Neurodevelopmental and Behavioral Features in Idic(15) Syndrome: A Case Report

Aspects neurodéveloppementaux et comportementaux du syndrome isodicentrique du chromosome 15 (idic (15)) : à propos d'un cas

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ABSTRACT

Isodicentric syndrome of chromosome 15 (Idic(15)) is a rare chromosomal disorder caused by an inverted duplication of the 15q11–q13 region, resulting in the presence of an extra chromosome. It is characterized by a broad neurodevelopmental phenotype, including hypotonia, psychomotor delay with intellectual disability, language impairment, epilepsy, and autistic traits. Owing to its clinical variability, early diagnosis may be challenging, particularly in the absence of seizures or dysmorphic features.

We report the case of a 2-year-and-10-month-old girl, born at term to non-consanguineous parents. At birth, she presented with transient respiratory distress and persistent axial hypotonia, with an otherwise normal physical examination. During follow-up, the patient exhibited global developmental delay, including delayed motor and language acquisition and reduced social interaction, without any seizures to date. Brain MRI was normal. Genetic analysis confirmed the diagnosis of Idic syndrome (15). Management was multidisciplinary (pediatric neurology, speech therapy, physical medicine).

This case highlights the early, often subtle, presentation of Idic syndrome(15) in the absence of epileptic seizures or facial dysmorphism, underscoring the need for genetic testing in children with unexplained hypotonia and developmental delay. Early identification allows for the implementation of appropriate multidisciplinary care, which can improve functional outcomes.

Keywords: reverse duplication 15q, idic (15), developmental delay, autism spectrum disorder, neurodevelopmental disorder

RESUME

Le syndrome isodicentrique du chromosome 15 (Idic(15)) est un trouble chromosomique rare causé par une duplication inversée supplémentaire de la région 15q11–q13, entraînant la présence d'un chromosome surnuméraire. Il se caractérise par un phénotype neurodéveloppemental large, incluant une hypotonie, un retard psychomoteur avec déficience intellectuelle, des troubles du langage, une épilepsie et des traits autistiques. En raison de la variabilité de sa présentation clinique, le diagnostic précoce peut être difficile en particulier en l'absence de dysmorphie ou de convulsions.

Nous rapportons le cas d'une fille âgée de 2 ans et 10 mois, née à terme de parents non consanguins. À la naissance, elle a présenté une détresse respiratoire transitoire et une hypotonie axiale persistante, avec un examen physique par ailleurs normal. Au cours du suivi, la patiente a présenté un retard global du développement, incluant un retard des acquisitions motrices et du langage et une interaction sociale réduite, sans crises épileptiques à ce jour. L'IRM cérébrale était normale. L'analyse génétique a permis de confirmer le diagnostic de syndrome Idic(15). La prise en charge était multidisciplinaire (neuropédiatrie, orthophonie, médecine physique). Ce cas met en évidence la présentation précoce, souvent discrète, du syndrome Idic(15) en l'absence de crises épileptiques ou de dysmorphie faciale, soulignant la nécessité d'un bilan génétique chez les enfants présentant une hypotonie et un retard du développement inexpliqués. Une identification précoce permet de mettre en

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place une prise en charge multidisciplinaire adaptée, susceptible d'améliorer les résultats fonctionnels.

Mots-clés : duplication inversée 15q, dup 15q, retard du développement, troubles du spectre autistique, trouble neurodéveloppemental

INTRODUCTION

The 15q duplication syndrome is a neurodevelopmental disorder caused by the presence of at least one additional copy of the 15q11.2–q13.1 chromosomal region. One specific subtype, idic(15), is characterized by a supernumerary marker chromosome. This marker results from an inverted duplication of the 15q11–q13 segment and is typically isodicentric (1). The condition is rare, with an estimated birth incidence of approximately 1 in 30,000 (2).

This subtype is generally associated with a more severe phenotype, including developmental delay, language impairment, epilepsy, and autism spectrum features (1,3). We report the case of a patient diagnosed with idic(15) syndrome, based primarily on clinical manifestations of global developmental delay, in the absence of dysmorphic features or epilepsy.

CASE PRESENTATION

We report the case of a 2-year-10-month-old girl who was admitted to our neonatal unit at birth for respiratory distress. She was delivered at 39 weeks of gestation by cesarean section to non-consanguineous parents following a well-monitored pregnancy complicated by gestational diabetes.

Prenatal ultrasound suggested esophageal atresia and an ovarian mass. At birth, the patient was a well-formed eutrophic newborn with no dysmorphic features, presenting with mild respiratory distress and stable hemodynamics. Neurological examination revealed axial hypotonia. Chest radiography excluded esophageal atresia, and the respiratory distress resolved within 24 hours, consistent with transient tachypnea of the newborn.

Postnatal abdominopelvic ultrasound confirmed a 20-mm ovarian cyst. Serum β-hCG levels were normal (1.46 mIU/mL), whereas alpha-fetoprotein levels were markedly elevated (20,247 ng/mL), with progressive normalization (3ng/mL at 18 months). Serial ultrasounds demonstrated normal female internal genitalia with transient maternal hormonal effects and complete regression of the cyst. A diagnosis of an incidental ovarian cyst was retained.

The clinical course was notable for persistent hypotonia and global developmental delay. Head control was achieved at 4 months, voluntary grasping at 9 months, and independent sitting at 15 months. She was able to stand with support at 16 months and walked independently at 2 years and 6 months. Vocalization of syllables began at 16 months.

The patient underwent Thyroid function testing, brain MRI, and electroencephalography, all of which were normal for age. Neurosensory investigations, including Brainstem Auditory Evoked Potentials and Visual Evoked Potentials, were also normal.

A karyotype was requested at one year of age and performed at two years, revealing the presence of a supernumerary marker chromosome. Fluorescence in situ hybridization (FISH) analysis demonstrated an inverted duplication of chromosome 15: 47, XX, +mar.ish idic(15) (D15Z4+,UBE3A+,PML-,UBE3A+,D15Za+).

At the age of 2 years and 10 months, the patient walked independently but exhibited significant language delay and limited social interaction. No seizures had been observed. Management remained symptomatic and includes speech therapy, physical rehab, and regular pediatric follow-up to monitor psychomotor development.

DISCUSSION

We report a 2-year-and-10-month-old girl presenting with neonatal hypotonia, which prompted close follow-up of her psychomotor development. This was later associated with global developmental delay and language impairment, with no seizures reported to date. Genetic evaluation through karyotyping and FISH analysis confirmed the diagnosis of idic(15) syndrome, characterized by an inverted duplication of chromosome 15.

Reports specifically addressing idic (15) remain limited and mainly consist of isolated case reports or small case series (3). A systematic review conducted in 2025 included only 38 publications. Among 421 cases of 15q duplication syndrome identified, 310 (74%) were diagnosed with idic (15) syndrome (4). The scarcity of reported cases worldwide reflects the rarity of this disorder.

In our patient, diagnosis was established at 2 years of age, compared with an average of 1.2 years reported in the literature (5). This delay may be explained by the absence of facial dysmorphia and epileptic seizures, as well as delayed referral for genetic consultation by the parents (karyotype requested at 1 year of age).

Dysmorphic features in idic(15) syndrome are usually absent or only mildly expressed, which may reduce clinical suspicion. Subtle craniofacial dysmorphic features may include a prominent forehead, laterally positioned eyebrows, down-slanting palpebral fissures, low-set auricles, a vaulted palate, a broad nasal bridge, a shortened philtrum, and ocular misalignment (6,7). These features were not observed in our patient.

Developmental delay is consistent finding in idic(15) syndrome. A case series of 22 patients reported profound intellectual disability in 85% of cases (8). Autistic spectrum features are also considered a hallmark of this syndrome, as demonstrated in our patient. In a U.S. cohort of 54 individuals, autistic traits were identified in 81% of cases (9). Clinicians should be particularly alert to diminished social interest and reduced eye contact.

Language development is markedly delayed, often

limited to echolalic speech, with understanding largely contextual and facilitated by gestures. During childhood, stereotyped movements are frequently observed (8).
Epilepsy is frequently associated with idic(15) syndrome. In a case series of 35 patients, 80% developed epilepsy, with a median age at onset of 3 years and 3 months (7). Seizure phenotypes are highly heterogeneous and may include infantile spasms with hypsarrhythmic EEG patterns, later evolving into a Lennox-Gastaut syndrome. Other seizure types such as tonic, atonic, and atypical absence have also been reported. Additionally, abnormal involuntary movements, particularly dystonic posturing, may occur (7).
although seizures have not been observed in our patient thus far, this remains consistent with the diagnosis, as seizure onset has been reported as late as 9 years of age in previously described cases (7).
Brain MRI is often normal in individuals with idic(15) syndrome, as in our patient., However, non-specific findings such as enlarged lateral ventricles or mild corpus callosum atrophy may occasionally be detected (2, 10). The combination of refractory epilepsy and specific behavioral manifestations previously mentioned contributes to a recognizable clinical pattern, that may help distinguish idic(15) syndrome from other neurodevelopmental disorders (8).
Management requires a multidisciplinary approach. Pediatric neurologists play a central role in monitoring psychomotor development and managing epilepsy when present. Speech therapy supports language acquisition, while physical rehabilitation improves hypotonia and promotes independent walking. In some cases, involvement of a child psychiatrist or developmental specialist may be necessary to enhance social interaction and adaptive skills.

CONCLUSION

The diagnosis of idic(15) syndrome can be challenging, particularly in the absence of dysmorphic features or seizures. Although epilepsy is common, it may develop later in childhood and should not delay diagnostic consideration. Early recognition allows timely multidisciplinary management and may improve developmental and social outcomes. Additional case reports are needed to better define the clinical spectrum of this rare syndrome.

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REFERENCES

[1] Lusk L, Vogel-Farley V, DiStefano C, Jeste S, Adam MP, Bick S, et al. Maternal 15q duplication syndrome. In: GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2016 Jun 16 [updated 2021 Jul 15].

[2] Battaglia A. The inv dup (15) or idic (15) syndrome (Tetrasomy 15q). Orphanet J Rare Dis. 2008 Nov;3(1):30.

[3] Bisba M, Malamaki C, Constantoulakis P, Vittas S. Chromosome 15q11-q13 Duplication Syndrome: A Review of the Literature and 14 New Cases. Genes. 2024 Oct 8;15(10):1304.

[4] Burkart S, Ries M, Romero V, Burau K, Schaaf CP, Hempel M. Unraveling the genomic architecture of supernumerary (iso-) dicentric chromosomes in Dup15q syndrome: Insight from a systematic literature-based study. Am J Med Genet A. 2025 Dec;197(12):e64186.

[5] Wheeler AC, Gantz MG, Cope H, Strong TV, Bohonowych JE, Moore A, et al. Age of diagnosis for children with chromosome 15q syndromes. J Neurodev Disord. 2023 Nov 7;15(1):37.

[6] Kim JS, Park J, Min BJ, Oh SK, Choi JS, Woo MJ, et al. A case of isodicentric chromosome 15 presented with epilepsy and developmental delay. Korean J Pediatr. 2012 Dec;55(12):487.

[7] Battaglia A, Bernardini L, Torrente I, Novelli A, Scarselli G. Spectrum of epilepsy and electroencephalogram patterns in idic (15) syndrome. Am J Med Genet A. 2016 Oct;170(10):2531-9.

[8] Battaglia A, Parrini B, Tancredi R. The behavioral phenotype of the idic(15) syndrome. Am J Med Genet C Semin Med Genet. 2010 Nov 15;154C(4):448-55.

[9] Hogart A, Wu D, LaSalle JM, Schanen NC. The comorbidity of autism with the genomic disorders of chromosome 15q11.2-q13. Neurobiol Dis. 2010 May;38(2):181-91.

[10] Czakó M, Till Á, Szabó A, Ripszám R, Melegh B, Hadzsiev K. Possible Phenotypic Consequences of Structural Differences in Idic(15) in a Small Cohort of Patients. Int J Mol Sci. 2019 Oct 5;20(19):4935.