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CASE REPORT

A New Case of a Neurodevelopmental Disorder and Myoclonic Dystonia Associated with the C.1404del Variant of the *ATP5F1A* Gene

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Abstract: ATP synthase (ATPase) is a mitochondrial enzyme responsible for the majority of ATP production. Disease phenotypes associated with mutations in ATPase subunits are extremely rare. To date, only four types of ATPase subunit mutations have been described in detail, with heterogeneous clinical manifestations ranging from hypotonia to epilepsy, movement disorders, developmental delay, and intellectual disability. In this work, in the form of a case report, we present a rare case of a patient with ATPase mutation and knowledge of the clinical symptoms associated with ATPase mutations has a positive benefit for neurological and medical practice, because as in the case of our patient, which was the whole life misdiagnosed with cerebral palsy until the *ATP5F1A* mutation was diagnosed.

Keywords: mutation, ATP synthase, dystonia, myoclonus, epilepsy, spasticity

Introduction

Case Report

In this case report, we present the case of a 44-year-old male patient, with negative family history, born at term by prolonged labor with the development of early asphyxiation syndrome and due to was diagnosed with cerebral palsy due to a motor and intellectual deficit practically from birth and epileptic seizures from the age of 4. Due to the gradual progression of the condition in terms of impaired walking, progression of active limb movement, involuntary movements of the left upper limb and urinary incontinence, he sought medical help again in recent years. The neurological examination revealed generalized dystonia with spasticity, craniofacial dysmorphism (mild microcephaly with high forehead and hypotelorism) and myoclonus in the left upper limb (Figures 1 and 2 and Videos 1, 2 and 3). Basic laboratory tests (complete blood count, basic metabolic panel including serum lactate level, lipid panel, coagulation panel, thyroid function tests and urinalysis) were normal. Brain MRI showed mild lateral asymmetry of the lateral ventricles in favor of the left side (Figure 3). The EEG was without significant abnormalities. On examination of memory functions, a mild cognitive deficit was found. Cognitive deficit was currently manifested mainly in the area of verbal memory (Montreal Cognitive Assessment test was 22/30). Given the polymorphic clinical picture, we proceeded to early genetic investigation in terms of whole-genome sequencing (WGS – the analysis was carried out by a private laboratory in Germany) where a rare mutation in the *ATP5F1A* gene was detected (heterozygous frameshift variant, c.1404del, p.Glu469Serfs*3). Whole-genome sequencing identified a heterozygous ATP5F1A variant, c.1404del (NM_004046.6), which creates a frameshift and a premature stop codon in exon 10 (p.Glu469Serfs*3). Although family members were unavailable for segregation analysis, we assessed the variant's impact via RNA sequencing in patient fibroblasts, ATP5F1A mRNA levels were significantly reduced (fold change = 0.59).

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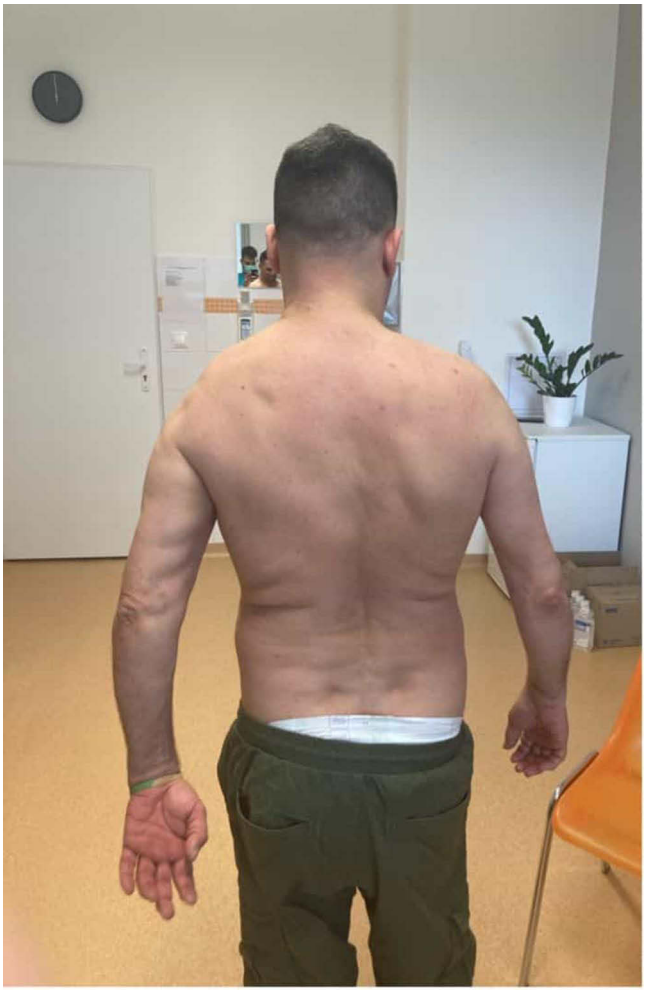

Figure 1 The neurological examination revealed generalized dystonia with dominant left upper limb disability.

Discussion

ATP synthase is a mitochondrial enzyme that is responsible for the majority of ATP production. It is located on the inner side of the mitochondrial membrane and consists of two parts (F0 and F1), which separately have additional subunits. Mutations in ATPase subunits are very rare, as evidenced by the fact that only 4 types of ATPase subunit mutations have been characterized so far (mutations in the gene for *ATP5F1E, ATP5PO, ATP5F1A and ATP5MC3*). The clinical picture of the mutations described so far was heterogeneous. The spectrum of symptoms ranged from hypotonia to epilepsy with premature death or variety of persistent abnormalities including movement disorders (mainly dystonia), developmental delay, intellectual disability, hyperlactatemia, and other neurological and systemic symptoms.[1,2]

The clinical symptoms of the published patients were very similar to those of the presented patient with confirmed mutation in the *ATP5F1A* gene, who was misdiagnosed with cerebral palsy since early childhood. There is no causal treatment for patients with these mutations and therapeutic options consist of symptomatic and supportive treatment only. Treatment with intramuscular botulinum toxin was indicated, which can positively affect dystonia and spasticity. Botulinum toxin also alleviated the above symptoms in this case. Oral antiepileptic drugs are recommended in patients with epileptic seizures; the presenting patient used a combination antiepileptic therapy of levetiracetam and timonil. Psychotherapy aimed at improving cognitive functions, speech therapy interventions, screening for possible dysphagia to

Figure 2 The neurological examination revealed generalized dystonia with dominant craniofacial dysmorphism.

prevent aspiration, and movement rehabilitation have a significant effect. In patients with dominant extrapyramidal symptoms (dystonia and myoclonus) surgical treatment in the sense of deep brain stimulation may be indicated, which we are considering in the patient, but no case of a patient with this mutation undergoing surgical treatment has been described so far. Given the individual clinical picture of patients and the extreme rarity of these types of mutations, their prognosis and length of survival are unclear.

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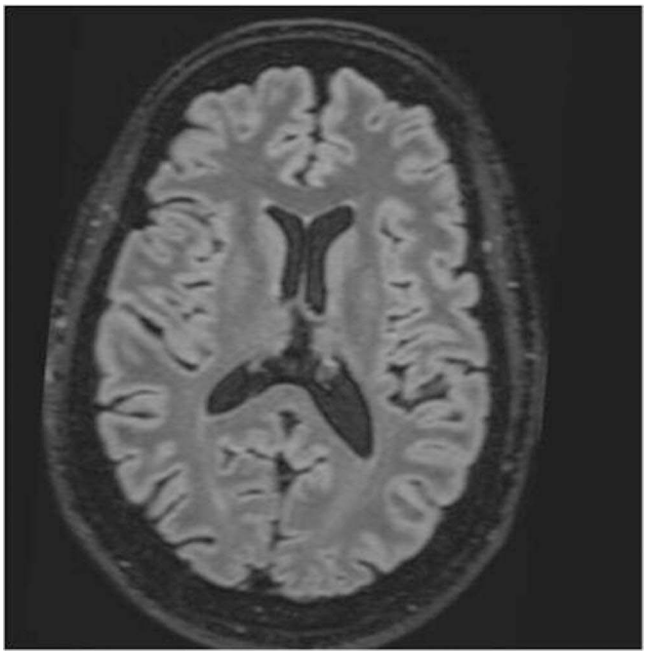

Figure 3 Brain MRI showed mild lateral asymmetry of the lateral ventricles in favor of the left side.

Conclusion

Mutational lesions of the nuclear genes encoding ATPase have not been sufficiently studied, leading to the hypothesis that there are other variations of ATPase mutations associated with previously described or novel clinical phenotypes. Therefore, it is important to discuss them and think about their presence in clinical practice, because there may be many patients with misdiagnoses mutations of these genes. Therefore, this publication can serve as a good example for doctors in clinical practice.

Abbreviations

WGS, whole genome sequencing; EEG, electroencephalography.

Ethical Compliance Statement

We confirm that the manuscript was approved by the ethics commission of the Faculty Hospital Trnava (Approval No. 2/2025/ETK). We confirm that we have read the journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines. Written consent for publication was obtained from the patient and his family members.

Consent for Publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images and Videos S1, S2 and S3.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically

reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest relevant to this work.

References

1. Zech M, Kopajtich R, Steinbrücker K, et al. Variants in mitochondrial ATP synthase cause variable neurologic phenotypes. *Ann Neurol*. 2022;91 (2):225–237. doi:10.1002/ana.26293
2. Harrer P, Krygier M, Krenn M, et al. Expanding the allelic and clinical heterogeneity of movement disorders linked to defects of mitochondrial adenosine triphosphate synthase. *Mov Disord*. 2025;40(7):1388–1400. doi:10.1002/mds.30209