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CASE STUDY

CLINICAL AND GENETIC INSIGHTS INTO SPINOCEREBELLAR ATAXIA TYPE 29

KLINICZNE I GENETYCZNE ASPEKTY ATAKSJI RDZENIOWO-MÓŻDŻKOWEJ TYPU 29

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Abstract

Introduction

Spinocerebellar ataxias (SCAs) denote a heterogeneous group of hereditary neurodegenerative disorders, most commonly presenting in adulthood. Nevertheless, few entities have their onset in childhood, including SCA type 29 (SCA29). It is associated with dominant pathogenic variants in the *ITPR1* gene, which encodes a calcium channel essential for Purkinje cell function. Clinically, SCA29 is characterized by early-onset cerebellar ataxia, global motor delay, and infantile muscular hypotonia.

Aim

The aim of this case report is to present detailed clinical and therapeutic management of an individual affected with SCA29.

Materials and methods

The patient is a 5-year-old boy born at term after an uneventful pregnancy. From infancy, he exhibited hypotonia, delayed attainment of milestones, and reduced responsiveness to visual stimuli. Since the age of 4 years, he has been walking only with bilateral support. The patient's cognitive development is normal, speech is inadequate for the age, dysarthric. Magnetic resonance imaging revealed cerebellar hypoplasia, a significant feature of SCA29. Trio-based whole exome sequencing identified a pathogenic heterozygous missense variant in the *ITPR1* gene: c.722G>A p.(Arg241Lys). The variant was absent from both parents, confirming its *de novo* character. Genetic testing combined with clinical findings led to a diagnosis of SCA29.

Conclusions

SCA29 is an ultra-rare disorder, which clinical manifestation overlaps with various other neurological entities, posing difficulties in differential diagnosis. Genetic analysis should be considered in any child exhibiting signs of ataxia of unknown etiology. Early diagnosis is of particular importance, as timely implemented interprofessional rehabilitation may enhance the children's development and facilitate access to patient support groups.

Keywords: early-onset spinocerebellar ataxia, *ITPR1* gene, SCA29, cerebellar hypoplasia

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Streszczenie

Wprowadzenie

Ataksje rdzeniowo-móżdżkowe (SCA) to zróżnicowana grupa dziedzicznych chorób neurodegeneracyjnych, które najczęściej ujawniają się w wieku dorosłym. Jednakże, niektóre z nich, w tym SCA29, mają swój początek już w dzieciństwie. Choroba ta jest spowodowana przez dominujące warianty patogenne w genie *ITPR1*, który koduje kanał wapniowy o wysokiej ekspresji w komórkach Purkinjego. Klinicznie SCA29 charakteryzuje się wczesną ataksją móżdżkową, globalnym opóźnieniem ruchowym i hipotonią mięśniową w okresie niemowlęcym.

Cel

Celem niniejszego opisu przypadku jest przedstawienie szczegółowego opisu klinicznego oraz postępowania rehabilitacyjnego u pacjenta z SCA29.

Materiały i metody

Pacjent to 5-letni chłopiec, urodzony o czasie z ciąży przebiegającej bez powikłań. Od okresu niemowlęcego występowała u niego hipotonia, opóźnione osiąganie kolejnych etapów rozwoju oraz ograniczona reakcja na bodźce wzrokowe. Od 4. roku życia chodzi wyłącznie z obustronną asekuracją. Rozwój funkcji poznawczych pacjenta jest prawidłowy, mowa dyzartryczna. Rezonans magnetyczny wykazał atrofię móżdżku, co jest istotną cechą SCA29. Sekwencjonowanie całego eksomu metodą trio zidentyfikowało patogenny heterozygotyczny wariant zmiany sensu w genie *ITPR1*: c.722G>A p.(Arg241Lys). Wariant ten nie występował u żadnego z rodziców, co potwierdza jego charakter *de novo*. Wynik badania genetycznego w korelacji z badaniami klinicznymi pozwolił na postawienie diagnozy SCA29.

Wnioski

SCA29 jest ultrarzadkim zaburzeniem, którego objawy kliniczne pokrywają się z objawami innych schorzeń neurologicznych, utrudniając przeprowadzenie diagnostyki różnicowej. U każdego dziecka wykazującego objawy ataksji o nieznanej etiologii należy rozważyć przeprowadzenie badań genetycznych. Wcześnie postawiona diagnoza ma szczególne znaczenie, ponieważ szybko wdrożona interdyscyplinarna rehabilitacja może poprawić rozwój dziecka i umożliwić uzyskanie dostępu do grup wsparcia dla pacjentów.

Słowa kluczowe: ataksja rdzeniowo-móżdżkowa o wczesnym początku, gen *ITPR1*, SCA29, hipoplazja móżdżku

Introduction

Spinocerebellar ataxias (SCAs) are a clinically and genetically heterogeneous group of hereditary neurodegenerative disorders, mostly inherited with an autosomal dominant pattern. The estimated frequency of occurrence of these conditions is between 2 and 7 per 100,000 people [1]. SCAs encompass a wide spectrum of over 40 distinct types of the condition, each exhibiting unique characteristics in terms of pathogenesis, demographics, and clinical manifestations [2]. The presentation of symptoms may vary depending on the specific SCA subtype, with patients potentially exhibiting additional neurological or non-neurological symptoms [3]. The most prevalent forms include motor development with gait ataxia and incoordination, dysarthric speech, nystagmus or ophthalmoplegia, and cognitive impairment [4]. The treatment of SCAs involves a combination of symptomatic pharmacotherapy and a range of rehabilitation methods, including speech therapy, physiotherapy based on coordination and balance exercises, and psychotherapy [5].

The diagnosis of SCA is made through a range of methods, including interviews, neurological examinations, genetic testing, and magnetic resonance imaging (MRI) scans. The most challenging aspect of this process is the execution of a proper neurological examination, which involves the assessment of key ataxia symptoms, specifically posture and gait, kinetic function, speech, and oculomotor function [6]. One of the methods of evaluating them is by implementing ataxia scales, such as the International Cooperative Rating Scale or the Scale for the Assessment and Rating of Ataxia. The employment of such scales assists in the process of objectification during the assessment [7]. Although, they can truly support in diagnostics, the scores have their limitations. These assessment tools are non-linear scales that assign differential weighting to individual ataxic manifestations. Patient performance may vary depending on several factors, including circadian influences, and the assessments retain a degree of examiner subjectivity [6].

The majority of cases are linked to an expansion of polyglutamine tracts through cytosine–adenine–guanine repeats [8]. Nevertheless, some subtypes have been observed to result from non-polyglutamine tract expansion or point mutations [9]. SCA type 29 (SCA29) is an ultrarare autosomal dominant condition that arises from point mutations, predominantly missense variants, in the *ITPR1* gene. The encoded protein corresponds to the inositol 1,4,5-trisphosphate receptor type 1, an endoplasmic reticulum-localized, ligand-gated calcium channel that plays a pivotal role in intracellular signalling pathways [10]. The encoded channel is abundantly expressed in Purkinje cells, where its activity is essential for the proper development and maintenance of cerebellar function [11].

The clinical manifestations of SCA29 are characterized by early-onset cerebellar ataxia,delayed acquisition of motor milestones, and infantile muscular hypotonia [12]. MRI consistently demonstrates cerebellar hypoplasia. Notably, the disorder exhibits a non-progressive or minimally progressive clinical course, in contrast to the allelic condition SCA type 15 (SCA15) [11]. Further data and scientific reports remain necessary in order to precisely delineate the characteristics and epidemiology of SCA29, in spite of the infrequency of this particular condition.

Aim

The aim of this case report is to present detailed clinical and therapeutic management of an individual affected with SCA29.

Patient, methods and results

The Polish patient, a boy of Caucasian origin born in July 2020 from his mother's first pregnancy, was delivered at 39 weeks of gestation. He weighed 3820 grams at birth and scored 10 on the Apgar scale. Both the pregnancy and the perinatal period were uneventful. Shortly after birth, a transfontanellar ultrasound revealed hypoplasia of the posterior brain structures. Physical examination also indicated muscle hypotonia in the shoulder and hip girdles.

During his first year of life, his developmental delay became increasingly evident. By the age of 5 months, he demonstrated impaired visual tracking of objects, and by the age of 10 months, he still had poor head control. An ophthalmological assessment revealed a poor visual response. Neurologically, he presented with global motor developmental delay, decreased muscle tone and myoclonic movements.

Further follow-up visits in 2022 continued to reveal delayed attainment of developmental milestones. At 16 months, a boy could only sit with support and was able to say a few words. He began articulating simple words around 18 months. However, speech development remained slow. By 19 months, he could sit independently and began to point with his fingers. A physical examination identified dolichocephaly, a narrow biparietal

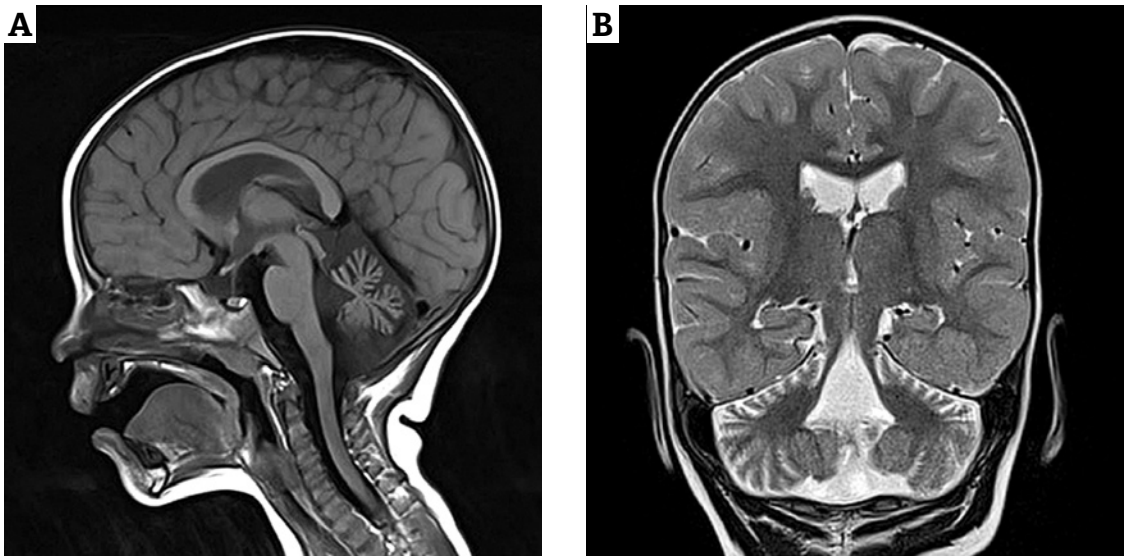
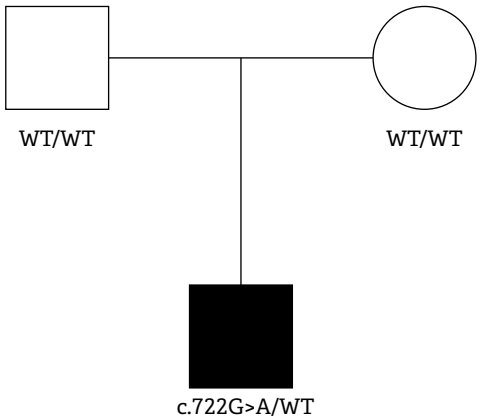


Figure 1. Magnetic resonance imaging head scan of the 2-year-old patient with visible atrophy of the cerebellar vermis and mild atrophy of the superior cerebellar hemispheres. **A**) Sagittal section. **B**) Frontal section

dimension, relatively large eyes, and bilateral symmetric hydroceles. MRI scan performed in February 2022 confirmed cerebellar atrophy (Figure 1). During a follow-up visit in 2022, the patient underwent a comprehensive neurological examination, including evaluation of meningeal signs, cranial nerve function, motor activity of the upper and lower extremities, trunk posture, deep tendon and abdominal reflexes, radicular signs, gait, and sensory modalities (touch, position, and vibration). The examination demonstrated generalized hypotonia, dolichocephaly, and gait impairment. Anthropometric measurements revealed a head circumference of 44 cm (below the 3rd percentile), a height of 92 cm (75th–90th percentile), and a weight of 11.3 kg (10th–25th percentile), corresponding to a body mass index of 13.35 kg/m^2. The patient was fully conscious, with a Glasgow Coma Scale score of 15/15.



WT – wild type

Figure 2. The pedigree of the described family. Filled symbol represents the affected individual, clear symbols represent the unaffected individuals

Genomic DNA analysis by trio-based whole exome sequencing was carried out in the patient and his neurologically healthy parents. It yielded a heterozygous *ITPR1* missense variant c.722G>A p.(Arg241Lys). The variant was previously reported and classified as pathogenic in Clinical Variant Database. The variant was absent from either parent, both of whom are neurologically healthy, which confirmed its *de novo* character (Figure 2).

By 2024, at 4 years of age, the boy could walk when supported by holding both shoulders. He attended regular therapeutic sessions, including work with a psychologist, a speech therapist, a physiotherapist, as well as dog and music therapy. A psychologist described him as being highly sensitive, both emotionally and sensorily. She underlined a marked improvement in his social interactions and that he was beginning to

show a sense of humour. Speech therapy evaluations noted dysarthric speech with good comprehension of verbal commands, but reduced intelligibility for people outside the immediate family. Focus has been placed on oral-motor skills, breathing, phonation, and speech clarity.

Currently, at the age of 5, the boy persists to show neurological signs, characterised by generally reduced muscle tone. His tendon and abdominal reflexes are present and symmetrical, his plantar responses are normal, and he exhibits no pathological reflexes. Nystagmus is also present. His speech remains dysarthric, though he can form short sentences of four to five words. His parents report ongoing sleep difficulties. In terms of motor functions, he can stand by the bed with support, rise to a standing position independently but unsteadily, crawl and walk with support, and sit on his own, although he requires additional torso stabilisation. Independent ambulation was not achieved.

The patient remains under the constant care of a physiotherapist – the Neuro-Developmental Treatment-Bobath method is utilized due to hypotonia and delayed motor function twice a week. This kind of therapy involves activating muscles using a gymnastic ball and stimulating lifting and head control. These exercises are also beneficial for his other problems, such as incorrect upright posture with asymmetry to the right, poor head control, and kyphosis of the spine when sitting. The exercises, prescribed by the physiotherapist, are performed on a daily basis by the child with his parents at home.

Further rehabilitation methods were introduced to support patient's motor development and improve his posture. In 2024, he was prescribed orthopaedic shoes to help distribute body weight correctly across the feet, which are generally worn for a few hours each day, primarily during ambulation or standing. A Baffin seat was also implemented in 2024 to stabilise his seated position, while a Lori standing frame was used to support proper hip joint development. These two elements are incorporated into routine activities, such as the intake of meals, the consumption of beverages, and the maintenance of dental hygiene, along with speech therapy and psychotherapy. Consequently, the patient achieves full linearity of posture. In June 2025, he started wearing a compressive vest to activate his abdominal muscles and improve his posture. Additionally, a Mustang walker was introduced in July 2025 to encourage activation of the lower limbs and facilitate gait mobilization. It is utilised on a daily basis.

Discussion

SCA29 is an ultrarare, autosomal-dominant, early-onset type of spinocerebellar ataxia, identified in the reported paediatric patient. Although this subtype has been infrequently described in the literature, an increasing number of reported cases now provides a framework for recognizing its core clinical features and the extent of phenotypic variability. These published observations allow for a meaningful comparison between previously documented presentations and the current case.

A 2017 case series and clinical review described a cohort of 21 individuals carrying pathogenic variants in the *ITPR1* gene, highlighting both shared and divergent clinical features within this population [13]. Among the most prominent characteristics of SCA29 was delayed motor development, typically manifested by poor head control and difficulties in achieving independent ambulation. As indicated in the article, the group of patients also exhibited symptoms consistent with hypotonia, dysarthric speech, and nystagmus. These symptoms have been described in the majority of patients with SCA29 in the literature [14]. Conversely, the review documented patients with features like hypertension, spasticity and intention tremor that were not exhibited by

the patient in study and have been rarely found in similar cases.

The *ITPR1* gene, which is responsible for encoding the inositol 1,4,5-trisphosphate receptor type 1, is a ligand-gated calcium channel that functions as a component of the membranes of the endoplasmic reticulum. The process of calcium ion release into the cytoplasm, initiated by the stimulation of inositol 1,4,5-trisphosphate, is a fundamental component of intracellular signalling pathways. The protein is densely expressed in Purkinje cells, making it essential for the proper functioning of the cerebellum [15]. Pathogenic variant of the *ITPR1* gene that causes SCA29, disrupts intracellular signalling pathways in Purkinje cells, leading to abruption of cerebellar function. Mutation can be identified not only in SCA29, but also in SCA15 and Gillespie syndrome (GLSP) and is significant for differential diagnosis [16]. Further studies are indicated to elucidate the underlying precise pathomechanism of SCA29.

In contradistinction to SCA29, GLSP is characterised by aniridia, in conjunction with other ophthalmic problems, including mydriasis and iris dystrophy. It has been observed that the condition may be inherited in either an autosomal-dominant or an autosomal-recessive pattern [17]. Conversely, SCA15 exhibits a high degree of clinical similarity to SCA29, a condition characterised by autosomal dominance and slowly progressive symptoms, yet its onset occurs in adulthood [18]. Therefore, it should be noted that a detailed interview and physical examination can be beneficial in establishing a diagnosis.

The management of SCAs is consistent across all types, encompassing pharmacological and physiotherapeutic approaches [19]. The investigation of SCAs for the purpose of developing curative therapies is limited to a small number of types. The majority of these are derived from antisense oligonucleotides and accumulate ataxin, including SCA type 1, SCA type 2, SCA type 3 and SCA type 7 [3]. The pharmacotherapy of SCAs is typically characterised by a symptomatic approach, with the utilisation of medications such as riluzole to enhance ambulatory function and speech, or the incorporation of supplements comprising coenzyme Q10 [19]. Although, the most important factor to be considered when seeking to improve SCAs is the implementation of a rehabilitation programme at the earliest opportunity, which is subsequent to a genetic diagnosis. It is recommended that all individuals, including those exhibiting mild symptoms, undergo physical therapy. Rehabilitation interventions have been demonstrated to be efficacious in improving functional performance, mobility, ataxic symptoms, and balance. In addition, the efficacy of physiotherapy in enhancing postural control in patients diagnosed with SCA has been well documented [5]. The literature suggests that technology-based rehabilitation approaches, including speech therapy and videogame-based interventions, represent valuable adjuncts in the management of SCAs by targeting communication deficits and promoting motor, cognitive, and sensorimotor functions through task-oriented, multisensory training [20]. Moreover, the implementation of speech therapy is crucial in order to enhance the quality of life of patients suffering from SCA. The potential benefits of this approach include the enhancement of small motor functions, respiratory function, and phonation, thereby contributing to the maintenance of clear speech [5].

It is important to note that SCA29 is one of a multitude of different types of SCAs, and it is rarely reported globally. The substantial heterogeneity observed among SCAs, both phenotypically and genetically, poses significant challenges in clinical trials, leading to difficulties in assessing disease progression and determining therapeutic interventions. Nevertheless, the reported findings may be useful in the development of evidence-based therapeutic strategies for ataxias and

illustrate genotype-phenotype relationships. In the context of rare inherited diseases, such as SCA29, case reports are typically pivotal in facilitating a systematic description of the condition, thereby serving as the primary source of clinical knowledge.

This study is limited by its single-case design and a five-year observational period, which precludes generalization of the findings. Additional case reports and larger-scale analyses are needed to further elucidate the clinical characteristics of SCA29 and to inform evidence-based management strategies.

Conclusions

The infrequency of SCA29 results in a paucity of literature and a corresponding deficit of knowledge about the management strategies that specialists can implement. Nevertheless, genetic testing in patients exhibiting ataxia symptoms is pivotal in order to obtain data and provide a management plan based on that evidence. It is evident that, taking into consideration the patient history that has been documented, the early diagnosis of both clinical and genetic aspects can facilitate the implementation of an appropriate rehabilitation and interdisciplinary therapy, with the aim of achieving optimal development of the child.

References

1. **Coarelli G, Coutelier M, Durr A**. *Autosomal dominant cerebellar ataxias: new genes and progress towards treatments.* Lancet Neurol 2023; 22: 735–749.
2. **Soong BW, Morrison PJ**. *Spinocerebellar ataxias.* Handb Clin Neurol 2018; 155: 143–174.
3. **Coarelli G, Wirth T, Tranchant C, Koenig M, Durr A, Anheim M**. *The inherited cerebellar ataxias: an update.* J Neurol 2023; 270: 208–222.
4. **Sullivan R, Yau WY, O'Connor E, Houlden H**. *Spinocerebellar ataxia: an update.* J Neurol 2018; 266: 533–544.
5. **Chien HF, Zonta MB, Chen J, et al**. *Rehabilitation in patients with cerebellar ataxias.* Arq Neuropsiquiatr 2022; 80: 306–315.
6. **Brooker SM, Edamakanti CR, Akasha SM, Kuo S, Opal P**. *Spinocerebellar ataxia clinical trials: opportunities and challenges.* Ann Clin Transl Neurol 2021; 8: 1543–1556.
7. **Matsugi A, Bando K, Kondo Y, et al**. *Effects of physiotherapy on degenerative cerebellar ataxia: a systematic review and meta-analysis.* Front Neurol 2025; 15: 1491142. DOI: 10.3389/fneur.2024.1491142.
8. **Paulson HL, Shakkottai VG, Clark HB, Orr HT**. *Polyglutamine spinocerebellar ataxias – from genes to potential treatments.* Nat Rev Neurosci 2017; 18: 613–626.
9. **Shakkottai VG, Fogel BL**. *Clinical neurogenetics.* Neurol Clin 2013; 31: 987–1007.
10. **Huang L, Warman-Chardon J, Carter MT, et al**. *Correction to: missense mutations in ITPR1 cause autosomal dominant congenital nonprogressive spinocerebellar ataxia.* Orphanet J Rare Dis 2022; 17: 143. DOI: 10.1186/s13023-022-02297-7.
11. **Romaniello R, Pasca L, Panzeri E, et al**. *Superior cerebellar atrophy: an imaging clue to diagnose ITPR1-related disorders.* Int J Mol Sci 2022; 23: 6723. DOI: 10.3390/ijms23126723.
12. **Ando H, Hirose M, Mikoshiba K**. *Aberrant IP_3 receptor activities revealed by comprehensive analysis of pathological mutations causing spinocerebellar ataxia 29. Proc Natl Acad Sci U S A* 2018; 115: 12259–12264.
13. **Zambonin JL, Bellomo A, Ben-Pazi H, et al**. *Spinocerebellar ataxia type 29 due to mutations in ITPR1: a case series and review of this emerging congenital ataxia. Orphanet J Rare Dis* 2017; 12: 121. DOI: 10.1186/s13023-017-0672-7.
14. **Casey JP, Hirouchi T, Hisatsune C, et al**. *A novel gain-of-function mutation in the ITPR1 suppressor domain causes spinocerebellar ataxia with altered Ca^{2+} signal patterns.* J Neurol 2017; 264: 1444–1453.
15. **Shimobayashi E, Kapfhammer JP**. *Calcium signaling, PKC Gamma, IP_3R1 and CAR8 link spinocerebellar ataxias and Purkinje cell dendritic development.* Curr Neuropharmacol 2018; 16: 151–159.
16. **Huang L, Warman-Chardon J, Carter MT, et al**. *Missense mutations in ITPR1 cause autosomal*

dominant congenital nonprogressive spinocerebellar ataxia. Orphanet J Rare Dis 2012; 7: 67. DOI: 10.1186/1750-1172-7-67.

17. **Ciaccio C, Taddei M, Pantaleoni C, et al**. *Phenotypic spectrum and natural history of gillespie syndrome. An updated literature review with 2 new cases*. Cerebellum 2024; 23: 2655–2670.
18. **Tipton PW, Guthrie K, Strongosky A, Reimer R, Wszolek ZK**. *Spinocerebellar ataxia 15: a phenotypic review and expansion*. Neurol Neurochir Pol 2017; 51: 86–91.
19. **Radmard S, Zesiewicz TA, Kuo SH**. *Evaluation of cerebellar ataxic patients*. Neurol Clin 2023; 41: 21–44.
20. **Lanza G, Casabona JA, Bellomo M, et al**. *Update on intensive motor training in spinocerebellar ataxia: time to move a step forward?* J Int Med Res 2019; 48: 300060519854626. DOI: 10.1177/0300060519854626.