe cases, seem to be the most useful alternative to minimize damage.

Keywords:
Lesch-Nyhan Syndrome; Lip/injuries; Self-Injurious Behavior/therapy; Dental Care for Children; self-biting and pain from self-mutilation

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Introduction

The Lesch-Nyhan síndrome (LNS) was first described by Lesch and Nyhan in 1964, they reported a pattern of neurological anomalies (choreoathetosis, self-aggression, intellectual disability and recurrent self-mutilation) in two brothers with hyperuricemia[1]. In 1967, Seegmiller et al. made a relation between this clinical symptom and the deficit of the hypoxanthine-guanine phosphoribosyltransferase (HPRT) enzyme codified by the HPRT1 gene, which is localized in the Xq26 chromosome[2-5]. The prevalence of LNS in newborns is variable, its rates in Canada, Spain and the United Kingdom are 1/380,000, 1/235,000 and 1/2,000,000, respectively[2,6].

The HPRT enzyme is responsible for the metabolism of purines and its deficiency leads to the accumulation of uric acid, whose crystals form in different organs and causing growth retardation, obstructive nephropathy, gout and musculoskeletal alterations[7]. The clinical phenotype varies according to the residual activity of the HPRT enzyme. An activity lower than 1.5% is a classic LNS (hyperuricemia and neurological alterations, such as motor disorders and self-mutilating behaviors); an enzyme activity between 1.5 and 20% lead to lower degrees of neurological alterations, hyperuricemia is a common symptom[8]. The neurological compromise only appears on males, since women are usually asymptomatic carriers.

The degree of compromise can be classified as *Grade 1 or no neurological manifestations*, they are independent and autonomous, they suffer from dystonia while exercising, and also have a slight attention deficit disorder and obsessive behaviors. *Grade 2 or mild neurological symptoms*, such as mild-moderate dystonia with independent walking, macrocytic anemia or mild intellectual disability. *Grade 3 or acute neurological symptoms* with acute generalized dystonia, but no self-mutilating behavior. And *Grade 4 "Classic Lesch-Nyhan Syndrome"*, which has a more severe phenotype, a complete deficiency of HPRT, acute generalized dystonia associated with choreoathetosis, ballism and behavior alterations, such as self-aggressive behaviors, cognitive impairment or megaloblastic anemia[9-12].

Reductions in the volume of the ventral striatum and absent prefrontal areas in the variable forms have been described in the classic LNS. This might explain the self-mutilating behavior and the response to a deep brain stimulation in some recently published cases[13].

The compulsive self-aggression and abnormal movements occur early (before the first year of life) and they are expressed as persistent bites in the oral mucosa, lips, tongue, fingers, and shoulders, which ends up in the total or partial destruction of the affected tissues. Despite having pain sensitivity, patients cannot control their self-aggressive behaviors[7,14,15].

The diagnosis must be suspected in infants with psychomotor retardation associated with renal lithiasis and early obstructive nephropathy with hyperuricemia and hyperuricosuria[10,11]. The enzymatic study allows evaluating the HPRT activity and the increase of the adenine phosphoribosyltransferase (APRTase) activity. At a molecular level, the gene mutation that codifies for HPRT1 must be sequenced[10,11].

The objective of the treatment is to relieve the hyperuricemia, however, it does not reduce neuropsychiatric manifestations[16]. The management of hyperuricemia prevents renal and musculoskeletal complications. The allopurinol inhibits the xanthine oxidase enzyme and blocks the conversion of xanthine and hypoxanthine into uric acid, which prevents uric acid crystalluria, renal lithiasis and gouty arthrosis[4,7,11,15-18].

Neurological dysfunctions are not totally comprehended, thus, there are no effective treatments for them. Benzodiazepines and gamma-aminobutyric acid (GABA) inhibitors, such as baclofen, can help treating dystonia and spasticity[11,19]. The anxiety of patients with LNS has been treated with benzodiazepines, which inhibit the reuptake of serotonin and atypical antipsychotic with different results in different patients[16]. The use of special devices to restrict the movement of limbs and to avoid mutilating lesions and programs for posture correction to prevent deformities are complementary alternative therapies[11]. Deep brain stimulation has been proved effective in the management of dystonia and behavior.

From a point of view of a dentist, the most performed surgical intervention in patients with LNS is the multiple dental extractions. It is, therefore, possible to prevent serious lesions in the oral mucosa, lips, and fingers[16]. It has been proposed the use of intraoral devices; however, they have a high percentage of failure due to an excessive overload, material fatigue and fracture of the device[20].

The objective is to report a self-mutilating behavior, which is valid for other pathologies with similar behaviors, such as congenital insensitivity to pain, severe mental retardation, Tourette syndrome, Riley Day syndrome, among others.

Clinical Case

Male patient, seven years old, with LNS due to an HPRT enzyme activity below 1%. He was treated with allopurinol to control the hyperuricemia, and trihexyphenidyl, clonazepam, and risperidone to control dystonia and the compulsive self-aggressive behavior, which had almost no response to behavioral symp-

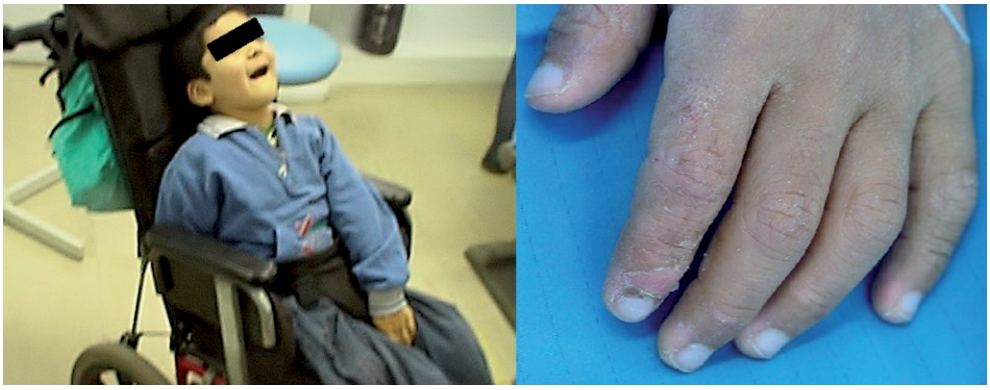

Figure 1. General physical examination. Patient with severe cognitive deficits and special devices to restrict the movement of limbs. Erosive injuries that in fingers and nails of upper extremities.

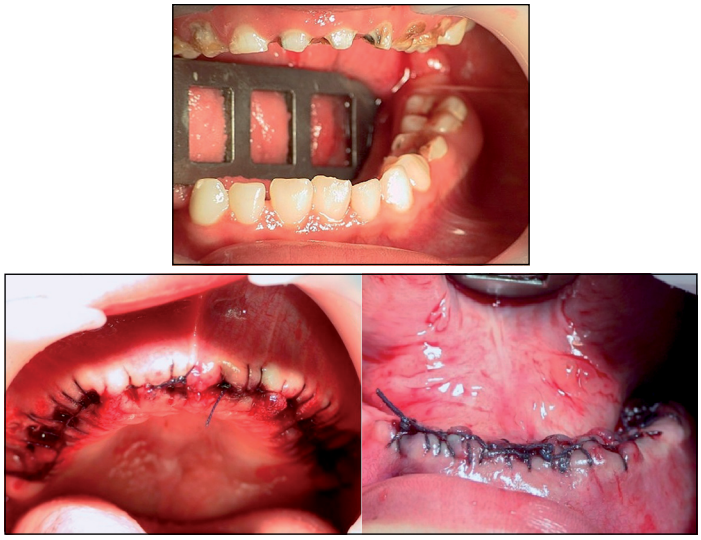

Figure 2. Intraoral examination. Mouth disease for generalized gingivitis and mixed first phase dentition, with presence of multiple cavities and severe crowns destruction of incisors and bimaxillary, temporary and permanent molars.

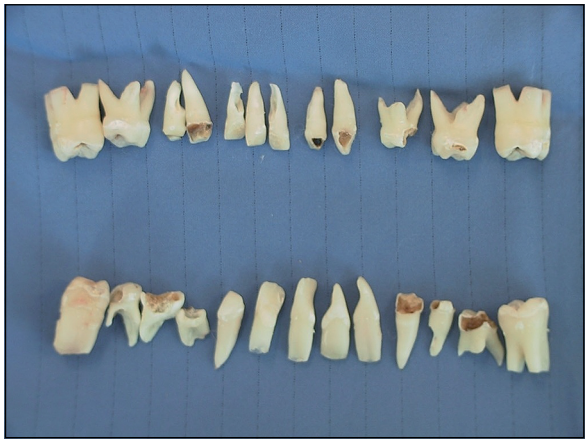

Figure 3. Surgical procedure: Multiple extractions.

toms. The patient had severe perioral and hand lesions, thus he was referred from the Department of Neurology to the Dental Unit for his evaluation and management of self-aggressions in finger, lips, and cheeks.

The physical examination showed an acute cognitive impairment, the absence of expressive language, acute dysarthria, generalized dystonia, choreoathetosis, and self-aggressive behavior. The patient was malnourished due to self-inflicted oral lesions (figure 1).

In an intraoral level, the mucosa membrane of the lower lip inner face and the jugal mucosa had a contused lacerated wound, which compromised the mucosa and submucosa; the gums were swollen in both maxillae, the tongue was mobile and had no lesions, the floor of the mouth was depressible and painless. The dentition was mixed, there were multiple dental caries and destruction of incisor crowns and bimaxillary molars, temporary and permanent teeth (figure 2). There were slightly bleeding abraded wounds in fingers and nails, which compromised the dermal and subdermal level.

The analysis of different therapeutic options, considering physical and cognitive capacities, degree of independence, self-care capacity, communication and compulsive self-mutilating behavior, which compromised perioral tissues, hands, shoulders and other surrounding areas), allowed the health care team to opt for the surgical extraction of all erupted deciduous and permanent teeth.

The surgical procedure consisted of multiple dental extractions and surgery of the residual alveolar ridges, which was performed in the operating room and under general anesthesia; there were no complications (figure 3). In the 7th postoperative day, the gums mucosa was healing and there were no signs of infection. A periodic follow-up was indicated, in order to evaluate the progress and the absorption of sutures. After the immediate postoperative period, the patient was able to eat, and after some time his quality of life significantly

improved, he gained weight and had no intraoral self-inflicted lesions.

After a month, the eruption of the permanent upper left central incisor led to new episodes of self-mutilation of the lower lip and fingers, and eating disorders. The decision of the health care team was the extraction of the tooth, which resulted in a positive progression, a significant improvement in the general status of the patients, feeding and there was no self-mutilation. After two months, the patient was discharged, he had an adequate nutritional state and had no signs of self-mutilation in hands or in the oral cavity (figure 4).

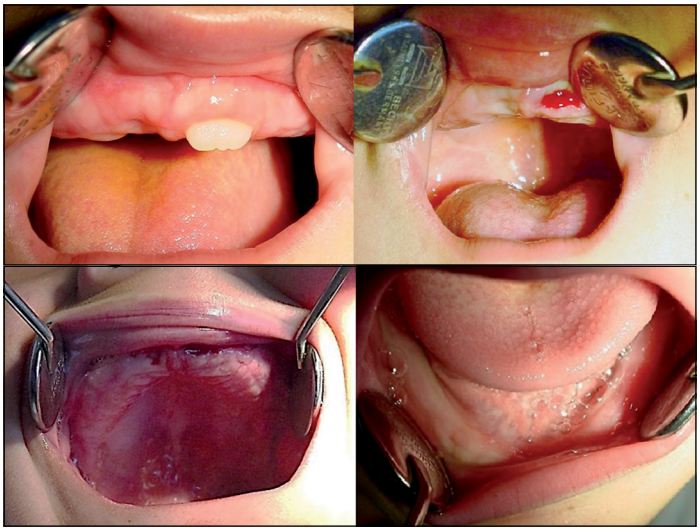

Figure 4. Post-operative control (2 month). Healthy alveolar ridges after teeth extraction.

Discussion

The LNS is a neurodegenerative disease, recessive X-related, which does not yet have a specific treatment for neuropsychiatric symptoms, which have a progressive course, without the possibility of late-stage psychological therapy and whose self-mutilating behavior is persistent.

The patient had a very low residual activity of the HPRT enzyme (lower than 1%), thus it was classified as *Grade 4 "Classic Lesch-Nyhan Syndrome"*, which is expressed as a more severe phenotype regarding self-aggressive behaviors and cognitive impairment.

Biting is the most common type of self-inflicted lesions, it involves the oral area, mainly the lower lip and tongue. 20% of the cases involve lesions in hands, shoulders, and knees[21]. In this report, it was possible to observe these behaviors, which were persistent despite the triple therapy.

The oral self-aggression behavior is a symptom difficult to control. Most of the available information in the literature are case reports, which makes it difficult to establish standard clinical treatments.

The current therapeutic approach is based on the multidisciplinary management, where the dentist can significantly collaborate to prevent future tissue lesions. In this case, the multidisciplinary team considered the extraction of deciduous and permanent teeth, which was the adequate treatment that leads to the recovery of damaged tissues and the nutritional state of the patient, in addition to the alleviation of the family psychological distress.

In this case, a pharmacological treatment was used as a first treatment in order to modify the behavior and muscular activity, however, the results were not favorable and there was a progression in health deterioration, in addition to multiple infections, which led to the option of multiple extractions[22].

The extraction of erupted teeth was an effective alternative in order to prevent future lesions, however, it is necessary to consider that edentulism generates an eating disability. Thus, each case must be studied carefully and personally, considering the opinion of the parents and the multidisciplinary team. The decision must be considered when psychological and therapeutic methods have failed, and this must be opportune since in some occasions when this method has been proposed, it led to deforming mutilations which are difficult to correct[22].

Nowadays, there are no standardized methods to prevent orofacial self-mutilation, therefore, new techniques that can prevent this type of lesions must be developed. The use of acrylic splints has been proposed, however, it had a low success rate and it also interferes with oral hygiene, it promotes the appearance of fungal infections and can promote new lesions or fracture of the splint, which could lead to respiratory risks[23].

Conclusion

Although being an uncommon disease, it is essential that the health care team knows about the LNS and understands the effects of self-mutilation on the family, in order to know how and when to proceed, and thus give patients and their family the best possible quality of life. Early dental extractions, as an effort to reduce self-mutilating lesions and pain at the initial phase of severe cases, can be a useful alternative.

Ethical responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World

Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

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Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

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