Diagnostic Criteria for Barth syndrome

Pediatric Neurology Setting
Diagnostic Criteria for Barth Syndrome in the Pediatric Neurology Setting

- A child with Barth syndrome could easily present in the pediatric neurologist’s office for an array of reasons.
- A floppy infant or child may be referred to the neurologist without any other relevant background information, and may turn out to have:
  - Cardioskeletal myopathy
  - A lipid myopathy
  - 3-methylglutaconic aciduria
- A geneticist, cardiologist or other specialist may refer a child to pediatric neurologist because they need his view to get a complete picture, either before or after the diagnosis has been made.
The neuromuscular symptoms of Barth syndrome are:

- Muscle affection mainly in a limb girdle distribution
- Moderate muscle wasting
- Moderate weakness, permitting unsupported walking
- Exercise intolerance
- Absence of contractures
- No involvement of bulbar musculature, with the exception of occasional mild facial muscle weakness
- No progression to wheelchair dependence, no involvement of extra-ocular muscles or diaphragm.
Diagnostic Criteria for Barth Syndrome in the Pediatric Neurology Setting

- A child with Barth syndrome showing Gowers’ sign on rising.
- Notice moderate muscle wasting.
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A boy with Barth syndrome showing

- lordotic back
- recurvated knees
Diagnostic Criteria for Barth Syndrome in the Pediatric Neurology Setting

- mild wasting of extremity muscles
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The facial appearance of Barth syndrome is not “diagnostic”, but experienced investigators point to a similarity in facial appearance in many affected boys.
Cardinal Characteristics besides neuromuscular involvement:

- Cardiomyopathy (frequently dilated)
- Neutropenia (chronic, cyclic or intermittent)
- Growth retardation (can appear as failure to thrive) before puberty
- 3-methylgluticonic aciduria, detectable by gas chromatography and mass-spectrometry
Diagnostic Criteria for Barth Syndrome in the Pediatric Neurology Setting

- **Major Clinical Hazards:**
  - Congestive heart failure
  - Risk of serious arrhythmia including sudden cardiac death
  - Serious bacterial infections
  - Hypoglycemia

- **Other major problems:**
  - Growth deficiency
  - Lack of stamina
Diagnostic Criteria for Barth Syndrome in the Pediatric Neurology Setting

- **Variable Clinical Problems:**
  - Frequent diarrhea
  - Recurrent aphthous ulcers
  - Hypoglycemia, including fasting hypoglycemia in the neonate
  - High incidence of minor congenital malformations
  - Low bone density
  - Reported chronic headaches and body aches especially during puberty
  - Feeding Problems
  - Reports of cognitive learning difficulties
Diagnostic Criteria for Barth Syndrome in the Pediatric Neurology Setting

**Diagnostic Testing**

- **Quantitative Urine Organic Acid Analysis**, including quantification of 3- methylgluticonic acid
- **Cardiolipin analysis of muscle, platelets, lymphocytes or cultured skin fibroblasts**
- **DNA sequence analysis** (Genetic testing of the tafazzin [G4.5] gene)
Patient- and family history

Ancillary examinations

Routine neurological examination and blood test

Cardiac examination: cardiomyopathy mainly dilated

Family history indicating maternal inheritance of cardioskeletal myopathy affecting only males. (this clue may be absent)

Moderate muscle weakness and wasting in limb-girdle distribution including Gowers’ sign; generally no contractures; normal creatine kinase in blood

Muscle biopsy: Routine histochemistry: lipid myopathy

EMG, nerve conduction velocity: normal

Specific examinations:
Urine: GCMS for 3-methylglutaconic acid
Blood/ muscle/ fibroblasts/ lymphocytes/ platelets for tetralinoleoyl cardiolipin

Proof of diagnosis:
Mutation analysis for TAZ-gene


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