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Case Report

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A rare cause of congenital hypotonia and bulbar palsy: a case of brown-vialetto-van laere syndrome type 1 in infancy

Abstract

This report describes the case of a pediatric patient, aged 9 months, presenting with delayed motor development, trunk and limb hypotonia, epileptic seizures, and hypoactive deep tendon reflexes. Genetic investigation identified a homozygous variant in the SLC52A3 gene, associated with Brown-Vialetto-van Laere Syndrome type 1 (BVVL1), a rare condition characterized by motor neuropathy, bulbar palsy, and sensorineural deafness. The patient underwent multiple interventions, including tracheostomy, gastrostomy, and high-dose riboflavin therapy. Despite clinical stabilization, challenges related to intestinal dysmotility and episodes of desaturation persist. The case reinforces the importance of early diagnosis and multidisciplinary management in rare diseases.

Keywords: brown-vialetto-van laere syndrome, congenital hypotonia, bulbar palsy, riboflavin, SLC52A3, case report

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Introduction

Brown-Vialetto-Van Laere Syndrome (BVVL) is a rare neurodegenerative disease of autosomal recessive inheritance, characterized by progressive pontobulbar palsy and bilateral sensorineural deafness.[1–3] The syndrome may also present with gait ataxia, limb weakness, optic atrophy, epilepsy, and respiratory impairment.[2] In summary, the disease is related to mutations in the SLC52A2 and SLC52A3 genes, which encode riboflavin transporters, an essential component for mitochondrial energy production.[2,3] Deficiency in riboflavin transport leads to the accumulation of toxic metabolites that are harmful to post-mitotic cells, such as neurons, resulting in severe clinical manifestations.[4]

The syndrome was first reported in 1894 by the French physician Charles Brown and subsequently by Vialetto and Van Laere.[5] According to available studies, the disease shows a female-to-male prevalence ratio of 3:1, generally manifesting a more severe clinical presentation in males. A possible differential diagnosis is Fazio-Londe syndrome, a disease also caused by riboflavin transporter deficiency but without sensorineural hearing loss.[2,6,7]

BVVL is a heterogeneous condition, and the first manifestations may occur from the neonatal period to the third decade of life.[4,8,9,10] Diagnosis is based on clinical signs, imaging studies, and genetic testing. Treatment, in turn, consists of riboflavin supplementation in patients with confirmed genetic mutation, and early initiation of therapy is highly related to the clinical course of the disease, potentially preventing the development of respiratory failure.[5,12]

Material and methods

This study is a descriptive and retrospective case report conducted at the Neurology Service of Hospital São Vicente de Paulo, affiliated with the School of Medicine of the University of Passo Fundo – RS. Data were collected through review of the medical records and analysis of complementary examinations. The report was prepared in accordance with the Research Ethics Committee (REC) guidelines, with consent obtained from the patient's legal guardian. The authors declare that they have no conflicts of interest related to this case report.

Case report

Table 1 A 9-month-old female infant, was admitted to a tertiary hospital on January 26, 2024, presenting with seizures associated with cyanosis and congenital hypotonia. The mother reported that the first seizure episode occurred at 4 months of age, characterized by clonic movements of the upper and lower limbs, accompanied by cyanosis and sphincter loss. Since then, the episodes became recurrent, with progressive increase in frequency and intensity. The patient also exhibited delayed motor development, with absence of head control and generalized hypotonia.

Table 1 Case report timeline

Age	Event
4 months old	First epileptic seizure
9 months old	Hospital admission
During hospitalization	Genetic diagnosis and riboflavin therapy
Post-treatment	Clinical stabilization with complications

Family history did not reveal known neuromuscular or genetic diseases, except for a paternal nephew who died at 5 months of age from glutaric aciduria type II, suggesting a possible genetic predisposition in the family. During investigation, the patient experienced cardiorespiratory arrest (CPA – ROSC 2 minutes), requiring intubation and phenytoin loading due to suspected seizure activity. However, electroencephalogram (EEG) did not demonstrate seizures. The patient was receiving Phenobarbital and Levetiracetam, without clinical control.

In this context, genetic testing for treatable diseases was collected, infectious screening was performed, and antibiotic therapy was initiated. Genetic testing identified a variant in the SLC52A3

gene, associated with Brown-Vialetto-van Laere Syndrome type 1 (BVVLS1); therefore, riboflavin therapy was initiated and progressively increased (75 mg/kg/day). Antibiotic therapy was discontinued due to absence of infection, and anticonvulsants were gradually reduced.

The patient showed improvement in the laboratory amino acid profile, but without clinical improvement. Additionally, she developed intestinal dysmotility, which was correlated with the increase in riboflavin dosage. For this reason, the medication was suspended for 48 hours and restarted at a lower dose (20 mg/kg/day), with good response. She remained on a nasogastric tube diet due to inability to feed orally and lack of dietary progression.

Gastrointestinal investigation was performed, and gastrostomy with fundoplication was required due to severe reflux. Furthermore, fiberoptic bronchoscopy with tracheoscopy revealed obstructive laryngomalacia and tracheobronchomalacia, requiring aortopexy with posterior tracheopexy.

The patient progressed well postoperatively in the intensive care unit, with withdrawal of sedation and vasoactive drugs. However, episodes of desaturation, cyanosis, and bradycardia related to crying recurred as the patient regained consciousness, requiring positive pressure ventilation (PPV).

The patient was discharged after 143 days of hospitalization. Currently, she remains stable, occasionally presenting cyanosis associated with crying and irritability, with good response to bag-valve-mask ventilation (Ambu). She tolerates gastrostomy feeding well, breathes via tracheostomy without effort (Ayre at 0.4 L/min), continues riboflavin therapy, and follows a multidisciplinary outpatient follow-up plan.

Discussion

BVVL1 is a rare neurodegenerative condition of genetic origin, characterized by dysfunction of the cranial nerves responsible for swallowing and breathing, leading to significant morbidity and risk of early mortality.[13] Mutation in the SLC52A3 gene directly impacts riboflavin transport, essential for mitochondrial energy metabolism and proper neuronal function.[14,15] Deficiency in this transport results in an exacerbated state of oxidative stress, compromising neuronal cell viability and favoring progressive neuropathy and autonomic dysfunction.[14]

The clinical presentation of the patient corroborates findings described in the literature, with early manifestations of congenital hypotonia, refractory seizures, bulbar palsy, and progressive respiratory failure. Riboflavin deficiency is associated with dysfunction in the mitochondrial respiratory chain, especially in enzymes dependent on flavoproteins, which may explain the worsening motor condition and intolerance to metabolic stress.[12,15]

Additionally, the presence of epileptic seizures not controlled with phenobarbital and levetiracetam suggests a direct impact of riboflavin deficiency on neuronal homeostasis and cortical excitability, as described in similar case reports.[16]

The development of intestinal dysmotility after initiation of high-dose riboflavin may be related to a reversible neurotoxicity mechanism. Evidence suggests that riboflavin influences the enteric nervous system and gut microbiota, both essential for gastrointestinal motility regulation (ref. 13),[13] which may be disrupted in transporter deficiencies.

The need for invasive interventions, such as tracheostomy and gastrostomy with fundoplication, reinforces the severity of bulbar insufficiency in these patients. Literature indicates that respiratory failure in these cases results from progressive weakness of respiratory muscles and bulbar incoordination, predisposing to aspiration episodes and ventilatory insufficiency.[4,9,15] Surgical approaches, such as the aortopexy performed in this patient, are frequently indicated to relieve upper airway obstruction caused by laryngomalacia, a condition often associated with severe neuromuscular disorders.[2]

The favorable response to riboflavin dose reduction suggests the importance of individualized treatment. Adjustments in therapy may be necessary to balance improvement in neuromuscular function with potential adverse effects related to hypersensitivity to increased riboflavin levels.[5,10] Furthermore, the ongoing need for assisted ventilation reflects the progressive nature of the disease and the requirement for strict longitudinal follow-up, focused on preventing respiratory and metabolic complications.[5]

Conclusion

This case report emphasizes the relevance of detailed clinical studies in rare diseases such as BVVL1, contributing to the improvement of differential diagnosis and therapeutic strategies. Documentation of atypical manifestations expands knowledge of the phenotypic spectrum of the syndrome, enabling physicians to identify subtle signs early and implement more effective interventions. Moreover, sharing clinical experiences assists in formulating more precise therapeutic guidelines, facilitating individualized treatment and improving patients' quality of life. Understanding the underlying pathophysiological mechanisms may contribute to new therapeutic approaches aimed at optimizing neuromuscular function and minimizing systemic complications of this devastating syndrome. Long-term follow-up is essential for continuous monitoring of neurological, respiratory, and nutritional status.

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Conflicts of interest

The author declares there is no conflict of interest.

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