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Mitochondrial Dysfunction in an Adolescent with Mental Health Problems: A Case Report

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Abstract | **Case Report**

We report the case of a 13-year-old boy with autism spectrum disorder (ASD), moderate intellectual disability, and severe conduct disorder in whom clinical and paraclinical findings suggested mitochondrial dysfunction. Neurodevelopmental assessment showed a WISC-V Full Scale IQ of 55 and ADI-R scores above diagnostic cut-offs. Laboratory tests revealed fluctuating hyperlactatemia (up to 3.56 mmol/L) and a cerebrospinal fluid lactate/pyruvate ratio of 72 (lactate 1.80 mmol/L; pyruvate 0.025 mmol/L), highly suggestive of a respiratory chain defect. Brain MRI demonstrated bilateral, symmetric T2/FLAIR hyperintensities of the corticospinal tracts. No alternative metabolic or genetic abnormalities were identified (normal amino acid profile, normal karyotype). A mitochondrial "cocktail" (coenzyme Q10, riboflavin, L-carnitine, alpha-lipoic acid) was initiated alongside multidisciplinary psychosocial management. This case underscores the importance of targeted metabolic evaluation in atypical or severe neuropsychiatric presentations, as early identification of mitochondrial involvement may inform tailored therapeutic strategies and improve outcomes.

Keywords: Autism Spectrum Disorder; Intellectual Disability; Conduct Disorder; Mitochondrial Dysfunction; Lactate/Pyruvate Ratio; Corticospinal Tract; Case Report.

INTRODUCTION

Mitochondria play a fundamental role in cellular functioning, particularly in the brain, an organ with high energy demand. Beyond their role in ATP production via oxidative phosphorylation, they are also involved in the regulation of oxidative stress, apoptosis, and calcium metabolism. Consequently, mitochondrial dysfunction—whether related to mutations in mitochondrial DNA (mtDNA) or nuclear DNA (nDNA)—can affect numerous neuronal functions and lead to neurodevelopmental and psychiatric disorders. Among these disorders, autism spectrum disorder (ASD) and intellectual disability (ID) are frequently cited in the literature as being associated with mitochondrial abnormalities. Studies have demonstrated impairment of the mitochondrial respiratory chain, pathogenic mtDNA mutations, and reduced mitochondrial density in some patients with ASD or ID. Furthermore, behavioral disturbances such as impulsivity, running away (elopement), or pathological lying, although rarely directly linked to mitochondrial diseases, may fall within the spectrum of neuropsychiatric manifestations related to cerebral energy dysfunction. Despite these observations, the relationship between mitochondrial disease and psychiatric disorders remains underexplored, particularly in complex cases combining ASD, ID, and behavioral disorders. This lack of data justifies better clinical and biological characterization of these patients, in order to determine whether a specific metabolic work-up could contribute to their management. In this context, we present the case of an adolescent with ASD, intellectual disability, and severe behavioral disorders, in whom biological and clinical abnormalities suggest mitochondrial involvement. Through this case and a narrative literature review, we explore the potential link between mitochondrial dysfunction and neuropsychiatric disorders.

METHODOLOGY

1. Clinical Case Analysis

This study is based on an in-depth analysis of a patient followed in child and adolescent psychiatry for a presentation combining autism spectrum disorder (ASD), intellectual disability (ID), and behavioral disorders (compulsive lying, elopement, emotional instability).

Data were collected from:

- Direct clinical observations (family interviews, behavioral assessments)
- Standardized neuropsychological evaluations (IQ scales, adaptive tests)
- Paraclinical investigations already performed during the patient's medical follow-up

2. Paraclinical Investigations

A biological and metabolic work-up was undertaken to search for evidence of mitochondrial dysfunction, including:

- Measurements of lactate, pyruvate, alanine, and urinary organic acids
- Extended blood panel (hepatic function, muscular enzymes, blood glucose, etc.)
- If necessary, a muscle biopsy (histology, enzymology)
- Genetic analysis targeting mitochondrial DNA (if available)

Clinical and biological results were interpreted according to diagnostic criteria proposed in the literature for pediatric mitochondrial diseases.

3. Narrative Literature Review

A literature review was conducted to contextualize the observed case and identify known links between mitochondrial diseases and neuropsychiatric disorders.

- Databases: PubMed, Scopus, Cochrane Library
- Keywords: "mitochondrial dysfunction," "autism spectrum disorder," "intellectual disability," "behavioral disorder," "psychiatric symptoms"
- Inclusion criteria: clinical studies, systematic reviews, case reports published between 2000 and 2024
- Exclusion: animal studies, articles without human clinical data

Relevant results were extracted, synthesized, and compared with the data from the presented case.

Complete Clinical Vignette

History and Family Context

Y., a 13-year-old Moroccan boy, the eldest of two siblings, born to second-degree consanguineous parents. Younger sister followed for intellectual disability. Father is a day laborer; mother is a homemaker.

Neonatal and Early Medical Data

- Monitored pregnancy, vaginal delivery without reported neonatal distress.
- Day 5: hematemesis after amniotic fluid inhalation (favorable course).
- At 8 months: first febrile urinary tract infection, later recurrences.
- Dermatologic follow-up for atopic eczema.
- No reported seizure history.

Psychomotor and Language Development

Global delay: head control at 6–7 months, sitting at 10 months, walking at 24 months (toe-walking gait intermittently persisting), first words at 30 months, first sentences at 4 years, full bladder/bowel control around age 5. Language remained poor, with immature articulation and phonological disorders.

Behavior and Adaptive Functioning

- Early childhood: hyperactivity, impulsivity, aggression, sensory hypersensitivity (noise/tactile), marked intolerance to change (feeding rituals, fixed placement), social withdrawal (no eye contact, does not respond to name).
- Anxious traits: fear of the dark, rain, and solitude.
- Adolescence: increasing sexual disinhibition (inappropriate physical contact, viewing and sharing pornography, repeated love letters to a caregiver), antisocial behaviors (compulsive lying, elopement, domestic arson, carrying a knife at school, verbal threats), chronic irritability, marked sleep disturbances, weight/appetite fluctuations. Affective worsening after the death of a close aunt (depressive mood, loss of initiative).

Psychometric Evaluations

Test	Result	Interpretation
WISC-V	Full Scale IQ = 55	Moderate intellectual disability
Vineland-3	Adaptive Composite = 57	Severe limitations across all domains
ADI-R	Social Interaction = 24 / Communication = 18 / Restricted Behaviors = 7	Above ASD diagnostic cut-offs

Psychiatric Examination

Initial mutism, avoidance of gaze, gestural responses. Subsequently: stereotyped language, poor prosody, restricted interests. Restricted affect, impaired emotional regulation. No frank productive syndrome (no persistent delusions or hallucinations).

Paraclinical Investigations

Domain	Key Results
Energy Metabolism	• Postprandial blood lactate: 88.22 mg/L (≈ 0.98 mmol/L) • Other blood lactate sample: 321 mg/L (≈ 3.56 mmol/L) • CSF: lactate = 1.80 mmol/L, pyruvate = 25 µmol/L (0.025 mmol/L) → L/P ratio ≈ 72 (highly suggestive of respiratory chain block)
Routine Blood Biochemistry	AST 18 U/L, ALT 11 U/L (normal) CK 164 U/L (upper normal) Ammonia 22.9 µmol/L (normal)
Plasma Amino Acid Profile	Normal
Karyotype	46,XY without anomaly
CSF Cytobacteriology	Clear, 1 WBC/mm³, negative culture
Brain MRI (07/10/2024)	Bilateral, symmetric T2/FLAIR hyperintensities of corticospinal tracts (corona radiata, internal capsule, cerebellar peduncles)—stable appearance; no contrast enhancement and no lactate peak on spectroscopy
Other	Amino acid chromatography: normal

Syndromic Diagnosis

1. **Autism Spectrum Disorder** (DSM-5)
2. **Moderate Intellectual Disability**
3. **Conduct Disorder** (aggression, property destruction, rule violations, deceit)
4. **Strong suspicion of mitochondrial disease** (fluctuating elevated blood lactate, CSF lactate/pyruvate ratio >25, MRI motor tract abnormalities, compatible clinical signs)

Current Therapeutic Plan ("Mitochondrial Cocktail")

Agent	Prescribed Dosage
Coenzyme Q10 100 mg	1 capsule morning & evening
Riboflavin 100 mg	1 capsule morning & evening
Oral L-carnitine 2 g/5 mL	1 ampoule/day
Alpha-lipoic acid 600 mg	1 tablet morning & evening

In parallel: multimodal child psychiatry management (ASD-adapted CBT, parental guidance, specialized educational support), sleep optimization, nutritional and neurological follow-up.

DISCUSSION

The presentation combines severe ASD, intellectual disability, severe behavioral disorders, and biological markers of mitochondrial dysfunction. Repeated elevation of blood lactate (up to 3.5 mmol/L) and especially the CSF lactate/pyruvate ratio of 72 are highly suggestive of a respiratory chain block (complex I or IV). Bilateral corticospinal tract hyperintensities, although nonspecific, are frequently encountered in pediatric mitochondrial encephalopathies. This observation reinforces a pathophysiological continuum: neuronal energy deficit → oxidative stress and neuroinflammation → alterations of social networks, impulse control, and synaptic plasticity. The "cocktail therapy" (CoQ10, riboflavin, carnitine, alpha-lipoic acid) aims to support oxidative phosphorylation and mitigate oxidative stress. Thus, this case illustrates the need for a systematic metabolic work-up in atypical or severe neuropsychiatric presentations. Identification of a mitochondrial disease opens the way to specific management likely to improve the developmental trajectory and quality of life of the child and family.

Several studies have demonstrated an increased prevalence of mitochondrial disorders in patients with ASD. A recent systematic review by Luna Payares *et al.,* (2024) identified mitochondrial metabolic alterations across a broad spectrum of neurodevelopmental and psychiatric disorders, including ASD, intellectual disability, and behavioral disorders. These alterations notably involve decreased activity of respiratory chain complexes, mitochondrial morphological abnormalities, and biochemical imbalances compatible with neuronal energy deficiency. The work of Scuderi *et al.,* (2023) confirms these observations, showing that 79% of autistic children studied presented mutations or alterations of the mitochondrial genome. Similarly, Valiente-Pallejà *et al.,* (2018) identified reduced mitochondrial DNA content in ASD/ID patients, suggesting a direct genetic and bioenergetic implication in these clinical pictures.

At the cerebral level, molecular imaging studies have revealed regional mitochondrial hypofunction. A positron emission tomography (PET) study demonstrated decreased availability of mitochondrial complex I in the anterior cingulate cortex of ASD patients. This region is involved in emotional regulation, social behavior, and adaptation—functions altered in our case. Behaviorally, disinhibition, impulsivity, pervasive rituals, marked affective possessiveness, and risk behaviors (weapon carrying, arson) observed in our

patient echo the publications of Rossignol & Frye (2015) and Marazziti *et al.,* (2012), which link mitochondrial dysfunction to various psychiatric disorders, notably mood disorders, schizophrenia, and impulse control disorders.

Another central aspect is the role of oxidative stress and neurocellular inflammation, well documented as mediators of mitochondrial damage in ASD. Thorsen (2020) and Gevezova *et al.,* (2020) demonstrated that these mechanisms exacerbate neuronal involvement, promote post-stress regressions, sleep disturbances, and behavioral irritability—elements found in our patient's evolution, particularly after the loss of a family member. The literature also supports the role of specific biomarkers. Bjørklund *et al.,* (2023) explored porphyrinuria as a reflection of mitochondrial dysfunction, while Shchelochkov *et al.,* (2024) identified mitochondrial alterations in propionic acidemia associated with ASD and severe ID.

Recent advances in understanding mitochondrial mechanisms also suggest that intercellular mitochondrial transfer via tunneling nanotubes could play a role in cerebral plasticity and neuronal resilience. This phenomenon, still under investigation, could explain certain clinical variations observed in affected patients. Moreover, recent models position mitochondria as central actors in premature cerebral aging, a phenomenon reported in some patients with ASD and mitochondrial dysfunction.

All these data corroborate the multidimensional nature of mitochondrial disease, which is not limited to simple energy deficiency but is part of a multisystem dysregulation affecting motor, cognitive, affective, and behavioral functions. In this context, our case confirms the importance of considering a targeted metabolic work-up in any patient presenting with atypical or severe ASD—particularly when extreme behavioral rigidity, atypical motor or sensory disorders, major sleep disturbances, or post-stress regression episodes are associated.

The confirmed diagnosis of mitochondrial disease in our patient thus sheds light on the understanding of his complex neuropsychiatric profile and opens the way to multidisciplinary therapeutic strategies combining behavioral management, family support, and targeted medico-nutritional interventions.

Conclusion

This clinical case highlights the potential role of mitochondrial dysfunction in the genesis of complex neuropsychiatric presentations combining autism spectrum disorder, intellectual disability, and severe behavioral disorders. Confirmation of mitochondrial disease in this patient strengthens the hypothesis that altered cerebral energy metabolism may underlie part of the observed clinical manifestations—particularly behavioral rigidity, post-stress regressions, and contrasts in social dynamics.

In the presence of atypical or severely disrupted clinical profiles, metabolic exploration is essential both to refine diagnosis and to consider targeted therapeutic approaches. This observation calls for systematically integrating the mitochondrial pathway into the evaluation of neurodevelopmental disorders with exacerbated behavioral presentation.

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