MITO 101 – Psychiatry

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Key Points:

- Neuropsychiatric problems are relatively common features of mitochondrial disease.
- Not all patients with mitochondrial disease develop neuropsychiatric symptoms.
- In children, mitochondrial disease can be associated with cognitive delay, regression, and autism spectrum disorders. In adults, mitochondrial disease can be associated with dementia.
- Depression, hallucinations and behavioral abnormalities can be associated with mitochondrial encephalopathies.
- Psychiatric symptoms can be difficult to recognize amidst cognitive impairment and other medical problems associated with a multi-system mitochondrial disorder.
- Recognizing and treating psychiatric disease with pharmacotherapy and behavioral interventions is important, as effective management can improve quality of life.

Clinical Investigation:

- A careful history, specifically eliciting behavioral and depressive symptoms, addiction, and cognitive impairment, are important in recognizing neuropsychiatric disease.
- Neuropsychological testing can uncover a subtle impairment; more precisely assess its extent, and help guide educational interventions in children and management in adults.
- It is important to ascertain what medications a patient with mitochondrial disease is taking, as drug side effects or interactions can exacerbate or cause neuropsychiatric symptoms.
- Magnetic resonance imaging (MRI) can identify potential new lesions underlying behavioral changes.
- Electroencephalography, including continuous monitoring, can identify if epileptiform activity is contributing to the neuropsychiatric symptoms.
- Given that mitochondrial diseases can affect multiple systems, laboratory testing may be indicated to rule out metabolic factors that can contribute to cognitive and behavioral impairment.

Neuropsychiatric features associated with mitochondrial disease (organized by genetic etiology)

- Single, large scale deletions causing Kearns-Sayre syndrome can be associated with visuospatial executive deficits, but rarely with psychiatric disease.
- Transfer RNA mutations in the mitochondrial DNA (mtDNA) causing encephalopathies are frequently associated with dementia and psychiatric...
symptoms, including depression, hallucinations, delusions, behavioral abnormalities, and autism spectrum disorders. Mutations in mtDNA protein-coding genes causing Leber’s hereditary optic neuropathy (LHON) do not seem associated with neuropsychiatric disease. However, mutations causing NARP/MILS (neuropathy, ataxia, retinitis pigmentosa/maternally inherited Leigh syndrome) commonly are associated with mental retardation.

Among nuclear DNA defects, primary coenzyme Q10 deficiency has been associated with often subtle neuropsychological deficits, but also with affective disease and behavioral abnormalities.

Among defects in intergenomic signaling, adenine nucleotide transporter (ANT1) gene mutations, POLG and PEO1 mutations have been associated with depression, less commonly paranoia, and personality disorders (avoidant, histrionic, or psychotic).

Management of mitochondrial psychiatric disease

- Depressive symptoms often respond to one of the newer antidepressants, including SSRI’s (selective serotonine re-uptake inhibitors). Older drugs including tricyclic antidepressants can be helpful, but should be used with caution because of their potential autonomic and cardiac side effects.
- Psychotic symptoms and significant behavioral problems respond to antipsychotics. Depending on the type of behavioral disturbance, more activating or more sedating drugs are chosen.
- Supportive counseling and psychosocial interventions are often helpful.
- In children, referral to appropriate early intervention or school special education services is indicated.

Acknowledgments:
The author is supported by NICHD PO1


