Case Report

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Case of Self-Mutilation –Lesch-Nyhan Syndrome

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ABSTRACT

Lesch-Nyhan syndrome involves a congenital error of purine metabolism, due to the absence (or very low levels) of hypoxanthine-guanine phosphoribosyltransferase (HPRT) enzyme (Lesch and Nyhan 1964). The classic clinical phenotype of LNS was first described by Michael Lesch and William Nyhan in 1964 and is characterized by hyperuricemia, intellectual disability, severe motor deficiency, and recurring self-mutilation (Lesch and Nyhan, 1964). Here we present a case of a 4-year-old male child with features of self-mutilation, aggression, and poor neck control and unable to sit and stand. we diagnosed him as a case of Lesch-Nyhan syndrome based on clinical features and slight hyperuricemia. Due to the lack of medical facilities, many cases of Lesch-Nyhan syndrome undergo unnoticed in many underdeveloped countries.

Keywords: lesch-nyhan syndrome; self-mutilation; lip injury; self-injurious behavior; global developmental delay.

INTRODUCTION

Lesch-Nyhan Syndrome (LNS) is a rare congenital disorder due to either a very low level or complete absence of hypoxanthine-guanine phosphoribosyl transferase (HPRT) activity. HPRT is an important enzyme of the purine salvage pathway which is encoded by HPRT1, a gene on the long arm of the X chromosome. The sequence errors in HPRT1 cause a wide range of mutations resulting in a spectrum of clinical disorders. It ranges from severe enzyme deficiency (less than two percent enzyme activity) with prominent behavioral and neurological impairments; to Lesch-Nyhan variants with only hyperuricemia-related symptoms like kidney stones, gout, and tophi (1). In 1964, Michal Lesch and William Nyhan were the first to describe the classic features of LNS as mental retardation, recurrent self-mutilation, and severe motor deficiency, with hyperuricemia (2).

Most patient with LNS is normal at birth. The features of developmental delay including poor head control, delayed sitting, hypotonia and athetoid movements may be present as early as three to six months. Although self-mutilation in form of finger chewing; lip and tongue biting may appear as soon as teeth develop, they are usually present between the age of two to sixteen years. (3). Early pediatric and/or neurological consultation for the patient with psychomotor delay can help diagnose HPRT deficiency. However, the clinical suspicion of LND is often delayed

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until significant self-mutilation.

Lack of knowledge of rare genetic diseases among medical and paramedical staff; and limitations of the health care system in geographically challenged parts of the world may have delayed diagnosis and management of such cases. We present a similar case from a rural part of Nepal, who was presented in our facility only after severe self-mutilation was evident

Case Presentation:

A 4-year-old male child born via cesarean delivery following an uneventful birth history presented to our hospital with complaints of self-injurious behaviors, irritability, aggression, and hypotonia. He started biting his lips, tongue, and fingers from the age of two, which gradually increased with age. This has led to marked deformities of the tongue, lips, and fingers. The tongue and lips had contusions and lacerated wounds, and the middle portion of the lower lip was missing. There were abraded wounds in the fingers and nails. He was so aggressive that his mother had to restrain him to prevent further self-injurious behavior. There were bruises on both forearms, as well as a handcuff mark from physical restraint. His hands were covered with big bedsheet to prevent further injury. He was hypotonic since early infancy, for which a brain MRI was done, which was found to be a normal scan. Developmental history revealed delayed gross motor and language milestones. He had poor eye contact, an inability to walk, and needed assistance for feeding.

He had a family history of similar findings in his elder brother, who died of respiratory complications at the age of 4 and half years. As his elder brother was suspected to have clinical findings because of complications of labor, this child was delivered by elective cesarean section to avoid such complications. There were no other close relatives in his family with similar illnesses. Laboratory investigation revealed a slight increase in serum uric acid levels. The mother denied further laboratory investigations and genetic evaluation was deferred.

DISCUSSION

LNS presents with the most severe clinical features among patients with HPRT deficiency. Delays in developmental milestones were common findings in most of the cases and many were diagnosed with Cerebral palsy at an early age until self-injurious behaviors were present (4)(5) (6). Self-injurious behavior can present in conditions like autism, Tourette syndrome, psychiatric illness, and idiopathic mental retardation. Moreover, intractable self-injurious behaviors including lip biting, finger chewing, and head banging, if present, along with hyperuricemia should always be suspected of complete HPRT deficiency (2). Commonly observed behaviors in previous cases were self-mutilation (hands, lips, buccal mucosa, and tongue), self-injury (scarring of face and hands), head banging, self-scratching, and hair pulling. The onset of such behaviors varied from as early as 11 months to 5 years of age ((7) (8) (5)). An observational study followed three cases of LNS and concluded that self-mutilation behavior appeared in all cases before three years of age, and was mostly influenced by biological, environmental, and social factors (4). Our case was also diagnosed as a case of cerebral palsy initially. He showed self-mutilating behavior at the age of two but was not suspected of LNS until presented in our center with severe self-mutilation. Although medical treatment of aggression and compulsive behaviors are still under study, an

early approach in conservative management of self-mutilation including dental extraction, mouth guard, and gum shield application was successfully used in previous cases (4,9). Severe self-mutilation in our case could have been prevented with similar approaches.

The common neurological features in most of the previous cases include hypotonia, dystonia, clonus, ballismus, dysarthria, choreoathetoid movements, spasticity, dysphagia along with cognitive impairments ((7) (5) (6) (10)). Torres and Puig conclude that the severity of neurological symptoms correlates degree of enzyme deficiency and is an important aspect to consider for prognosis. According to their proposed classification of HPRT deficiency, the case with complete HPRT deficiency has motor syndrome as severe action dystonia superimposed on a baseline hypotonia, resulting in an inability to stand up and walk (3). Our case has similar neurological findings, as he is wheelchair-bound and requires complete personal care for daily activities.

Respiratory conditions should be primarily monitored in the cases of LND as it can be a major cause of mortality. Kostadinov et al, in their case series, described eight cases of LNS having multiple episodes of severe respiratory arrest with or without coma, loss of consciousness, cyanosis, and obtundation. Five of them ended up dying of unexplained causes in various course of time (10) and the elder brother of our case who also presented with the features of LNS died of respiratory complications. Most previous cases had increased serum uric acid and increased urinary uric acid to creatinine ratio. As hyperuricemia is a common finding of LNS, these laboratory findings along with phenotypic features of LND can be an essential tool in early suspicion of LND. Our case also had increased serum uric acid levels along with classical clinical features of LND including self-mutilation, which further supported our diagnosis.

The definitive diagnosis of LND is made either with enzymatic essay, with low or undetectable HPRT activity and increased APRT activity; or molecular testing by HPRT1 gene sequencing. Most of the previous cases had extremely low or undetected HPRT activity and/or mutation of the HPRT1 gene ((7) (9) (5). However, some of the cases were diagnosed based on clinical features and hyperuricemia alone. As enzymatic essay and genetic testing were not feasible in our center and the case was noncompliant with treatment, the presumptive diagnosis of LNS was made based on classic clinical features, hyperuricemia, and a history of similar findings in his elder brother.

CONCLUSIONS

LNS can go undiagnosed until the stage of severe self-mutilation, although neurological and developmental features are present at an early age. Many parts of the world lack proper medical facilities and motivation for enzymatic and genetic testing. Knowledge of classic findings in LND and a series of common labs including serum uric acid levels can help early suspicion of the disease and prevent disfigurement due to self-mutilation.

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