ROHHAD

- Rapid-onset Obesity with Hypothalamic dysfunction, Hypoventilation and Autonomic Dysregulation
- Diagnostic criteria:
  - Onset of alveolar hypoventilation and obesity after 1.5 y
  - Evidence of hypothalamic dysfunction
    - Obesity
    - Hyperprolactinemia
    - Central hypothyroidism
    - Disordered water balance
    - Failed growth hormone stimulation test
    - Cortisol deficiency
    - Delayed or precocious puberty

Etiology

- Genetics?
  - PHOX2B mutations → Congenital Central Hypoventilation Syndrome
  - Not present in ROHHAD
  - Study of 7 triads including twins with whole exome found no clear genetic correlate
  - Familial case reports – Monogenic?
- Immune mediated?
  - Association with neural crest tumors (33%)
  - Lymphocytic inflammation on histology, CSF analysis
  - Intrathecal oligoclonal bands
- No biomarker has been found
- Partial response to immune modulatory therapies
**Congenital Central Hypoventilation Syndrome (CCHS, PHOX 2B)**
- Prader-Willi syndrome
- Bardet-Biedl syndrome
- Alstrom syndrome
- Congenital leptin deficiency
- Neurometabolic disorders – mitochondrial, amino acid, and neurotransmitter
  - ROHHAD previously thought to be an isolated serotonin deficiency

**Rapid onse: Obesity**
- Over 6 -12 months
- Usually 30+ lbs
- Hyperphagia

Age 2 years  Age 3 years

**Hypoventilation**
- Blunted response to hypercarbia → hypoxemia
- Obstructive sleep apnea
- Central sleep apnea
- Hypopnea
- Daytime hypoventilation → Tracheostomy
- Months to years after onset of obesity
Respiratory
- Shallow breathing
- Central sleep apnea

Cardiac
- Arrhythmia (typically bradycardia)
- Blood pressure dysregulation
- Cardiorespiratory arrest

Altered sweating

Behavioral dysregulation
- Mood instability
- Developmental delay
- Seizures
- Ataxia

Evaluation
- Polysomnography
- Chest/abdomen Imaging
- Cardiac evaluation
- Nutrition evaluation
- Endocrine evaluation
  - Water balance
  - Pituitary function
Evaluation

- MRI brain
  - Bilateral basal ganglia hypodensities
  - Rathke’s cleft cyst
  - Hypointensity of pons, midbrain
  - Diffuse cerebral atrophy
  - Normal
- CSF
  - Normal
  - Inflammatory markers
  - Oligoclonal bands
  - Normal neurotransmitters
Autoimmune disorders of the CNS

- NMDA – receptor
- AMPA – receptor
- LGI-1
- CASPR-2
- GABA-A – receptor
- GABA-B – receptor
- IgGNS
- Contactin-2

CNS Autoimmunity

Future Directions:

- Studies currently enrolling – Use of cyclophosphamide in treatment of ROHHAD
- International ROHHAD Registry
- 10-year observational period

Resources: