OBJECTIVES

- Understand the approach to diagnosis of juvenile parkinsonism (JPD)
- Discuss the long-term course of symptoms and treatment responses in our patient
- Recognize signs and symptoms of Neuronal Inclusions Inclusion Disease (NID)
- Review literature on JPD and NID

PATIENT PRESENTATION

2001-2003 (Ages 8-10 years old):
- New onset articulation difficulties with progression to anarthria
- Inability to eat due to chewing difficulty

2004 (Age 11 years old):
- Stumbling, losing balance
- Increased stiffness noted in limbs
- Depression, anxiety (started Lexapro)
- Saw local neurologist
- Tested CK, Thyroid, Fragile X, Chromosome microarray (all normal)
- EMG: initially abnormal (possible NMJ disorder but poor patient tolerance of test)

Early 2005 (Age 12 years old)
- Needed assistance to walk
- Drooling, fatigue
- MRI: normal
- Terting for myasthenia gravis, Wilson’s Disease, negative, Huntington’s Disease
- Alpha fetal protein, pyruvate, lactate, Vitamin E, immunoglobulins: normal

June 2005 (Age 12 years old)
- Brief insufficient cardiopulmonary trial, minimal effect
- Referral to Rochester Pediatric Movement Disorders Clinic

October 2005 (Age 12 years old)
- Seen at University of Rochester Pediatric Movement Disorders Clinic
- Initial Exam: tremor, bradykinesia, rigidity, postural instability, cogwheeling, dystonia
- PARKIN, PINK1 gene testing negative

DISEASE COURSE

- Hematogenous spread of mediastinal and cervical lymph nodes
- NID remains in central nervous system

NEUROPATHOLOGY CONFIRMS DIAGNOSIS OF NID

- Inferior olivary complex neuron
- Tectum

Hematoxylin and eosin stained sections of inferior olivary complex neuron and tectum in postmortem analysis of the patient. Both slides show eosinophilic inclusion bodies characteristic of Neuronal Inclusions Inclusion Disease. Not shown here is ubiquitin immunoreactivity, which was positive. Immunoreactivity to SUMO-1 antibodies is pending.

REFERENCES

- Giovanni R, Juan R, Neuronal Inclusions Inclusion Disease; no longer a pain in the butt. Neurology. 2011 Apr 19;76(16):1361-9

DISCUSSION

- NID is a rare cause of JPD
- Also called Neuronal Inclusions Inclusion Disease
- Very rare with fewer than 40 cases reported in the literature
- Affects central, peripheral and autonomic nervous systems
- Can be sporadic or familial
- Signs and symptoms:
  - Parkinsonism
  - Cerebellar ataxia
  - Chorea
  - Dystonia
  - Nystagmus
  - Pyramidal signs
  - Seizures
  - Cognitive impairment
  - Peripheral neuropathy
  - Autonomic instability

- Oculogyric crises, early onset dopa-induced dyskinesias, and gastrointestinal dysfunction can be clues to diagnosis
- Antemortem diagnosis can be done
  - Rectal biopsy (although often avoided due to associated pain)
  - Skin biopsy may be a helpful test
- Postmortem brain pathology diagnosis
  - Neuronal eosinophilic hyaline inclusions
  - Immunoreactivity to ubiquitin and small ubiquitin-related modifier 1 (SUMO-1) antibodies

TAKE HOME POINTS

- Juvenile Parkinsonism itself is not common and Neuronal Inclusions Inclusion Disease is a rare cause of JPD
- When approaching the etiology of JPD, first consider if the onset if symmetric or asymmetric
- NID tends to be dopa-responsive initially with early-onset dyskinesias
- Our patient demonstrated many of the non-motor symptoms that have been described in NID (oromotor symptoms, autonomic disturbances, cognitive regression, seizures)
- Microscopic findings confirm diagnosis with typical inclusions