Journal of Neonatal Research and Pediatrics Care

Chembio Publishers
Right Choice for Researchers

Case Report *Volume 2; Issue 2*

Extreme reduction of serum uric acid in patients with Lesch-Nyhan Disease: Reduction of Nephrolithiasis

Nyhan WL*, Eddey GE, Haldaman K and Rohey KC

Department of Pediatrics, University of California San Diego, USA

***Corresponding author:** Dr. William Nyhan, Department of Pediatrics, University of California San Diego and Rady Children's Hospital, San Diego, CA, USA, Tel No: 619-543-5337; Email: wnyhan@ucsd.edu

Received Date: October 03, 2019; **Published Date:** October 22, 2019

Abstract

Lesch-Nyhan disease (LND) or Lesch-Nyhan Syndrome (LNS) is an X-linked recessive disorder of the purine salvage pathway in which hyperuricemia, is associated with gout and uric acid nephrolithiasis. It is also characterized by cognitive impairment, dystonia and dramatic behavioral manifestations, including the hallmark self-injurious behaviors.

Keywords: Lesch-Nyhan disease; Lesch-Nyhan Syndrome; Nephrolithiasis; Dystonia

Abbreviations: LND: Lesch-Nyhan Disease; LNS: Lesch-Nyhan Syndrome

Introduction

The HPRT1 gene is located on the long arm of the X chromosome, and over 600 different mutations have been identified [1]. As an X-linked recessive mutation it occurs predominantly in males, but there have been several documented cases of classic LND in females, in some instances a consequence of nonrandom inactivation of the paternal X chromosome [2]. In others, especially twins, it reflects a skewed pattern in which there is preferential inactivation of one X in the affected twin and the other in her normal twin [3]. Matheny is an ideal place for such observations because the patients are under observation 24 hours a day for years. In contrast, most patients are seen by a physician for a small fraction of their lives. This is the purpose of this report to describe two patients with the disease.

Case 1

GB was a 37 year old individual with the classic form of Lesch-Nyhan disease. He had simple conversations at times demonstrating a child-like demeanor, yet always personable – at least in the company of individuals that made him feel safe. He had long used protective devices to prevent severe self-injury. He was noted to be an excellent observer as demonstrated by the following example: when his nurse was changing the feeding tube on his roommate…if she left the room without connecting the tubing properly or forgetting to turn the feeding pump on, (despite his dysarthria) he reminded the nurse to return and complete her task. In addition, he memorized on a week to week basis the schedules of all his nurse and PCA caretakers and was highly cognizant of when his parents were to visit and take him home. Another example of his skills: At one time he was told that his primary caregiver was taking about 4 weeks off for a family emergency. On the day his caregiver was expected be back, GB was startled that he had not returned. No one else

Citation: Nyhan WL, et al. Extreme reduction of serum uric acid in patients with Lesch-Nyhan Disease: Reduction of Nephrolithiasis. J Neo Res Pedia Care 2019, 2(2): 180018.

remembered the anticipated return date and when his caregiver returned, it turned out GB was the only person who remembered the correct date of return.

He had been a resident at Matheny Medical and Educational Center for 25 years. At one time his serum uric acid had been allowed to rise to 7.5 and 7.7 and 8.2 mg/dl. Later he had migratory swelling with erythema of his hands and hands/wrists.

Case 2

ZL was a 23 year old individual with the classic form of Lesch-Nyhan disease who was first diagnosed at the age of 16, having previously carried the diagnosis of Tourette syndrome. His self-injurious behaviors were minimal. His predominant form of abnormal behaviors was verbal aggressiveness.

Discussion

The self-injurious behavior is not under the patient's control nor does the patient desire it. These self-destructive behaviors usually begin between ages one and six and often escalate as the patient ages and the patient is more physically able to cause self-injury. The first manifestations of physical self-injury are lip biting, finger biting, and biting of the oral cavity. Modes and patterns of self-injury have been described in [4] and are often specific to each individual patient and reoccur consistent over the life-span. Self-injury usually involves biting, usually of the lips and fingers. Forms of self-injury include eye-poking, head banging, fingers in wheelchair spokes, and extension of arms in doorways. Outwardly directed aggressive behaviors include hitting, kicking, head-butting, biting others, spitting, and inappropriate remarks.

When oral self-injury is present, removal of the teeth is completely effective to prevent facial disfigurement. Removal of teeth is often difficult for families (and healthcare providers) to accept. Decisions regarding dental extraction are ideally made by physicians who are expert in the comprehensive care of patient with this disorder [5]. Protective devices are essential to safeguard the patient from himself. Treatment with allopurinol is designed to minimize the possibility of uric acid nephropathy. Maximizing the excretion of hypoxanthine and minimizing that of xanthine is the objective of doses. Hyperuricemia is a consequence of aberrant activity of the enzyme hypoxanthine-guanine hosphoribosyltransferase (HPRT).

Although strength is normal, individuals with classic LND are non-ambulatory. The dystonia is continuous, characterized by sustained or intermittent muscle contractions causing abnormal and repetitive, patterned movements. The dystonia is superimposed on hypotonia and can be initiated or worsened by voluntary action. In addition, anxiety, a component of this disorder, worsens the dystonia and exacerbates self-injury. Patients with LND can be very engaging and personable. It is interesting that parents often believe IQ scores obtained are artificially low and reason that low performance is secondary to LND behavior.

Moderately high doses of allopurinol in the 650 mg level would decrease the serum uric acid level modestly. Our patients have used doses as high as 1200 mg per day without side effects. If there are very high levels of urinary xanthine excretion, then the likelihood exists for the formation of xanthine stones. But if the curve can be shifted to the production of a higher accumulation of hypoxanthine, this may decrease stone formation. Hypoxanthine is soluble. Dosage is recommended to make hypoxanthine maximum and xanthine minimal. Total purine excretion remains the same.

References

1. Lesch M, Nyhan WL (1964) A familial disorder of uric acid metabolism and central nervous system function. Am J Med 36: 561-570.

2. Fu R, Ceballos-Picot I, Torres RJ, Larovere LE, Yamada Y, et al. (2014) Genotype-phenotype correlations in neurogenetics: Lesch-Nyhan disease as a model disorder. Brain 137(5): 1282-1303.

3. De Gregorio L, Nyhan WL, Serafin E, Chamoles NA (2000) An unexpected affected female patient in a classical Lesch-Nyhan family. Molec Genet and Metab 69(3): 263-268.

4. De Gregorio, Jinnah HA, Harris JC, Nyhan WL, Schretlen DJ, et al. (2005) Lesch-Nyhan disease in a female with a clinically normal monozygotic twin. Molecular Genetics and Metabolism 85: 70-77.

5. Sweetman L, Nyhan WL (1967) Excretion of hypoxanthine and xanthine in a genetic disease of purine metabolism. Nature 215(5103): 859-860.