SEPTO OPTIC DYSPLASIA
IN CHILDREN
KATHY CLARK PNP-BC
UNIVERSITY OF MICHIGAN HEALTH SYSTEM

OPTIC NERVE HYPOPLASIA
SYNDROME IN CHILDREN
KATHY CLARK PNP-BC
UNIVERSITY OF MICHIGAN HEALTH SYSTEM

I HAVE NO CONFLICTS TO DISCLOSE.
KATHY CLARK NP
OBJECTIVES
Describe and define SOD/ONH
Discuss pituitary hormone needs in children with SOD/ONH
Explain the differences between typical child development and that of children who are visually impaired

WHAT IS SOD/ONH?
- Optic Nerve Hypoplasia
- Pituitary abnormalities
- Midline brain defects

HISTORY
1941 – Reeves associated optic nerve hypoplasia with agenesis of septum pellucidum
1956 – de Morsier coins “SOD” but it is not ONH
1970 – Hoyt makes association with 9 patients who have ONH and growth hormone deficiency; 4 had missing septum pellucidum
SOD – AT LEAST TWO OF THREE
Abnormal central brain structures
Optic nerve hypoplasia
Pituitary hormone abnormalities

OPTIC NERVE HYPOPLASIA
The prevalence of ONH is about 1:10,000
Leading cause of (non cortical) blindness in infancy
Small nerves carry less information to the brain
- nystagmus or strabismus by 1-3 months
  10% have normal vision
  34% no light perception; 80% “legally” blind

ABNORMAL BRAIN STRUCTURES IN ONH
Pituitary gland - absent, ectopic, or underdeveloped
Corpus callosum – most predictive, most prevalent
Septum pellucidum – less prognostic
Arachnoid cyst – rarely needs shunting
Hypoplasia of the cerebellum
Microcephaly
Seizure disorders not uncommon
**BIG WORDS – BUT WHAT IS IMPORTANT?**

<table>
<thead>
<tr>
<th>Corpus Callosum</th>
<th>Septum Pellucidum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Associated with developmental delay</td>
<td>Just not that interesting</td>
</tr>
<tr>
<td>1.8-2/10,000 absent in 2.3% of DD individuals</td>
<td>Can occur with absence of corpus callosum</td>
</tr>
<tr>
<td>49% have other CNS abnormalities</td>
<td>Presence of SP does not rule out endocrinopathy</td>
</tr>
<tr>
<td>ONH only in 10% of individuals with absent corpus callosum</td>
<td></td>
</tr>
</tbody>
</table>

**ANATOMY**

![Brain Anatomy Diagram](Image1)

**ANATOMY**

![Corpus Callosum Diagram](Image2)

Intact Corpus Callosum  
Agenesis of the Corpus Callosum
ANATOMY

HYPOTHALAMUS

- Controls the pituitary gland
- Has many other functions
  - temperature regulation
  - hunger
  - thirst
  - sleep regulation
- Does not influence intelligence

PITUITARY GLAND

- Two lobes - anterior and posterior
- Anterior pituitary hormones control the release of hormones from other glands
  - thyroid – TSH – T3 and T4
  - adrenal gland – ACTH - cortisol
  - ovary/testis – GnRH – testosterone or estrogen
  - oxytocin (labor) and prolactin (milk)
  - releases growth hormone - GH
- ADH hormone (posterior pituitary)
- Controls water loss in the kidney
Spectrum of clinical presentations and endocrinological findings of patients with septo-optic dysplasia: A retrospective study

Ayse Pinar Cemeroğlu / Tarin Coulas / Lora Kleis


Age at diagnosis, years 0.7±1.2 (0–7)
Mean±SD; range

Duration of follow-up, years 6.3±4.9 (0–18)
Mean±SD; range

Current age, years 7.0±5.1 (0.2–20)
Mean±SD; range

Maternal age, years 22.2±4.8 (15–36)
Mean±SD; range

Male: female, n 46:34

1st child of the mother, % 64

Adoption at birth, n (%) 5 (8)

Positive family history, n (%) 3 (3.8)

<table>
<thead>
<tr>
<th>Age at diagnosis, years</th>
<th>0.7±1.2 (0–7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of follow-up, years</td>
<td>6.3±4.9 (0–18)</td>
</tr>
<tr>
<td>Current age, years</td>
<td>7.0±5.1 (0.2–20)</td>
</tr>
<tr>
<td>Maternal age, years</td>
<td>22.2±4.8 (15–36)</td>
</tr>
<tr>
<td>Male: female, n</td>
<td>46:34</td>
</tr>
<tr>
<td>1st child of the mother, %</td>
<td>64</td>
</tr>
<tr>
<td>Adoption at birth, n (%)</td>
<td>5 (8)</td>
</tr>
<tr>
<td>Positive family history, n (%)</td>
<td>3 (3.8%)</td>
</tr>
</tbody>
</table>
SPECTRUM OF CLINICAL PRESENTATIONS AND ENDOCRINOLOGICAL FINDINGS OF PATIENTS WITH SEPTO-OPTIC DYSPLASIA: A RETROSPECTIVE STUDY

AYSE PINAR CEMEROGLU / TARIN COULAS / LORA KLEIS

Hypothalamic-pituitary dysfunction, n=44

<table>
<thead>
<tr>
<th>Hypothalamic-pituitary dysfunction, n=44</th>
<th>Age of onset, years Mean±SD; range</th>
<th>Frequency %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Growth hormone deficiency</td>
<td>1.8±1.2 (0–8)</td>
<td>55</td>
</tr>
<tr>
<td>Central hypothyroidism</td>
<td>1.2±1.9 (0–8)</td>
<td>70</td>
</tr>
<tr>
<td>Secondary/tertiary adrenal insufficiency</td>
<td>0.5±0.6 (0–8)</td>
<td>50</td>
</tr>
<tr>
<td>Central diabetes insipidus</td>
<td>0.8±1.2 (0–1.5)</td>
<td>30</td>
</tr>
<tr>
<td>Central precocious puberty</td>
<td>7.3±0.5 (7–8)</td>
<td>9</td>
</tr>
</tbody>
</table>

ENDOCRINE AND PUBERTAL DISTURBANCES IN OPTIC NERVE HYPOPLASIA, FROM INFANCY TO ADOLESCENCE

OLIVER J. DAVAN, DONALD R. MCCLELLAN, MICAH L. OLSON, PAMELA GARCIA-FILION

INTERNATIONAL JOURNAL OF PEDIATRIC ENDOCRINOLOGY 2015 2015:8

Methods: A retrospective chart review was conducted on a cohort of children with ONH between January 2005 and March 2013. Endocrine dysfunction was determined based on laboratory evidence of hormone deficiency or hormone replacement. Pubertal disturbances were characterized based on presence of micropenis, Tanner staging, menarche and hormone replacement. Pituitary abnormalities were classified using MRI findings. Descriptive statistics were used, and comparisons between groups were performed using the chi-square test.

Results: During the study period, 101 patients underwent an endocrine evaluation (median age: 2.3 years [0.76 – 6.5]). Hypopituitarism was present in 73% of patients with growth hormone deficiency (56%) and hypothyroidism (54%) being the most common. Pubertal disturbances (n = 19) were common; micropenis in 31% (13/42) of males and 2% with precocious puberty. Half of adolescents (n = 6/11) were diagnosed with gonadotropin deficiency. Patients with MRI pituitary abnormalities were more likely to have endocrine dysfunction than those without (p = 0.004). The sensitivity and specificity of MRI pituitary abnormalities for hypopituitarism was 54% and 92%, respectively.
GENETICS OF SOD
A genetic diagnosis can be made in less than 1% (5-10% in research)
Can be caused by mutations in HESX1, OTX2, SOX2, SOX3; many other genes control specific developmental pathways
Evidence of epigenetic factors
There is overlap in the genetic pathways in development of the hypothalamus and the pituitary
Spontaneous mutation, as rarely reoccurs in families

RISK FACTORS FOR SOD
No known cause – sporadic occurrence
These abnormalities occur at 4-6 weeks gestation
Young maternal age reported
Primigravida common
Maternal smoking; some studies note drug/alcohol use
Breech presentation - 32%
Males 2 or 3:1 in some studies

PITUITARY AND ENDOCRINE ISSUES IN ONH
Growth hormone deficiency
Cortisol deficiency
Thyroid deficiency
ADH deficiency (diabetes insipidus)
Precocious puberty
GnRH Pubertal hormone deficiency
GROWTH HORMONE IN CHILDHOOD

The main hormones of intrauterine growth are insulin and thyroxine, not growth hormone. GH maintains normal blood sugar in infancy. Liver conversion to IGF-1 prompts skeletal growth. GH is essential to achieve normal adult height and bone health. Increases lean mass.
CORTISOL

- Stress hormone
- Controls blood sugar and water/salt balance, blood pressure
- Daily rhythm - highest in morning
- Medication forms:
  - liquid unstable but easiest for babies
  - pills/liquid must be given 3 times per day
  - injection when ill/injured/vomiting

THYROID

- Essential for growth
- Brain growth - no substitute
- Sets metabolic rate
- May be picked up on newborn screening
- Should not be combined with other medications

ANTI DIURETIC HORMONE – ADH (VASOPRESSIN)

- ADH makes kidney hang on to water; too much water loss also means loss of salts
- People with Di drink because they urinate too much; they do not urinate because they drink too much
- Waterwaterwater means less food and less hunger
- Inadequate treatment means dehydration
- DDAVP comes as injection, nasal spray, nasal liquid, oral tablets
- Hard to distinguish from psychogenic water drinking
SEX HORMONES

Can be too early, or not at all in SOD
Too early? Too short!
Essential to good health, not just social needs
Sex hormones prompt sexual changes and
Improve bone density
Increase muscle mass
Prompt growth spurt
Finalize growth – by closing the epiphyses

SEX HORMONES

While no parent delights in puberty, consider these issues in children with profound developmental challenges
Fracture risks in non ambulatory children
Delayed puberty means a taller adult
Sexualized behaviors are not typically the challenge that families dread
Not all “precocity” needs to be treated, and delaying puberty out of fear may have unintended negative consequences

GROWTH, BEHAVIOR, AND DEVELOPMENT IN VISUALLY IMPAIRED CHILDREN

“Blindisms” vs autism
Hand flapping, eye tapping, twirling

Autism even more likely with lower IQ; difficult to assess as some parameters are visual

Motor skill delays – not predictive!
It may show intelligence to take things slow in an unsafe world
**COMMON PHYSICAL PROBLEMS OF ONH BABY**

- Hypoglycemia
- Prolonged jaundice
- Small external genitals – boys and girls
- Nystagmus
- "Overdue" post date
- Poor feeding

**INFANTS WITH ONH**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>David</td>
<td>Brayden</td>
</tr>
</tbody>
</table>

- Chaotic parents with substance abuse issues
- Constant crying, poor sleep
- GH, TSH, ACTH deficient
- GH, TSH, ACTH
- No sleep cycle
- Teen parents, moving house to house
- Profound obesity
- Great grandmother now caring for him

**CARE NEEDS IN INFANCY**

- Early On referral
  - Suck, swallow may be impaired
  - Hypotonia may be present
  - Tummy time help needed to prevent plagiocephaly
- Visual therapy
- Support and encouragement - especially for young or first time parents
- Be prepared to call them at least every two weeks
CHILDHOOD CHALLENGES

- Sensory integration
- Oral defensiveness
- Sleep abnormalities
- Temperature regulation
- Bathroom issues - DI, constipation
- Temperment and personality style
- Weight gain
- ?Autism

HOW VISUALLY IMPAIRED CHILDREN LEARN

- Use of other senses, but may become overwhelmed
- No, they do not all “love” music and noise
- Will not “see” others eating, which is key in beginning spoon feeding
- Will become defensive and fearful if others do not provide verbal directions and explanations
- Gross motor skills may be very delayed
- Poor vision limits free playing and exploration
- Obesity is common due to low use of big muscles

SENSORY INTEGRATION AND ORAL DEFENSIVENESS

- Delayed coordination of suck and swallow, slow progression to solids
- No visual cues – incoming bottle! Spoon!
- One choking episode, however mild, can be so traumatic that the child refuses similar textures
**Sleep Issues**

“Non 24”
Melatonin
Clonidine
Sleep disorders are a major cause of behavior problems
Don’t expect children with poor sleep to be tired and want to nap! Wild and disobedient is more common

**Temperature Dysregulation**

Too hot, too cold

Good for parents to know “normal” for their child

May need bedroom A/C

**Bathroom Issues**

Sensory integration means both ends of the tube
Poor muscle tone impairs bowel elimination
Odd dietary habits, low fiber diets
Delayed potty training
Is it DI, or psychogenic water drinking?
**TEMPERAMENT AND PERSONALITY STYLES**

- Echolalia
- Verbal tics
- Can perseverate and need redirection
- Thrive with routines
- Generally affectionate individuals
- Parents can help diminish “blindisms”

---

**8 YEAR OLDS WITH ONH**

<table>
<thead>
<tr>
<th>Ella</th>
<th>Jayden</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adopted at birth</td>
<td>Non verbal</td>
</tr>
<tr>
<td>Uses a cane</td>
<td>GH, levoxyl, cortef</td>
</tr>
<tr>
<td>Some food aversion</td>
<td>Completely dependent, can stand with support</td>
</tr>
<tr>
<td>Learning braille, top student in 2nd grade</td>
<td>Oral aversion led to Gtube</td>
</tr>
<tr>
<td>Isolated GH deficiency</td>
<td>Developed seizures at age 6 years</td>
</tr>
</tbody>
</table>

---

**TEENS WITH ONH**

<table>
<thead>
<tr>
<th>Maggie</th>
<th>Chase</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 feet tall at age 17</td>
<td>5’6 and still growing at 17</td>
</tr>
<tr>
<td>Helps herself to water</td>
<td>3rd child of 19 year old mother</td>
</tr>
<tr>
<td>Affectionate, obedient</td>
<td>In high school, raises livestock in the city, wants to be a farmer</td>
</tr>
<tr>
<td>Autistic; not potty trained</td>
<td>Depression</td>
</tr>
<tr>
<td>Missing all hormones</td>
<td>Visual field defects</td>
</tr>
<tr>
<td>2nd child, post HS educated family</td>
<td></td>
</tr>
<tr>
<td>Can detect light</td>
<td></td>
</tr>
</tbody>
</table>
FAMILY RESOURCES

- Magic Foundation  www.magicfoundation.org
- NIH – NINDS booklet on line
- Hormone.org
- http://www.hormone.org/hormones-and-health/the-endocrine-system
- nodcc.org – Disorders of the corpus callosum
- Facebook (of course)
- Pinterest