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CASE REPORT

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Lesch–Nyhan syndrome: A rare occurrence

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ABSTRACT

Human populations display a marked variation in their patterns of health and disease. This variation may have multiple underlying causes, which may not be completely in the hands of an individual. One such condition is "Lesch–Nyhan Syndrome," a rare inherited disorder caused by a deficiency of the enzyme hypoxanthine-guanine phosphoribosyltransferase (HGPRT), produced by mutations in the *HPRT* gene located on the X chromosome, where persons affected are cognitively impaired and have behavioral disturbances and uncontrollable self-injury causing habit. This paper is a case report of this extreme condition.

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Syndrome; self biting; behavioral; chromosome

Introduction

Lesch–Nyhan syndrome (LNS) is an extremely rare X-linked recessive error of purine metabolism due to severe inborn deficiency of hypoxanthine-guanine phosphoribosyltransferase (HGPRT) enzyme. This enzyme is present in the highest concentration in basal ganglia and is vital for normal metabolism of hypoxanthine [1,2]. Affected individual is shown to have behavioral disturbances, cognitive impairment, and an uncontrollable habit of causing self-injury. Clinically, this compulsive self-biting behavior usually begins with the eruption of teeth. This is associated with the development of hyperuricemia, cerebral palsy, mental retardation, dysarthric speech, choreoathetosis initially and spasticity and dystonia later. The self-mutilating behavior persists and can result in the partial or total destruction of the lower lip and/or amputation of fingers, toes, and sometimes of the tongue [1]. The survival beyond 20 years of age is an exception. The cause of death is mostly renal or respiratory complications. The estimated prevalence of LNS is 1 in 380,000 live births in Canada and 1 in 235,000 live births in Spain, and it has been rarely reported from India [3].

The most distinctive symptom in such children is the compulsive self-mutilating behavior. They may also show symptoms of head snapping and banging, arching the spine, etc. Though they are sensitive to pain, they cannot control the behavior of self-injury. However, they are relieved when inhibited from hurting themselves [4].

Several treatment approaches have been tried with varied results to manage the various abnormalities of the syndrome. Allopurinol has been tried to reduce uric acid. It prevents the development of renal and musculoskeletal injury and leads to a significant increase in life expectancy, by delaying renal failure, which is the common cause of death in early childhood [5,6]. However, it has no effect on the behavioral, cerebral, and neurological manifestations of the disorder [7–9]. Use of drugs like benzodiazepines, neuroleptics, antidepressants, chloral hydrate, and anticonvulsive drugs, etc., has been found to be useful in controlling self-mutilating habit [10,11]. Therapeutic trials with botulinum toxin A (BTX-A) [12], dopamine replacement therapy, and gabapentin for deep brain stimulation in globus pallidus have given positive results [13,14]

This paper is a case report of this condition.

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Case Report

A 2-year-old male child reported to the dental clinic of Department of Pediatric and Preventive Dentistry, Faculty of Dentistry, Delhi with the chief complaint of the habit of self-biting, and parents desiring extraction of teeth present in his mouth. On taking complete history, the parents revealed that the child had developed this self-biting habit at 9 months of age, which coincided with the eruption of teeth. Though ulcers would heal spontaneously after bandaging, recurrence was seen within a day after its removal. The patient also had a habit of pulling his own teeth; as a result, mandibular deciduous anteriors were missing (Fig. 1). He was the only child born to non-consanguineous parents after a normal gestation/pregnancy. Examination revealed that the patient had bit his own tongue and lip leading to visual disfigurement (Figs. 1 and 2). A single, well-defined, scarred region with ragged margins was present over the left forearm (Fig. 3) along with scratching of the skin behind the right ear (Fig. 4). According to the parent, the patient has himself bitten on his arm and removed the flesh of that part. Neurological examination showed chorea, hyper-reflexia, and positive Babinski's sign. Regional lymphadenopathy was not present. Other symptoms included, change in the color of the urine. Complete blood and urine investigations, along with DNA analysis were advised. In DNA analysis, the deletion was found in position c.213 Del C in *HPRT* cDNA, corresponding to Exon 3 in genomic DNA. The serum uric acid levels were 7.1 mg/dLI (normal 1.7–5.8 mg/dl). After complete assessment, final diagnosis as Lesch–Nyhan syndrome was made. The patient was referred to a neurosurgeon and pediatrician for further pharmacological management of the condition.

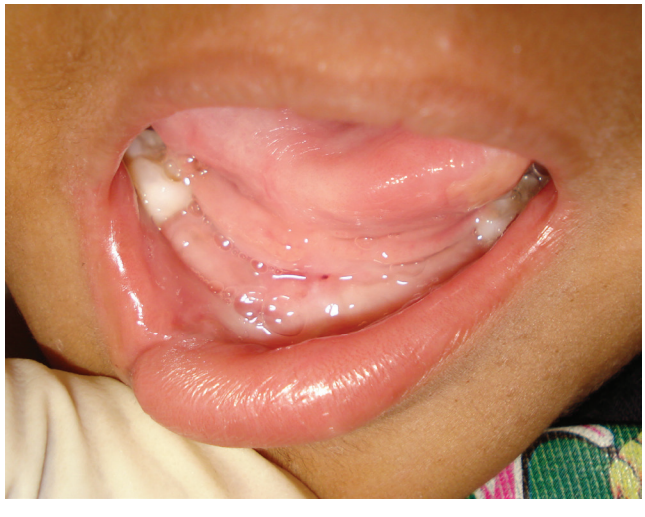

Figure 1. Intraoral appearance with missing mandibular anteriors.

Discussion

Lesch–Nyhan syndrome is an extremely rare genetic disorder, having behavioral, neurological, developmental, and biochemical abnormalities. The symptoms of Lesch–Nyhan syndrome may appear as early as 6 months of age, with the presence of orange-colored deposits (urate crystals) in the urine of the infants due to high levels of uric acid. In the present case, the parent was not able to confirm the same; however, they did mention about the different color of urine. Urine investigations also confirmed the presence of high levels of uric acid in urine. In older children, deposits of sodium urate in cartilaginous tissues can lead to the formation of visible "bulges" called tophi. In untreated young adult patients, urate crystals may also be found in

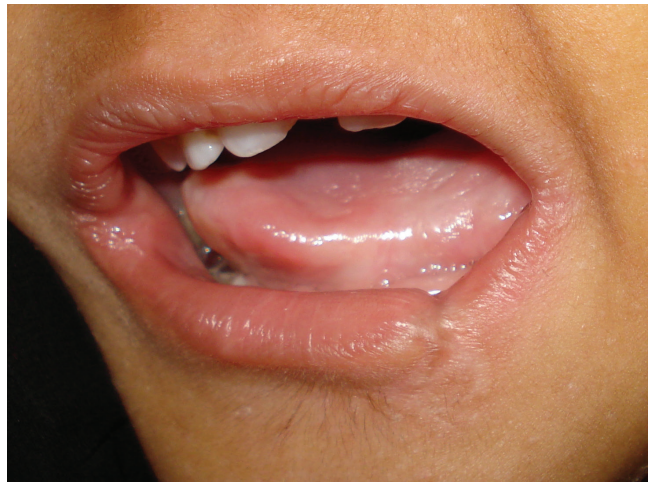

Figure 2. Disfigurement of lip and tongue.

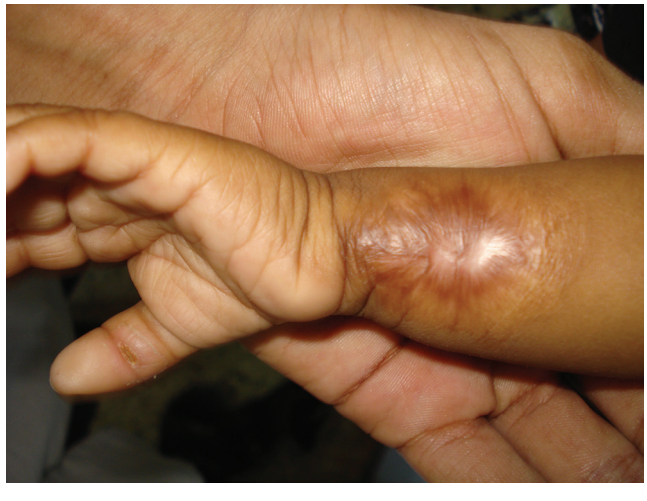

Figure 3. Scarred region of the left forearm.

the joints, causing episodes of pain and swelling of the joints. Neurological symptoms usually begin before the age of 12 months. These may include initial dystonia, chorea, hypotonia with difficulty in sitting and holding the head upright, grimacing, etc. Eventually, most children experience hypertonia, spasticity, and hyperreflexia [8,15].

Compulsive self-injury behavior like persistent biting of the lips, tongue, fingers, and shoulders is one of the most difficult conditions to manage and may result in the partial or total destruction of perioral tissues. Self-mutilation behavior can be present in other syndromes like Familial dysautonomia, Cornelia de Lange syndrome, etc [15]. However, this is the most striking feature of the Lesch–Nyhan syndrome, being present in almost 85% of the cases [15,16]. In the present case also, the child reported with a severe self-mutilating habit, which developed at the age of 9 months, leading to severe disfigurement of the oral structures.

Several studies have been conducted to understand the pathogenesis of the neurologic disorders of the Lesch–Nyhan syndrome, such as self-mutilation, but the mechanism still remains unclear. Though several drug trials have been performed, they have given questionable results in improving the severe self-destructive behavior [17–19]. Extraction of some or all teeth may be considered an effective means to prevent persistent self-destruction; still, it is a highly invasive approach with long-term oral disability. Authors have suggested the use of an intraoral appliance for restricting the self-injurious biting and protecting the oral and peri-oral structures, or even other parts of the body.

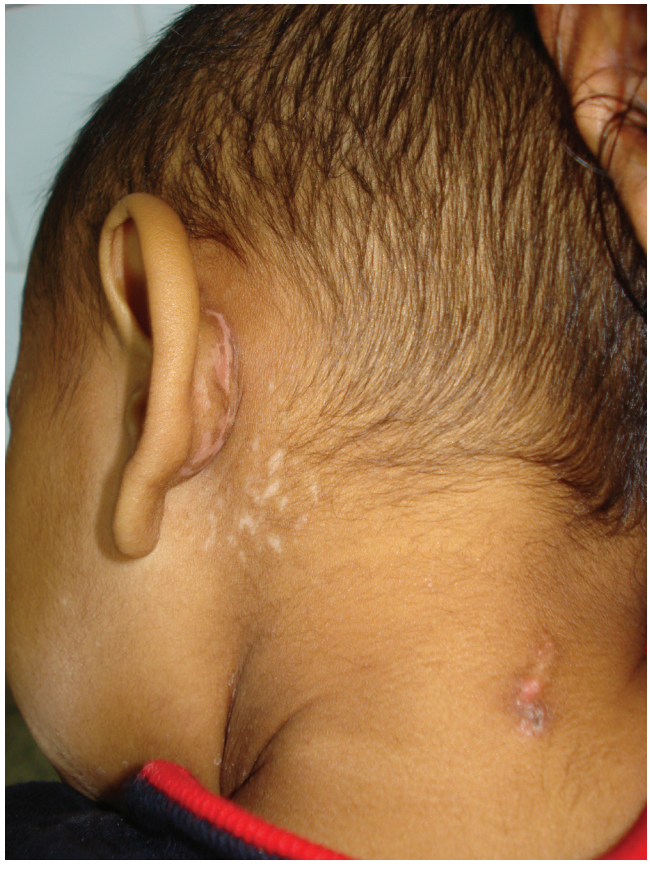

Figure 4. Scratched area behind the right ear.

In a case of an adult female with cerebral palsy and mental retardation, leading to chronic lip biting, Macpherson [20] used a maxillary osteotomy to create an anterior open bite. Postsurgical evaluation after 13 years showed that the anterior open bite was still present with no further episodes of lip biting. This could make orthognathic surgery an option for cases where the conservative approach has failed [21]. Behavior modification techniques designed to reduce self-mutilating behaviors have been useful to some extent. Olson and Houlihan [22] advocated the combination of physical restraints, behavioral treatment, and pharmaceutical therapy for the management of the self-destructive behavior. Though in this case, the patient had a severe self-mutilating habit, the use of an intraoral appliance or maxillary osteotomy was not a very useful option, as the child was just 2-year old. Hence, the patient was referred to a neurosurgeon and pediatrician for pharmacological intervention.

Complete management of Lesch–Nyhan syndrome involves dealing with specific symptoms that are present in each individual. Specialists in various fields like pediatrician, orthopedist, neurosurgeon, physical therapists, dental surgeon, and other health care professionals need to systematically and comprehensively plan an affected child's treatment.

Conclusion

Lesch–Nyhan syndrome is an extremely rare disorder, associated with behavioral, neurological, and developmental and biochemical abnormalities. Not many cases have been reported of the same. Hence, no standard methods have been established as yet for the prevention and management of self-injurious habit in patients with Lesch–Nyhan syndrome. Appropriate preventive methods need to be used for each individual patient based on close observation. Whether to go ahead with an oral appliance or employing more invasive approaches will vary from case to case. However, at a younger age, management of cases further becomes difficult and pharmacological management appears to

be a preferable option. More reporting of cases and studies on various management approaches is needed to effectively deal with such cases and provide them relief.

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