

SEPTO OPTIC DYSPLASIA IN CHILDREN

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OPTIC NERVE HYPOPLASIA SYNDROME IN CHILDREN

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I HAVE NO CONFLICTS TO DISCLOSE.

KATHY CLARK NP

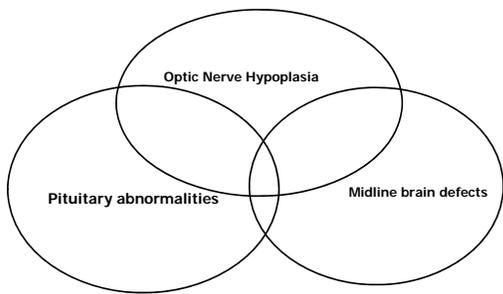
OBJECTIVES

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?



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?

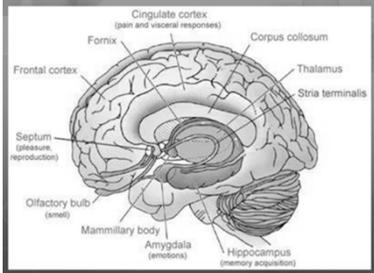
Corpus Callosum

Associated with developmental delay
1.8-2/10,000
absent in 2.3% of DD individuals
49% have other CNS abnormalities
ONH only in 10% of individuals with absent corpus callosum

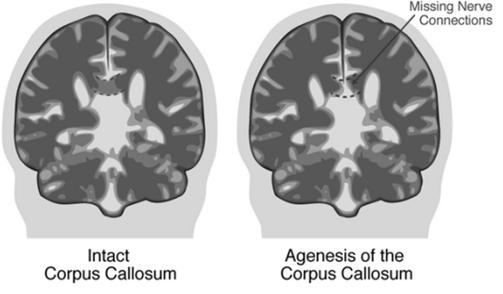
Septum Pellucidum

Just not that interesting
Can occur with absence of corpus callosum
Presence of SP does not rule out endocrinopathy

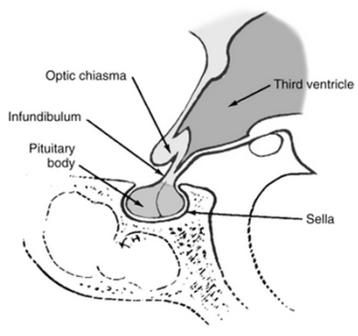
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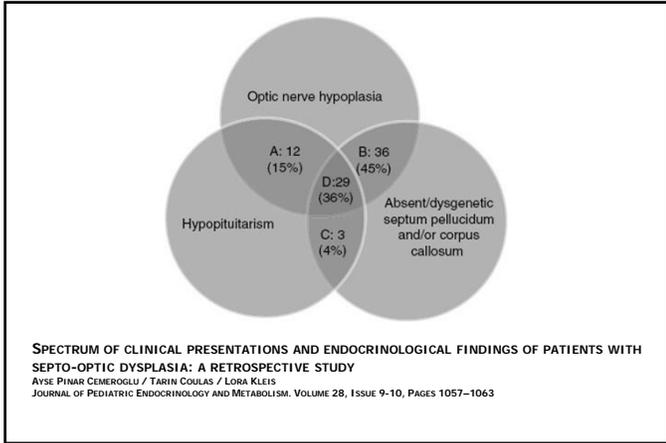


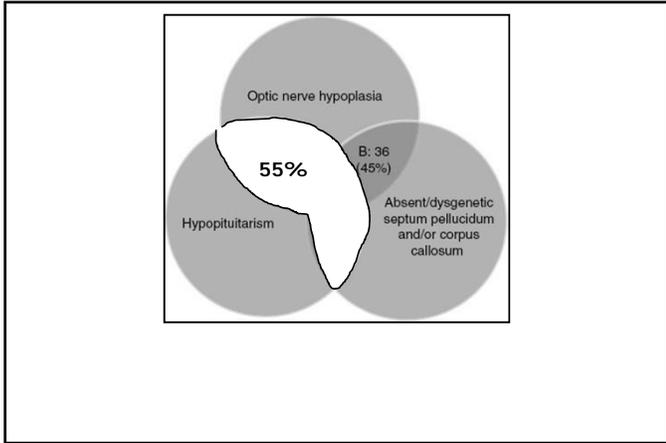
HYPOTHALAMUS

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 CEMEROGLU / TARIN COULAS / LORA KLEIS
 JOURNAL OF PEDIATRIC ENDOCRINOLOGY AND METABOLISM, VOLUME 28, ISSUE 9-10, PAGES 1057-1063

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) ^a

Clinical findings, %	
Clinical optic nerve hypoplasia, unilateral	6
Clinical optic nerve hypoplasia, bilateral	90
Blindness (unilateral or bilateral)	44
Hypothalamic-pituitary dysfunction	55
Seizures	27.5
Behavioral issues	22.5
Autism spectrum	10
Cognitive delay	42.5
Other clinical findings, n (%)	
Limb/hand anomaly	2 (2.5)
Cleft lip/cleft palate	2 (2.5)
MRI findings, %	
Optic nerve hypoplasia	96
Septum pellucidum (absent/hypoplastic)	85
Corpus callosum (absent/hypoplastic)	32
Pituitary hypoplasia/ectopic pituitary	9*
Other additional MRI findings	36

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Age at diagnosis of the endocrine dysfunction – all occurred by age 8 years

Hypothalamic-pituitary dysfunction, n:44	Age of onset, years Mean±SD; range	Frequency %
Growth hormone deficiency	1.85±2.2 (0-8)	55
Central hypothyroidism	1.2±1.9 (0-8)	70
Secondary/tertiary adrenal insufficiency	0.53±0.84 (0-8)	50
Central diabetes insipidus	0.85±1.2 (0-3.5)	30
Central precocious puberty	7.3±0.5 (7-8)	9

ENDOCRINE AND PUBERTAL DISTURBANCES IN OPTIC NERVE HYPOPLASIA, FROM INFANCY TO ADOLESCENCE
 OLIVER J OATMAN, 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 = 4/8) 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

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

David

Brayden

- Chaotic parents with substance abuse issues
- Constant crying, poor sleep
- GH, TSH, ACTH deficient
- Constant mild infections

- Teen parents, moving house to house
- Profound obesity
- Great grandmother now caring for him
- GH, TSH, ACTH
- No sleep cycle

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

Ella

- Adopted at birth
- Uses a cane
- Some food aversion
- Learning braille, top student in 2nd grade
- Isolated GH deficiency

Jayden

- Non verbal
- GH, levoxyl, cortef
- Completely dependent, can stand with support
- Oral aversion led to Gtube
- Developed seizures at age 6 years

TEENS WITH ONH

Maggie

- 5 feet tall at age 17
- Helps herself to water
- Affectionate, obedient
- Autistic; not potty trained
- Missing all hormones
- 2nd child, post HS educated family
- Can detect light

Chase

- 5'6 and still growing at 17
- 3rd child of 19 year old mother
- In high school, raises livestock in the city, wants to be a farmer
- Depression
- Visual field defects

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



