



A Preventive Approach to Oral Self-mutilation in Lesch-Nyhan Syndrome: A Case Report

Tae-Sung Jeong, DDS, PhD¹ Ji-Hyun Lee, DDS² Shin Kim, DDS, PhD³ Ji-Hoon Kim, MD⁴
 Ruwaida G.H. Tootla, BChD, MDentSci, PhD⁵

Abstract

Lesch-Nyhan syndrome is a rare X-linked recessive disorder of purine metabolism, caused by complete absence of the enzyme hypoxanthine-guanine phosphoribosyl transferase. Persons affected with this incurable disease are developmentally and physically delayed, and suffer from self-injurious behavior. The most typical feature results in partial or total destruction of perioral tissues. The purpose of this paper was to discuss a case of Lesch-Nyhan syndrome with self-mutilative behavior and lip injuries, including some suggestions of a preventive approach avoiding the extraction of teeth. A soft mouthguard fabricated to prevent the destruction of perioral soft tissues and combined psychiatric pharmacologic therapy proved to have satisfactory results. (*Pediatr Dent* 2006;28:341-344)

KEYWORDS: LESCH-NYHAN SYNDROME, SELF-MUTILATION, MOUTHGUARD

Received November 30, 2005 Revision Accepted February 8, 2006

Lesch-Nyhan syndrome is a rare X-linked recessively inherited disorder. It was first described in 1964 by Lesch and Nyhan in a study of 2 brothers.¹ It is a disorder of purine metabolism causing hyperuricemia and hyperuricosuria with resultant accumulation of sodium urate crystals in the joints, kidneys, central nervous system, and other tissues of the body. The clinical symptoms include impaired kidney function, joint pain, and a progressive neurological disorder, resulting in retardation of mental and motor development. The most distressing aspect of the syndrome, however, is the compulsive urge for self mutilation.² This self-inflicted damage is progressive and protective restraints need to be utilized. Partial to complete amputation of fingers, nose, lips and tongue are the most common.^{3,4}

Over the years, various forms of treatment including pharmacological and dental management have been introduced in an attempt to prevent self-mutilation in Lesch-Nyhan syndrome. The main indication is to prevent the self-mutilative behavior nonsurgically before evolving to surgical procedures.^{3,5-7} Several pharmacological trials have been performed to improve the severe self-destructive behavior with questionable effectiveness.^{8,9}

The purpose of this case report was to present a Lesch-Nyhan syndrome patient who was treated successfully with noninvasive approaches, including a soft mouthguard and psychiatric pharmacologic therapy to prevent further damage of perioral soft tissues.

Case description

A 4-year-old boy was referred to the Department of Pediatric Dentistry, Pusan National University Hospital, Busan, Korea, by his family physician for evaluation of involuntary self-mutilation of the lower lip and a finger. The medical history demonstrated that he had Lesch-Nyhan syndrome and cerebral palsy. He was receiving a 2-mg daily dose of diazepam to relieve the biting action with limited success. Family history indicated that his elder brother, with the same disease, had broad tissue destruction of the perioral region—necessitating the extraction of most of his permanent teeth to prevent further soft tissue destruction (Figure 1). According to the familial pedigree, the mother was a carrier of the recessive X-linked gene which causes Lesch-Nyhan syndrome.

Upon clinical examination, the patient had a self-mutilated wound on both the lower lip and a finger caused by the primary central incisors. Spontaneous strong tonic biting motions caused the lower lip to be trapped between the upper and lower anterior teeth. This resulted in significant and repeated soft tissue trauma and infection, with the loss of normal lip architecture (Figure 2). Intraoral examination was completed with some difficulty, but revealed a caries-free, intact primary dentition minus 2 lower central incisors that were previously extracted by a dental practitioner. The patient's oral hygiene was fairly good. Except for marginal

¹Dr. Jeong is associate professor, ²Dr. Lee is a graduate student, and ³Dr. S. Kim is professor and chair, all in the Department of Pediatric Dentistry, College of Dentistry, Pusan National University, Busan, Korea; ⁴Dr. J-H Kim is assistant professor, Subdivision of Child-Adolescent Psychiatry, Department of Psychiatry, College of Medicine, Pusan National University; and ⁵Dr. Tootla is clinical assistant professor of Pediatric Dentistry, Department of Orthodontics and Pediatric Dentistry, School of Dentistry, University of Michigan, Ann Arbor, Mich.
 Correspond with Dr. Jeong at tjeong@pusan.ac.kr



Figure 1. Facial photograph of patient's elder brother (Lesch-Nyhan syndrome), showing broad tissue destruction on the perioral tissues. Most of his permanent teeth had already been extracted to prevent further tissue destruction.

gingivitis, the remaining intraoral soft tissues were within normal limits. Radiographs were not available.

An impression of the maxillary arch was taken under sedation with chloral hydrate and hydroxyzine. A soft mouthguard was constructed on the working cast using Biostar (Scheu-Dental, Iserlohn, Germany). The maxillary dental arch was covered with a mouthguard made of soft resin material. Simultaneously, psychiatric analysis by a child psychiatrist involved an interview and observation. The patient had been biting his lower lip since 12 months of age.

During toddlerhood, the patient had been cared for in a nursing home, after which the parents were directly involved in his care. The psychiatric report indicated that, whenever the patient was frustrated, he mutilated himself to control anxiety and express aggression. Hence, the pharmacologic approach was aimed at breaking this destructive cycle of events. Sertraline 12.5 mg and risperidone 0.25 mg were prescribed to control the anxiety and self-mutilating behavior. Seven days into pharmacotherapy, the dosages of both medications were doubled. At day 15, the self-mutilating behavior and agitation were markedly reduced and the patient's interaction with his mother improved. Within 1 month, the frequency of self-mutilating behavior was less than a single attempt per week. Remarkably, 4 months of pharmacotherapy resulted in a complete disappearance of the self-mutilating behavior without any adverse effects.

During the periodic dental monitoring phase, the patient appeared to be well adapted to the soft mouthguard. The



Figure 2. Patient with ulcer, scarring, and loss of tissues from the lower lip as recorded at the initial examination.

reduced frequency of overall self-mutilation included fewer lip bites in the first 2 weeks of mouthguard and pharmacotherapy. Within a month, the patient had stopped biting his lower lip and the lip wound had healed completely with only a slight scar (Figure 3a). By 3 months, the self-mutilated damage of the lower lip was satisfactorily reduced. At the 6-month recall visit, a new soft mouthguard was fabricated as the former was ill-fitting. At the 1-year follow-up period, the treatment outcome was very promising. The mother was highly satisfied, and the patient appeared to be very comfortable and less agitated, with no evidence of new self-injurious lesions (Figure 3b).

Discussion

Orofacial self-mutilative behavior almost invariably appears during infancy in children suffering from Lesch-Nyhan syndrome, resulting in the loss of tissue from various body sites. From the dental point of view, self-mutilation can result in massive destruction of the lower lip and, to a lesser degree, of the upper lip. Extraction of primary and permanent teeth are frequently advocated as a solution. The mere extraction of the incisors, however, has not proven effective in preventing further self-injury. Permanent canines and perhaps premolars and molars may also be involved.⁶

Self-mutilation resulting from the teeth is managed with several modalities. The most commonly used oral device is a soft mouthguard. Other appliances^{3,10,11} include:

1. bite blocks;
2. a combination of extraoral and intraoral appliances covering the chin and held in place with a rubber band around the head or with a headgear on the neck-strap;
3. various types of shields that guard the tongue and lips from direct injury;
4. acrylic trays designed to force the lower lip anteriorly seated on the lower teeth; and
5. lip bumpers soldered onto orthodontic bands or stainless steel crowns.

These methods have the advantage of preserving the teeth, but patient cooperation is so poor that it is hard to expect any effective results. Also, devices covering skin or soft tissue may cause drooling and dermatitis.^{7,10} In the present case, at the parent's request, the remaining primary



Figure 3a. Patient at the 12-month recall visit; complete wound healing was found following dental mouthguard and psychiatric pharmacologic therapy.

dentition was retained. While a soft mouthguard was being fabricated, a thorough psychiatric consultation was sought. Following psychiatric assessment and induction of appropriate pharmacotherapy to modify and/or relieve the aggressive behavior, the custom-made soft mouthguard was delivered to limit soft tissue injuries. A soft mouthguard is often chosen as the first device to prevent perioral injuries. In this case, after 6 months, the soft mouthguard needed replacement as it became ill-fitting and there was a change in its physical properties. Therefore, it is necessary to maintain periodic dental reviews to reassess the need for replacement, based on individual need.

Self-mutilation resulting from dysfunction of dopamine in basal ganglia has been confirmed in animal models.¹² In this model, animals typically exhibit behaviors such as oral and limb stereotypes, increased locomotion, sniffing, rearing, and self biting to the level of self-mutilation. Also, some pharmacological agents such as pemoline, which increases dopamine transmission, can result in self-injurious behavior in rodents.¹³ 5-HT also can cause self-injurious behavior. 5-HT antagonist mianserin seems to attenuate the oral stereotype.¹⁴ Risperidone and other serotonin-dopamine antagonists are relatively unique in their pharmacological profile compared to other antipsychotic agents.¹⁵ In this case, 4 months of therapy with risperidone 0.5 mg and sertraline 25 mg reduced self-mutilating behavior and anxiety without any adverse effect up to a 1-year follow-up period. The patient's psychiatrist should:

1. closely monitor and decide on the pharmacotherapy period based on individual patient needs; and
2. liaise with the dentist who should plan appropriate management accordingly.

Long-term clinical studies evaluating the overall effects of this drug regimen on the self-mutilating behavior of Lesch-Nyhan patients is desirable, but adequate patient numbers in any one center would be limited.

In conclusion, there are no standard methods for the prevention of this self-mutilation. Appropriate preventive methods need to be developed for each patient based on reasonable consideration. As an alternative treatment to



Figure 3b. The patient seemed satisfied with the appliance.

extraction, a therapy combining psychiatric, pharmacologic, and dental soft mouthguard treatment may be a viable option in treating transient and acute episodes of self-injurious behavior involving the lower lip. On this basis, this approach for preventing tooth induced self-mutilation warrants further study.

Acknowledgement

This work was supported by Pusan National University Research Grant.

References

1. Lesch M, Nyhan WL. A familial disorder of uric acid metabolism and central nervous system function. *Am J Med* 1964;36:561-570.
2. Jenkins EA, Hallet RA, Hall RG. Lesch-Nyhan syndrome presenting with renal insufficiency in infancy and transient neonatal hypothyroidism. *Br J Rheumatol* 1994;5:392-396.
3. Chen LR, Liu JF. Successful treatment of self-inflicted oral mutilation using an acrylic splint retained by a headgear. *Pediatr Dent* 1996;18:408-410.
4. Nyhan WL, Wong DF. New approaches to understanding Lesch-Nyhan disease. *N Eng J Med* 1996;334:1602-1604.
5. Sugahara T, Mishima K, Mori Y. Lesch-Nyhan Syndrome: Successful prevention of lower lip ulceration caused by self-mutilation by use of a mouthguard. *Int J Oral Maxillofac Surg* 1994;23:37-38.
6. Dicks JL, Lesch-Nyhan syndrome: A treatment planning dilemma. *Pediatr Dent* 1982;4:127-130.
7. Lee JH, Beerkowiz RJ, Choi BJ. Oral self-mutilation in the Lesch-Nyhan syndrome. *J Dent Child* 2002;69:66-69.

8. Anderson LT, Hermann L, Dancis J. The effect of L-5-hydroxytryptophan on self-mutilation in Lesch-Nyhan disease: A negative report. *Neuropadiatrie* 1976;7:439-443.
9. Van Moffaert M. Management of self mutilation. Confrontation and integration of psychotherapy and psychotropic drug treatment. *Psychother Psychosom* 1989;51:180-186.
10. Saemundsson SR, Roberts MW. Oral self-injurious behavior in the developmentally disabled: Review and a case. *J Dent Child* 1997;64:205-209.
11. Fardi K, Topouzelis N, Kotsanos N. Lesch-Nyhan Syndrome: A preventive approach to self-mutilation. *Int J Paediatr Dent* 2003;13:51-56.
12. Breese GR, McCown TJ, Baumeister AA, Emeric SG, Frye GD, Mueller RA. L-DOPA induced self-biting in rats treated with 6-hydroxydopamine(6-OHDA) as neonate: Models of self-mutilation observed in Lesch-Nyhan syndrome. *Fed Proc* 1984;43:928.
13. King BH, Cromwell HC, Hoa TL, et al. Dopaminergic and glutamatergic interaction in the expression of self-injurious behavior. *Dev Neurosci* 1998;20:180-187.
14. Plech A, Brus R, Kalbflesch JH, Kostrazewa RM. Enhanced oral activity responses to intrastriatal SKF 38393 and m-CPP are attenuated by intrastriatal Mianserin in neonatal 6-OHDA lesioned rats. *Psychopharmacology* 1995;119:466-473.
15. Sumiyoshi T, Kido H, Sakamoto H, Urasaki K, Suzuki K, Yamaguchi N, Mori H, Shiba K, Yokogawa K. In vivo dopamine-D2 and serotonin-5-HT2 receptor binding study of risperidone and haloperidol. *Pharmacol Biochem Behav* 1994;47:553-557.

Abstract of the Scientific Literature



Emdogain Does Not Prevent Root Resorption in Reimplanted Teeth

The aim of this study was to evaluate the effectiveness of Emdogain on the periodontal healing of avulsed teeth prior to and after the onset of ankylosis. The present study was performed at the Trauma Centre of the University Hospital of Copenhagen, Denmark. Sixteen teeth in 7 patients (mean age=12.4) comprised the new trauma study group, whereas 11 teeth in 7 patients (mean age=12.7) were enrolled in the previous ankylosis group. Newly traumatized teeth sustained a combined wet and dry extraoral time of 25 to 270 minutes prior to reimplantation. Previously ankylosed teeth were diagnosed as such through their metallic tone on percussion testing. Newly avulsed teeth and those extracted upon evidence of ankylosis were treated with extraoral retrograde root canal therapy with gutta percha and IRM if not previously completed. Emdogain was applied to the root surface and into the saline rinsed alveolar socket. The teeth were splinted for 7 days and then a follow-up program was undertaken at 3 weeks and 2, 6, and 12 months post reimplantation. In the new trauma group, ankylosis occurred in 50% of teeth after 2 months and all teeth by 1 year post injury. In the previously ankylosed group, 72% were ankylosed again by 2 months and all teeth by 4 months post reimplantation.

Comments: Emdogain has been reported to be effective in the treatment of marginal periodontitis, where root surfaces are necrotic or injured. This study shows that Emdogain displays minimal effectiveness in cessation or prevention of ankylosis secondary to tooth reimplantation. Ankylosis of reimplanted teeth is a grave complication leading to infraocclusion and possible tooth loss. Dentists must inform their patients of this sequelae at the time of injury and maintain a rigorous follow-up regimen to address these complications. **JMK**

Address correspondence to Dr. J.O. Andreasen, Department of Oral and Maxillofacial Surgery, University of Copenhagen (Rigshospitalet), Blegdamsvej 9, Copenhagen-2100, Denmark.

Schjott M, Andreasen JO. Emdogain does not prevent progressive root resorption after replantation of avulsed teeth: a clinical study. *Dent Traumatol* 2005;21:46-50.

15 references