Cite as: Saraswati PVA, Gunawan PI, Irmawati M: Self-injury behaviour in children with intellectual disabilities, suspected Lesch–Nyhan syndrome: a rare genetic case. Pediatr Med Rodz 2025; 21 (3): 154–158

Received: 31.08.2024
Accepted: 04.11.2024
Published: 15.10.2025

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Self-injury behaviour in children with intellectual disabilities, suspected Lesch–Nyhan syndrome: a rare genetic case

Zachowania samouszkadzające u dzieci z niepełnosprawnością intelektualną w kontekście podejrzenia zespołu Lescha–Nyhana: opis rzadkiego przypadku genetycznego

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https://doi.org/10.15557/PiMR.2025.0022

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Abstract

Intellectual disability is a deficit in intellectual functioning that impairs adaptation to daily life and may lead to behavioural disorders. Self-injury behaviour is a form of behavioural disorder which has an association with intellectual disabilities in children. Self-injury behaviour can be present in certain genetic syndromes, such as Lesch–Nyhan syndrome. A two-year-old boy with developmental delay was unable to sit, crawl, and talk. He had a habit of biting his lips, tongue, and fingers frequently. His uric acid level was 7.3 mg/dL. The patient was diagnosed with behavioural and emotional disorder with global developmental delay due to suspected Lesch–Nyhan syndrome. In this case, self-mutilating behaviour, global developmental delay, and motor impairment were observed. Integrated management through behavioural therapy and combination pharmacologic interventions represents the current therapeutic approach. Self-mutilating behaviour accompanied by motor impairment may give rise to physical deformity and decrease a child's quality of life if not diagnosed and treated early.

Keywords: self-injury, intellectual disability, behavioural disorder, Lesch–Nyhan syndrome

Streszczenie

Niepełnosprawność intelektualna to deficyt funkcji poznawczych, który utrudnia codzienne funkcjonowanie i może prowadzić do zaburzeń zachowania. Jednym z takich zaburzeń są zachowania samouszkadzające, często obserwowane u dzieci z niepełnosprawnością intelektualną. Mogą one także współwystępować z niektórymi zespołami genetycznymi, takimi jak zespół Lescha–Nyhana. W pracy opisano przypadek dwulatka z opóźnieniem rozwojowym, który nie potrafił siadać, pełzać ani mówić. Często gryzł wargi, język i palce. Stężenie kwasu moczowego wynosiło 7,3 mg/dl. U chłopca stwierdzono zaburzenia zachowania i kontroli emocji wraz z globalnym opóźnieniem rozwojowym, prawdopodobnie w przebiegu zespołu Lescha–Nyhana. Rozpoznano zachowania samouszkadzające, globalne opóźnienie rozwojowe oraz zaburzenia motoryczne. W takich przypadkach zalecane podejście terapeutyczne obejmuje terapię behawioralną w skojarzeniu z farmakoterapią. Nieleczone lub zbyt późno rozpoznane zachowania samouszkadzające, zwłaszcza przy współwystępowaniu zaburzeń motorycznych, mogą prowadzić do deformacji fizycznych i znacząco obniżać jakość życia dziecka.

Słowa kluczowe: samookaleczanie, niepełnosprawność intelektualna, zaburzenia zachowania, zespół Lescha–Nyhana

INTRODUCTION

Intellectual disability (ID) refers to a heterogeneous group of conditions affecting approximately 3% of the population, characterised by an intelligence quotient (IQ) below 70. Children with ID frequently experience behavioural disorders, which can complicate daily life and may either mask or reveal underlying organic or psychiatric conditions. The management of behavioural disorders in children with ID often requires a multidisciplinary approach, addressing common disorders such as sleep disturbances, agitation, and self-injury behaviour (SIB)[1].

SIB is defined as a deliberate act that causes physical harm to one's own body. It is frequently associated with ID, with prevalence rates ranging from 7% to 22%, and is often linked to pervasive developmental disorders or genetic syndromes, including Lesch–Nyhan (LNS), Cornelia de Lange, Fragile X, Prader–Willi, and Tourette syndromes[2]. While approximately 10% of typically developing two-year-olds may engage in behaviours such as head-banging during tantrums as part of normal development, these behaviours generally subside as communication skills develop. However, in children with ID, this developmental trajectory is delayed, and SIB may persist into adolescence[1]. Once established, SIB can be particularly challenging to manage, although it may diminish with age in cases where impulsivity is well-controlled[3].

This case report presents the diagnosis and management of a child exhibiting self-injurious behaviour in the context of suspected LNS, a rare genetic condition. In the absence of confirmatory metabolic or genetic testing, the diagnosis remains tentative, and the focus of this report is on the clinical presentation and management strategies employed to address the child's psychomotor impairments and self-harming behaviours[3].

CASE REPORT

A two-year-old boy was brought to the paediatric clinic at Dr. Soetomo Hospital, with the primary concern of an inability to sit independently. According to his mother, he also exhibited a compulsive habit of biting his thumbs, lips, and tongue, causing injuries and bleeding. This self-injurious behaviour could only be interrupted by physically restraining the child's hands, which in turn triggered crying and tantrums. Additionally, the patient demonstrated difficulty understanding spoken commands and delayed motor development, including an inability to lift his head due to hypotonia. No family history of similar conditions was reported, and both pregnancy and postnatal periods were uneventful.

The boy was delivered by a midwife following a full-term pregnancy, with a birth weight of 3,400 g. He cried immediately at birth and displayed no signs of cyanosis or jaundice. He is the second of two children and lives with his parents and sister. The mother reported no infections or significant illnesses during pregnancy, and both parents had completed junior high school. The patient had no history of hospitalisation, and his mother had never sought medical attention for his self-harming behaviours. The boy received all necessary immunisations and was breastfed until the age of 1 year, after which he was transitioned to formula milk.

On physical examination, the patient's lower lip and tongue appeared hypoplastic, but there were no signs of anaemia or jaundice. Examination of the chest and abdomen was unremarkable. Both upper and lower extremities were hypotonic, and there were lacerations on both thumbs due to biting. Despite these findings, the child was alert, active, and cooperative during the examination. Neurological assessment revealed no gross abnormalities, and anthropometric measurements indicated that the patient was underweight, normocephalic, and stunted in growth. Head magnetic resonance imaging showed no significant findings, and laboratory results revealed elevated uric acid (7.3 mg/dL) and creatinine (0.3 μmol/L) levels, while all other parameters were within normal limits.

The patient was referred to the physiatry department for further management. He was prescribed fluoxetine (1 mg) and folic acid (0.5 mg) to be taken orally in the morning, along with haloperidol (0.1 mg) to be administered at night. Behavioural therapy was also planned to address his self-injurious tendencies. Additionally, an IQ test was scheduled to assess for ID, with a suspicion of LNS, a rare genetic disorder. The onset of LNS symptoms, typically occurring between 3 and 9 months of age, corresponded to the patient's clinical history.

Despite the patient exhibiting signs of a behavioural disorder, specifically self-harming behaviours such as lip-biting, a formal diagnosis of ID could not be confirmed pending the IQ test. Moreover, the required testing for hypoxanthine-guanine phosphoribosyltransferase (HPRT) enzyme deficiency, essential for confirming LNS, was not available in Indonesia at the time of evaluation[4]. This lack of accessibility to diagnostic tests, especially in resource-limited settings, often delays the timely diagnosis and management of LNS[5].

DISCUSSION

The present case of a two-year-old boy with significant developmental delays and SIB, notably characterised by compulsive lip, thumb, and tongue biting, offers a unique opportunity to examine the intersection between behavioural disorders, ID, and suspected LNS. This case highlights several notable aspects, including the severe nature of self-harm, the early onset of psychomotor delays, and the complex interplay between diagnostic limitations and management strategies in a resource-constrained setting.

SIB in children with developmental delays and ID is a well-documented phenomenon, with prevalence rates ranging from 7% to 22% among this population[6]. However, the severity of SIB in this case, leading to physical deformities

 DOI: 10.15557/PiMR.2025.0022

such as hypoplastic lips, is less common and aligns with more extreme cases of self-mutilation, typically associated with genetic syndromes such as LNS[2]. In LNS, SIB is almost universal, with all affected individuals exhibiting self-mutilating behaviours such as biting the lips, fingers, and other body parts. These behaviours typically begin within the first year of life; similar behaviours were observed in this case, starting at around 7 months of age[4].

By comparison, in other genetic syndromes such as Cornelia de Lange, Fragile X, and Prader–Willi, the onset of SIB tends to occur later and is often less severe[7]. The compulsive nature of the behaviour, as well as its resistance to environmental modulation (requiring physical restraints), further supports a genetic aetiology, most likely LNS[8]. However, without confirmatory genetic or biochemical testing (such as HPRT enzyme analysis), the diagnosis remains tentative, highlighting a key limitation of this case.

The pathophysiology of SIB in LNS is thought to be multifactorial, involving both neurobiological and biochemical mechanisms. LNS is caused by mutations in the *HPRT1* gene, leading to a deficiency of the enzyme HPRT. This enzyme plays a crucial role in the purine salvage pathway, recycling purines for DNA synthesis. HPRT deficiency results in the accumulation of uric acid in blood and tissues, leading to gout, kidney stones, and other systemic complications[9].

Of particular relevance to this case is the neurological and behavioural component of LNS, which remains incompletely understood. The deficiency of HPRT is believed to disrupt dopaminergic pathways, particularly within the basal ganglia, leading to motor dysfunction and the characteristic self-injurious behaviours[10]. Guanosine triphosphate (GTP), which is crucial for dopamine synthesis, is hypothesised to be deficient in neurons reliant on the purine salvage pathway. This GTP deficiency may impair dopaminergic signalling, contributing to both the neurological symptoms and the impulsive, repetitive self-harm seen in LNS patients[11]. Involvement of the basal ganglia, specifically lesions affecting the striatal dopamine pathways, has been demonstrated in neuroimaging studies of LNS patients.

In this case, the patient's elevated uric acid level (7.3 mg/dL) provides indirect evidence of a metabolic abnormality consistent with LNS. However, normal creatinine levels and the lack of overt renal symptoms (e.g. kidney stones) suggest that the metabolic consequences of HPRT deficiency, if present, have not yet fully manifested. This emphasises the importance of early diagnosis and ongoing monitoring in suspected cases of LNS, as systemic complications may progress over time[12].

The diagnosis of LNS remains challenging, particularly in settings where advanced genetic and metabolic testing is unavailable. In this case, the absence of confirmatory HPRT enzyme analysis or genetic testing represents a significant limitation, preventing a definitive diagnosis. The lack of access to these diagnostic tools, seen in many developing countries like Indonesia, highlights the need for greater availability of specialised diagnostic resources in such regions[13].

The patient's clinical presentation, with early-onset psychomotor delays and severe SIB, strongly suggests a genetic aetiology. The lack of a family history of similar conditions, while notable, does not rule out LNS, as approximately one-third of cases arise from de novo mutations[14]. Furthermore, the absence of cognitive testing, such as an IQ assessment, limits the ability to fully assess the extent of ID in this patient, which is typically moderate to severe in LNS. ID in LNS is frequently accompanied by impulsivity, aggression, and poor social functioning, all of which were observed to varying degrees in this patient[15].

The management of SIB in patients with suspected LNS or other forms of ID is complex and requires a multidisciplinary approach. In this case, a combination of pharmacological and behavioural therapies was employed, with the patient receiving fluoxetine, haloperidol, and vitamin supplementation (B_6 and B_{12}). This pharmacological approach aimed to reduce impulsivity and self-harm, with fluoxetine, a selective serotonin reuptake inhibitor (SSRI) targeting mood instability, and haloperidol, an antipsychotic, addressing aggressive behaviours.

The use of haloperidol and fluoxetine in this case aligns with existing literature on the pharmacological management of SIB in children with ID. Haloperidol has been shown to reduce aggression and self-injurious behaviours in several studies, particularly in cases where dopaminergic dysfunction is implicated, as seen in LNS[2]. However, long-term use of haloperidol is associated with significant side effects, including extrapyramidal symptoms, which were not observed in this patient but remain a concern for future management. Fluoxetine, meanwhile, has demonstrated efficacy in reducing impulsivity and mood-related components of SIB, although its use in young children remains controversial due to the potential risk of increased suicidal ideation[16].

Non-pharmacological interventions, including behavioural therapy, were also planned for this patient. Behavioural therapy, particularly through positive reinforcement and environmental modifications, has been shown to be effective in reducing SIB in children with developmental disabilities. However, in cases of severe, compulsive self-harm, behavioural interventions may need to be supplemented by pharmacological treatments, as was done in this case[3]. The need for physical restraints in this patient, while necessary to prevent further injury, highlights the severity of his condition and the limitations of current therapeutic approaches in managing such extreme behaviours.

Several limitations were encountered in the management of this case. First, the lack of confirmatory diagnostic testing represented a major challenge, as the clinical suspicion of LNS could not be definitively proven without genetic or biochemical confirmation. This limitation not only affects the diagnosis but also complicates the long-term management of the patient, as the prognosis and treatment strategies for

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confirmed LNS differ from those for other causes of ID and SIB. For example, patients with confirmed LNS may benefit from specific treatments aimed at reducing uric acid levels, such as allopurinol, which was not considered here due to diagnostic uncertainty[17].

Second, pharmacological interventions, while necessary, carry the risk of side effects, especially with long-term use. Haloperidol, in particular, can induce extrapyramidal symptoms and tardive dyskinesia, which could further complicate the patient's motor dysfunction[7]. Additionally, the use of fluoxetine in young children, while effective in this case, remains controversial due to its association with an increased risk of mood swings and suicidal ideation[16].

Third, the reliance on physical restraints to manage SIB reflects a limitation in available therapeutic options. While restraints were effective in preventing immediate harm, their use is associated with ethical concerns and potential long-term developmental consequences, as they can limit the child's ability to engage in normal activities and social interactions[2]. Moreover, restraints may exacerbate psychological and social issues over time.

This case contributes to the existing literature by highlighting the challenges of managing severe SIB in a child with suspected LNS in a resource-limited setting. The early onset of SIB, combined with developmental delays and the absence of confirmatory testing, underscores the importance of clinical suspicion and timely intervention. Moreover, the case emphasises the need for improved access to diagnostic tools, such as genetic and enzyme testing, in resource-constrained environments to facilitate early diagnosis and appropriate management[15].

Furthermore, this case provides insights into the use of combined pharmacological and behavioural interventions in managing severe SIB. The successful reduction in self-harm behaviours through the use of haloperidol and fluoxetine, while noteworthy, also highlights the need for ongoing monitoring and awareness of potential adverse effects with long-term use[2]. The case also raises important ethical considerations regarding the use of physical restraints in paediatric patients and the need for alternative, less restrictive interventions[4].

Further research is needed to explore alternative therapeutic strategies for managing SIB in children with ID and suspected genetic syndromes like LNS. Specifically, the development of novel pharmacological agents targeting the underlying biochemical and neurological dysfunctions in LNS could provide more effective and targeted treatments[18]. Additionally, the implementation of early genetic screening programmes in resource-limited settings could facilitate earlier diagnosis and support more tailored interventions for children with suspected genetic disorders[19].

CONCLUSIONS

In this case, the child's severe self-injurious behaviour, particularly compulsive lip-biting, firmly suggested a genetic syndrome, most likely LNS. The diagnosis of LNS, though unconfirmed due to the lack of genetic and metabolic testing, remains a strong clinical consideration based on the patient's presentation and elevated uric acid levels. Management of suspected LNS, as demonstrated in this case, focuses on symptomatic control through a combination of behavioural and pharmacological interventions.

Behavioural therapy, particularly positive reinforcement strategies, plays a pivotal role in reducing self-injury, though its effectiveness may be limited in cases of severe compulsive behaviour, such as seen in this patient. Pharmacological management, including antipsychotics such as haloperidol and mood stabilisers like fluoxetine, aims to address the underlying impulsivity and mood dysregulation that drive self-injurious behaviour. In confirmed cases of LNS, medications such as allopurinol, which reduce uric acid levels, may also be incorporated into the treatment plan to address the metabolic complications of the syndrome.

Early detection and intervention in children exhibiting SIB are crucial to improving long-term outcomes. While the absence of confirmatory diagnostic testing posed a limitation in this case, the combination of clinical suspicion and multidisciplinary management provided meaningful symptomatic relief. Continued research into more effective and targeted therapies, along with improved access to diagnostic tools, will be essential for enhancing the quality of life for children with suspected or confirmed LNS.

Conflict of interest

The authors do not report any financial or personal connections with other persons or organisations which might negatively affect the content of this publication and/or claim authorship rights to this publication.

Acknowledgments

We express our gratitude to the patient and his parents for being cooperative. To Head Department of Child Health, University Airlangga/ Dr. Seotomo General Hospital, doctors and nurses for their support for this case report.

Author contribution

Original concept of study; final approval of manuscript PVAS, PIG, MI. Collection, recording and/or compilation of data; analysis and interpretation of data; writing of manuscript: PVAS. Critical review of manuscript: PIG, MI.

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DOI: 10.15557/PiMR.2025.0022