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
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- ...mild wasting of extremity muscles
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 gaschromatography and mass-spectrometry
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**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
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- **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
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Diagnostic Testing

- Quantitative Urine Organic Acid Analysis, including quantification of 3-methylglutaronic 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

Routine neurological examination and blood test

Ancillary examinations

Cardiac examination: cardiomyopathy mainly dilated

Neutropenia (may not be present on single examination)

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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