

Recurrent Familiar Ataxic Syndrome in a 2-Years-Old Child Affected by ATP1A3 Mutation: A Case Report

Rapaccini V*, Pasini A, Nunziata L, Pitzianti M and Miconi F

Pediatric Clinic, Università Tor Vergata, Rome, Italy

Abstract

ATP1A3 mutations have been recognized in children with different neurological phenotypes. We describe a patient with a diagnosis of ATP1A3 mutation inherited from his mother. The ataxic syndrome occurred at 18 months with cerebellar symptoms and psychomotor regression, after an infectious episode. The same clinical manifestations were found in his mother. This is the first case of a subject under 2-years-old with ataxic syndrome and ATP1A3 mutation inherited from his mother affected by the same cerebellar manifestations.

Keywords: Diagnosis; Mutation; Clinical; Symptoms

Introduction

Now, several phenotypes have been recognized in infants and children presenting ATP1A3 mutations, including Rapid-onset Dystonia Parkinsonism (RDP), Alternating Hemiplegia of Childhood (AHC), and Cerebellar ataxia, Areflexia, Pes cavus, Optic atrophy, and Sensorineural hearing loss (CAPOS) [1]. These diseases cause acute onset of neurological symptoms, but the predominant neurological manifestations differ with particularly early onset of hemiplegic/dystonic episodes and mental decline in AHC, ataxic encephalopathy and impairment of vision and hearing in CAPOS syndrome and late onset of dystonia /parkinsonism in RDP. One of the most frequent syndromes associated with ATP1A3 mutations is Childhood Alternating Hemiplegia, an intractable neurological disorder characterized by recurrent episodes of alternating hemiplegia accompanied by other paroxysmal symptoms [2]. We describe the case of a child who is not affected by any of these three syndromes but shows signs of cerebellar damage such as dysmetric abnormalities and marked difficulties in static and dynamic balance. His mother, affected by the same ATP1A3 mutation, shows a similar clinical picture characterized by ataxic and dysmetric symptoms.

Case Presentation

A 2-years-old child suffered from Acute Ataxia in 2016. The patient was born through FIVET with an external paternal donor, therefore he inherited part of the genetic attitude of the mother. He was born at term from a monitored and regular pregnancy; the weight at birth was 3270 Kg, good neonatal conditions were referred. Regarding to psychomotor development, head control was present at 3 months, trunk control was present at 8 months; despite autonomous walking has not yet been acquired, upright gait was acquired at 12 months. Concerning the communicative and linguistic development, parents reported that the stages of gestural development have been normally acquired (indicative gesture, hello); the first words were pronounced at 12 months, the first sentences with subject, verb and object were present at 18 months; parents do not refer doubts about the child's comprehension skills. At 18 months, after an acute infectious episode, it was described the onset of a generalized hypotonous associated with an ataxic syndrome; dysmetric elements were also present. He was recovered at the Bambino Gesù Pediatric Hospital in Rome with the diagnosis of ataxic syndrome of a genetic nature (mutation of ATP1A3 gene). During hospitalization, several diagnostic tests were performed including laboratory tests for screening of infectious diseases, cerebral TC (without contrast), Sensory Evoked Potential (SEP) and Electroneurography (ENG). Laboratory tests, Sep and ENG resulted normal. Cerebral TC was performed under

baseline conditions in a situation of urgency with x-care technique. The images were partly altered by the presence of technical movement artifacts; with these limits no, gross focal alterations of encephalic tissues had been recognized. The supra and subtentorial ventricular system resulted normal for morphology and size; the representation of subarachnoid spaces of cranial base was normal, but it was difficult to evaluate that because of the convexity of the structure. Cognitive development was examined through the administration of the Griffiths Scale from which emerged at 19 months a Global Quotient value of 91 and an Age Development of 17 months in relation to a Chronological Age of 19 months. These parameters suggest an adequate psychomotor development. The neurorehabilitative clinical examination showed good general conditions, the patient was described as an alert child with a tendency to exercise a marked control on the surrounding environment mediated by the adult figure, emerged also an important difficulty in separating from his mother. The control of the trunk was present, the child could pass from supine to prone and viceversa, he crawled but he showed slight difficulties in cross movements. At last, from the physiotherapy evaluation emerged an impairment of posturo-motor control, of static and dynamic equilibrium, difficulties in motor activity and gait deficit.

Overall at present, the neuropsychological profile is characterized by a greater motor impairment compared to an adequate cognitive potential [3]. The current clinical picture significantly compromises the relational aspects and the autonomy of the child who needs a constant support and a supervision of the adult associated with clinical periodic checks.

Discussion

ATP1A3 gene specifically encodes the Na,K-ATPase 3 subunit, exclusively present in neurons, where it is thought to be responsible for restoration of basal intracellular Na concentrations after sustained activity.

The $\alpha 1$ and $\alpha 3$ Na^+/K^+ ATPases can be considered prime candidates

*Corresponding author: Rapaccini V, Pediatric Clinic, Università Tor Vergata, Rome, Italy, Tel: +39 06 7259 3099; E-mail: rapaccinivalentina@gmail.com

Received June 11, 2018; Accepted June 13, 2018; Published June 18, 2018

Citation: Rapaccini V, Pasini A, Nunziata L, Pitzianti M, Miconi F (2018) Recurrent Familiar Ataxic Syndrome in a 2-Years-Old Child Affected by ATP1A3 Mutation: A Case Report. J Clin Case Rep 8: 1133. doi: [10.4172/2165-7920.10001133](https://doi.org/10.4172/2165-7920.10001133)

Copyright: © 2018 Rapaccini V, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

for maintaining neuronal excitability. A3 isoform has approximately four-fold lower Na⁺ affinity compared to a1 and is specifically required for rapid restoration of large transient increases in Na⁺ intracellular concentration. Conditions associated with a3 deficiency are likely aggravated by suprathreshold neuronal activity [4]. This could be explained by the fact that infectious episode can determine an increase in body temperature because of the fever which may attempt the intrinsic vulnerability of neurons.

Conclusion

We describe the first case in literature of hereditary ATP1A3 mutation in a subject under 2 years old affected by a clinical picture characterized by dysmetric and ataxic symptoms. The child was the son of a woman who presents the same genetic mutation and is affected by ataxic syndrome [5]. The patient doesn't show signs of other neurological diseases generally associated with mutation in the ATP1A3 gene such as Rapid-onset Dystonia Parkinsonism (RDP), Alternating Hemiplegia of Childhood (AHC), and Cerebellar ataxia, Areflexia, Pes cavus, Optic atrophy, and Sensorineural hearing loss (CAPOS). However, the onset of his cerebellar symptomatology followed an acute infective episode as well as it can happen in syndromes associated with ATP1A3 mutation. The same mutation was present in his mother who presented the same onset of cerebellar symptoms. At the age of 18 months she suffered from ataxia and a generalized hypotonus after a febrile infectious episode; afterwards, since the age of six, she showed recurrent ataxic episodes

with convulsions and loss of consciousness. The child's clinical picture and onset of symptomatology were correlated with those of his mother, who is affected by the same ATP1A3 mutation [6]. These elements lead to the hypothesis that there is a specific timing for the onset of the symptomatology. In relation to his mother's recurrent symptoms, the child has carried out a rehabilitative therapy to improve the control of the trunk and is subjected to periodic check up to the age of 6 years.

References

1. Holm TH, Lykke-Hartmann K (2016) Insights into the pathology of the $3 \text{ Na}^+/\text{K}^+$ -ATPase ion pump in neurological disorders: Lessons from animal models. *Front Physiol* 7: 209.
2. Jun J, Hirose S, Shi XY, Ishii A, Hu LY, et al. (2016) Treatment with oral ATP decreases alternating hemiplegia of childhood with *de novo* ATP1A3 mutation. *Orphanet J Rare Disease* 11: 55.
3. Kirshenbaum GS, Dachtler J, Roder JC, Clapcote SJ (2015) Characterization of cognitive deficits in mice with an alternating hemiplegia-linked mutation. *Behav Neurosci* 129: 822-831.
4. Panagiotakaki E, De Grandis E, Stagnaro M, Heinzen E, Fons C, et al. (2015) Clinical profile of patients with ATP1A3 mutations in alternating hemiplegia of childhood: A study of 155 patients. *Orphanet J Rare Dis* 10: 123.
5. Hunanyan AS, Fainberg NA, Linabarger M, Arehart E, Leonard AS, et al. (2015) Knock-in mouse model of alternating hemiplegia of childhood: Behavioral and electrophysiologic characterization. *Epilepsia* 56: 82-93.
6. Yang X, Gao H, Zhang J, Xu X, Liu X, et al. (2014) ATP1A3 mutations and genotype-phenotype correlation of alternating hemiplegia of childhood in Chinese patients. *PloS one* 9: 97274.