CERPO
Centro de Referencia Perinatal Oriente
Facultad de Medicina, Universidad de Chile

Seminario
Diagnóstico Prenatal de Displasia Septo-óptica

Dr. Cristian Contreras
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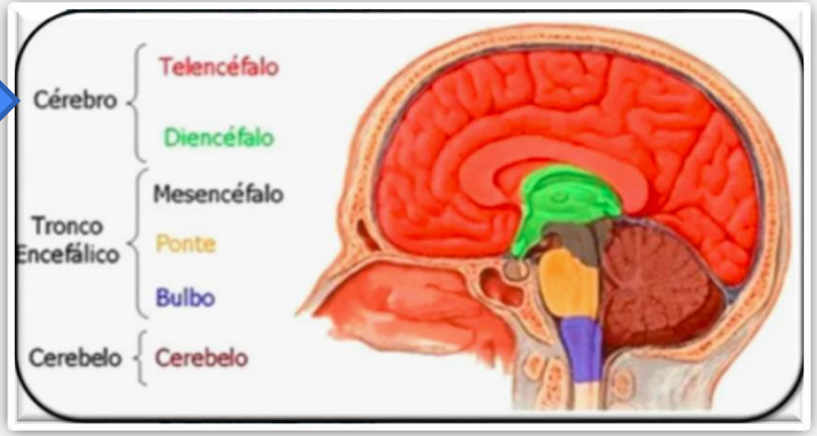
Introducción

Desarrollo del prosencéfalo consta de 3 partes (proceso inducción ventral)

- Formación de vesículas del prosencéfalo
- Clivaje
- **Formación de línea media → CSP, CC, fórnix.**



Definición

Tno. Congénito de formación de línea media

Incidencia 2-53 en 100000 (depende de criterio)

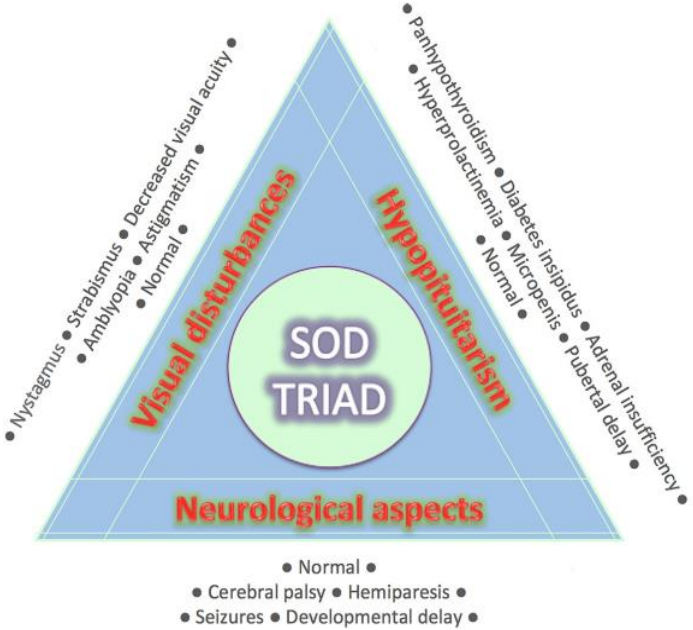
Sd. De Morsier (describió en 1956)

Tríada clásica (sólo en 30-47%):

- Agenesia de estructura línea media (CSP, CC)
- Hipoplasia nervio óptico
- Hipoplasia hipotálamo-hipofisiario.

Dg. con 2 de los 3.

Heterogéneo en penetrancia y desafiante.



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Etiopatogenia

Genética

HESX1 → prosencéfalo y adenohipófisis
- Variantes homo y heterocigotas asociadas a SOD

SOX2, SOX3, OTX2
- Asociados a nervio óptico y C. calloso.

De novo, aunque se han descrito patrones AR (más raro AD)

Ambiente

Drogas: anticonvulsivantes, antidepresivos, antieméticos,

Infecciones Virales

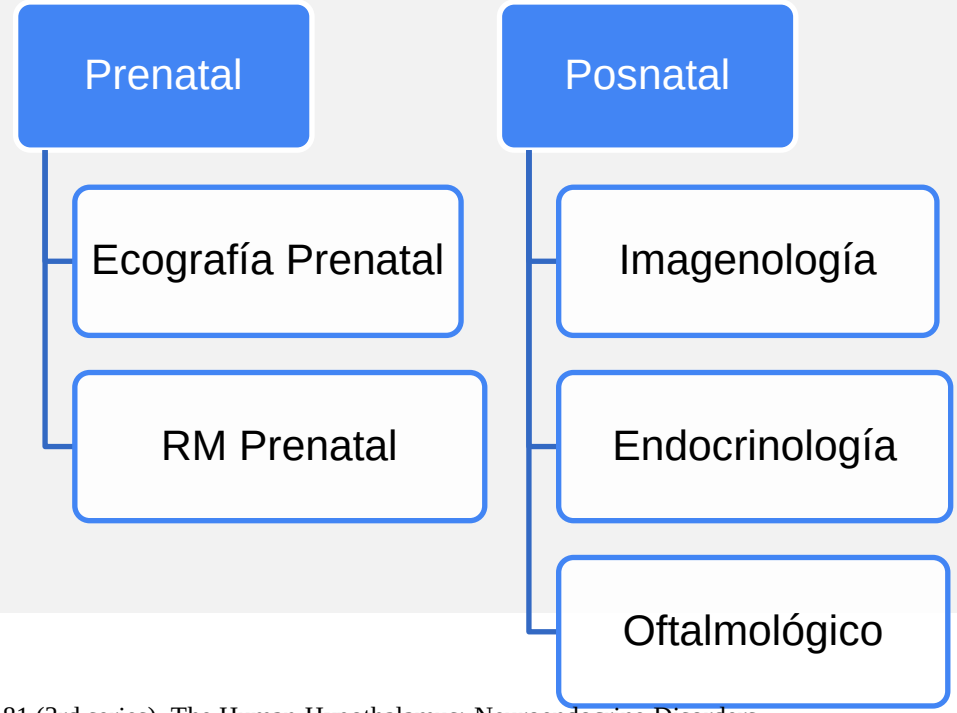
Edad materna < 22 años (factor consistente)

OH, TBQ

Insulto vascular A. cerebral ant.

Fenotipo (SOD)

Diagnóstico



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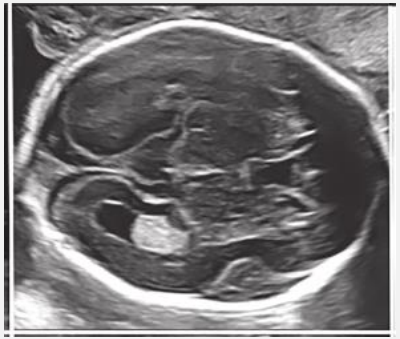
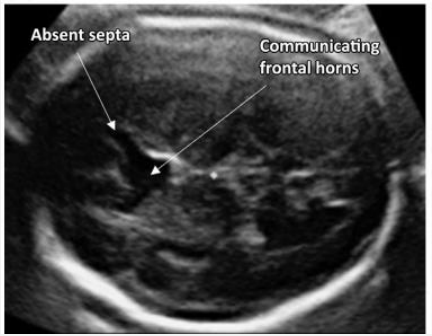
Diagnóstico Prenatal

- Hallazgos imagenológicos explican 90% trastornos neurológicos

- **Ausencia CSP 75-80% (parcial o completa**
- **Fusión fórnices 60%**
- **Hipoplasia nervio óptico**



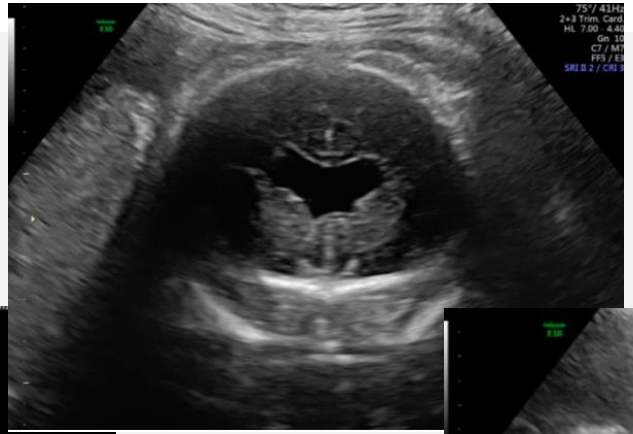


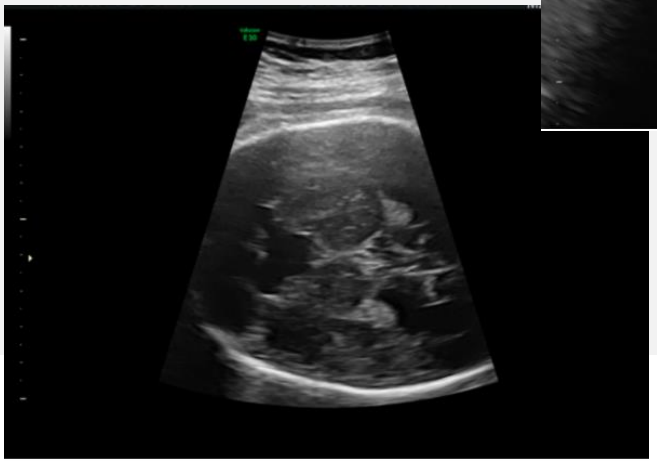
- Aquiasmia, anoftalmia y microftalmia
- Anomalías Cuerpo Calloso
- Anomalías Hipofisiarias (RM)
- Anomalías hipocampales
- Quistes aracnoideos (12.5%)

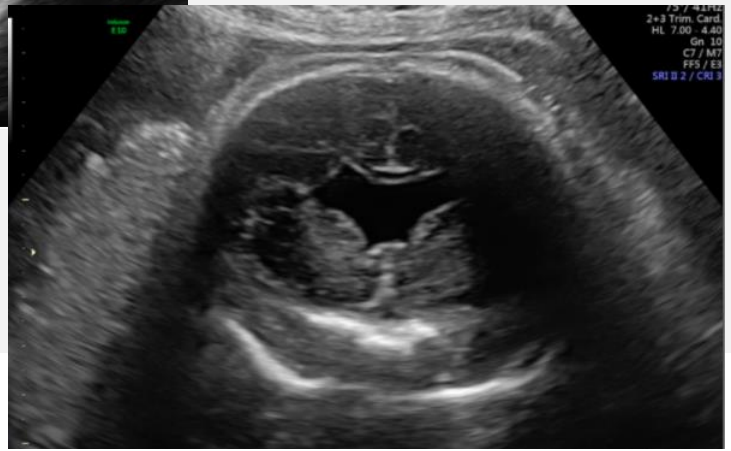
Tamar Borkowski-Tillman, Prenatal Diagnosis. 2020;40:674–680

SMFM Anomalies Consult Series #3. Am J Obstet Gynecol 2020.

Diagnóstico Prenatal







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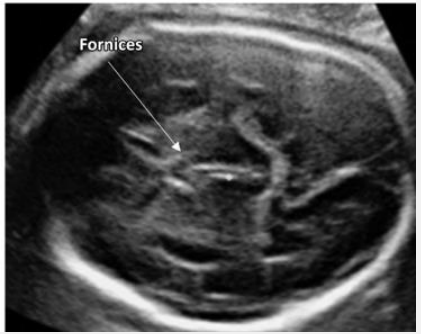
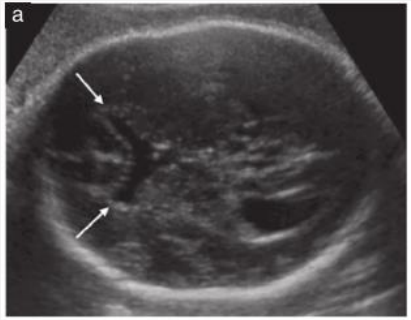
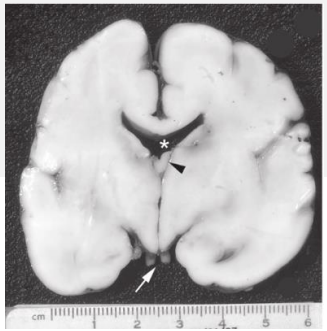
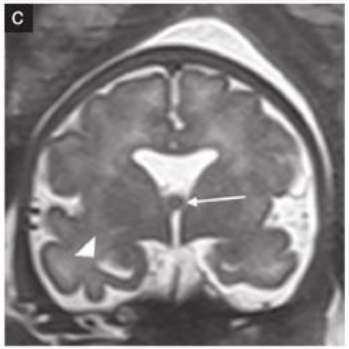


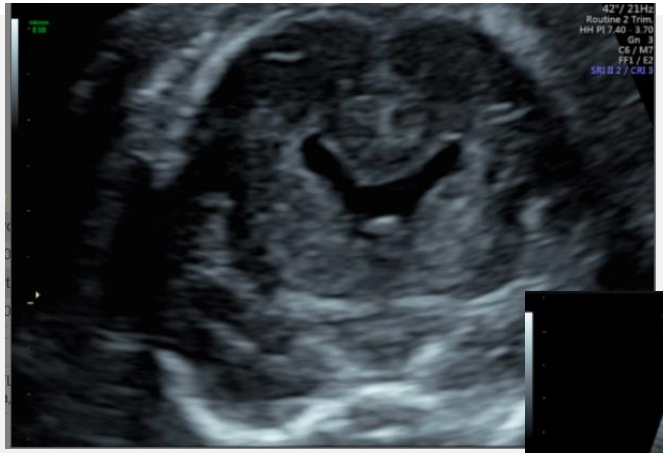


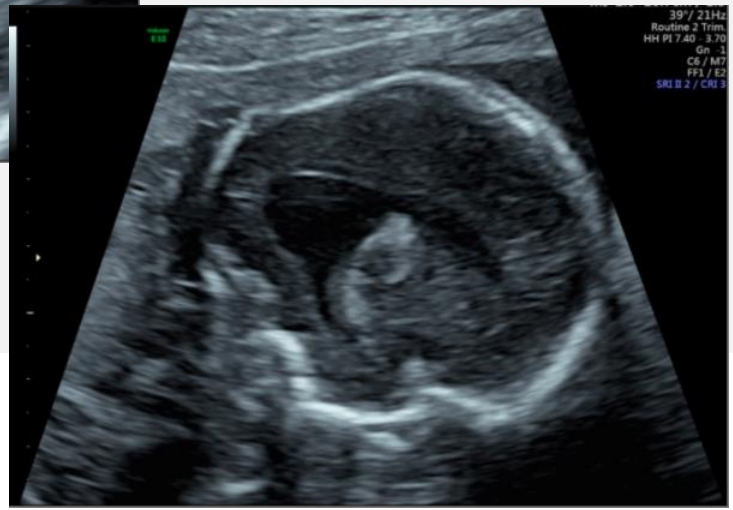


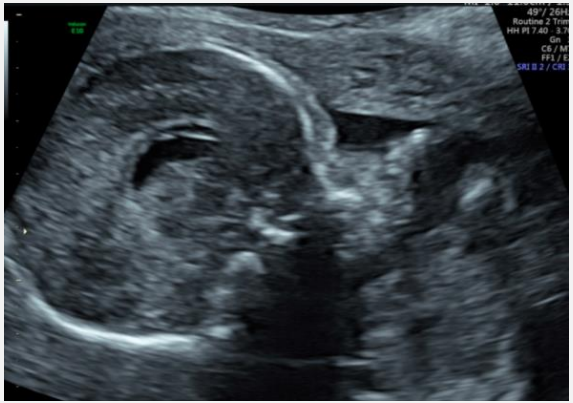


Tamar Borkowski-Tillman, Prenatal Diagnosis. 2020;40:674–680.

Diagnóstico Prenatal

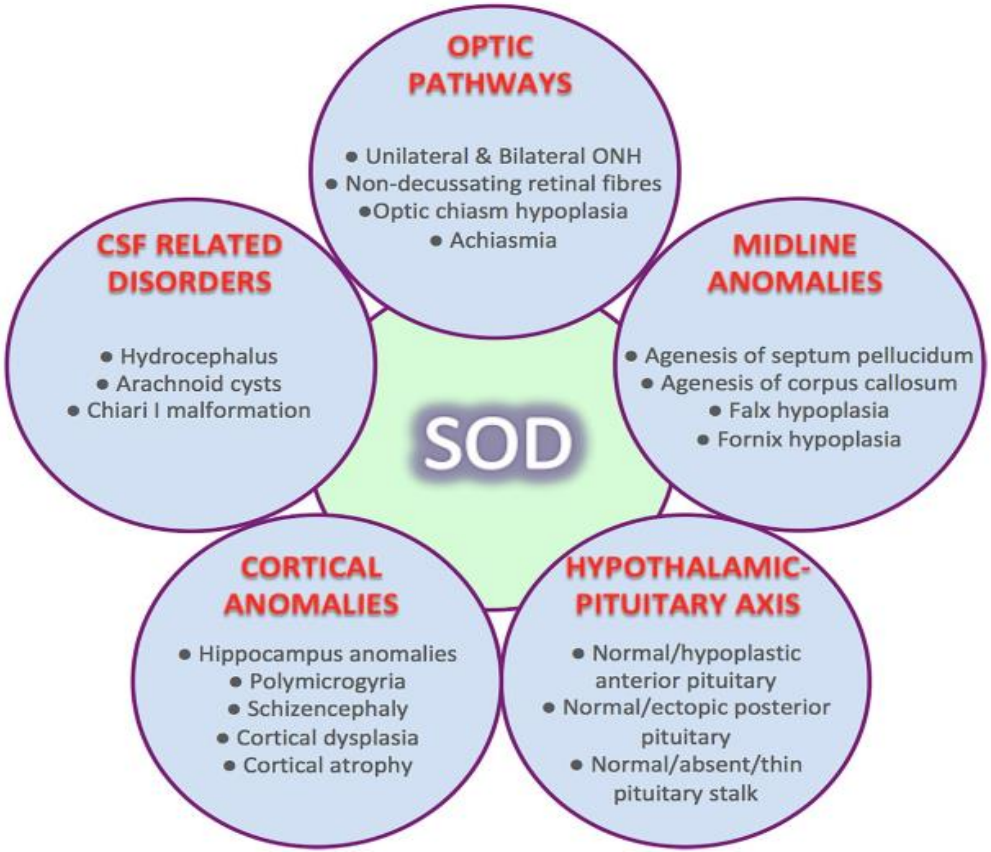






Diagnóstico Prenatal

- Frente a anomalías del CSP, derivar a centro terciario
- Neurosonografía
- RM Fetal
- Tener presente que no es posible realizar dg. definitivo prenatalmente



Asociaciones

- Hidrocefalia

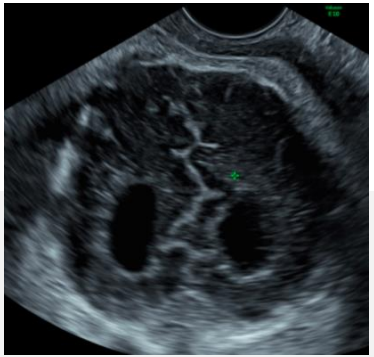
Migración Neuronal
- Lisencefalia
- Hetororopias de MG

Organización Neuronal
- Polimicrogiria

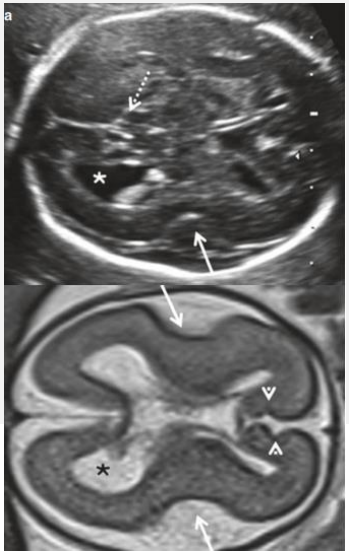
SOD plus (+ Tno. Dllo cortical)

Espectro SOD (Por ej: fisura labiopalatina, etc)

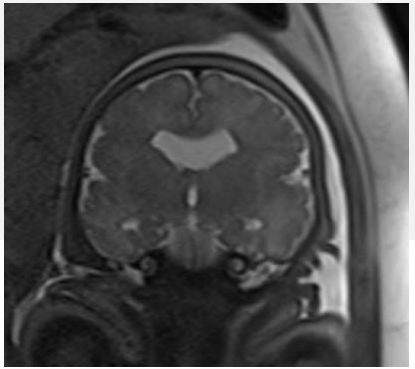
Riesgo muy bajo de anomalías cromosómicas asociadas.



Heterotopia



Lisencefalia



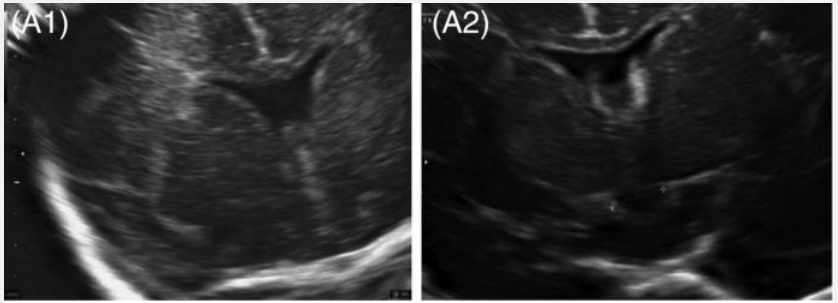
Polimicrogiria

Diagnóstico Diferencial

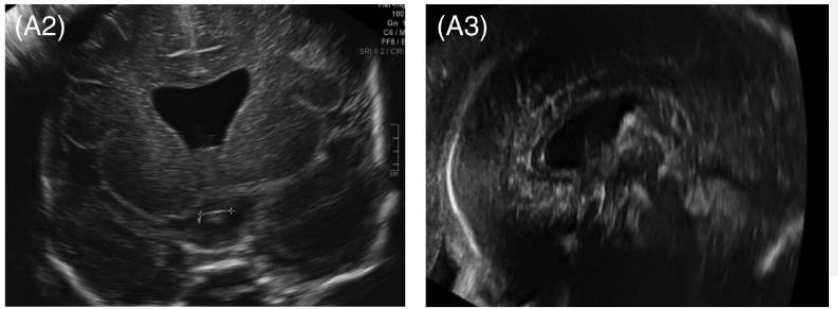
D. Dif de Agenesia de CSP

- Agenesia aislada
- Holoprosencefaia
- Ventriculomeglia severa
- Hidranencefalia
- Agenesia CC (y sus casusas)
- Esquizencefalia

Hipoplasia de nervio óptico



Agenesia CSP con outcome normal



Agenesia/Disgenesia CC

Tamar Borkowski-Tillman, Prenatal Diagnosis. 2020;40:674–680.

Diagnóstico Diferencial

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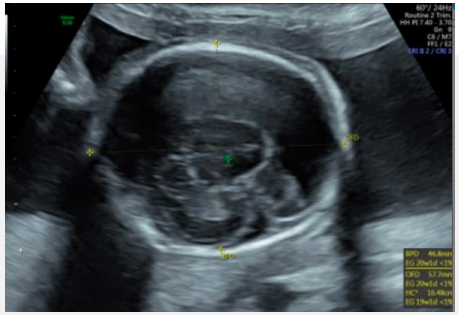
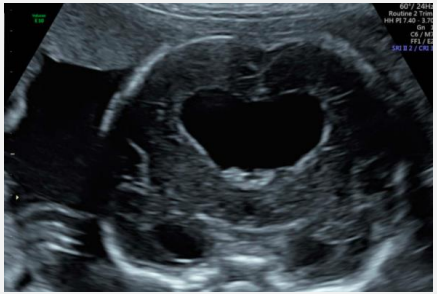
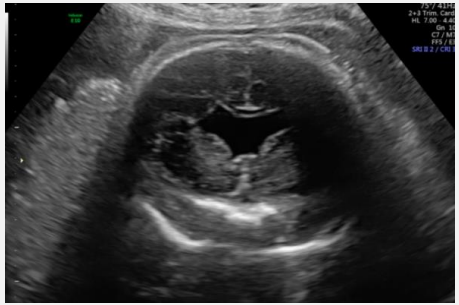


Holoprosencefalia Semilobar



Ventriculomegalia severa



Esquizencefalia

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- Holoprosencefaia
- Ventriculomeglia
- Hidranencefalia
- Agenesia CC (y sus casusas)
- Esquizencefalia

Hipoplasia de nervio óptico

Systematic approach to MRI reporting for SOD patients

Questions to be answered when reporting MRI scan in SOD

1. Is the anterior pituitary of normal size?
2. Is the posterior pituitary present, and what is its location?
3. Is the pituitary stalk present, and what is its size?
4. What are the sizes of optic nerves and optic chiasm?
5. Is the septum pellucidum present?
6. Are there other midline abnormalities (e.g., corpus callosum dysgenesis)?

Adapted from Hellström A, Aronsson M, Axelson C et al. (2000). Children with septo-optic dysplasia–how to improve and sharpen the diagnosis. Horm Res Paediatr 53: 19–25 and Webb et al. (2009).

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Fetal Ultrasound and Magnetic Resonance Imaging Findings in Suspected Septo-Optic Dysplasia

A Diagnostic Dilemma

Amy Maduram, MD, Nikdokht Farid, MD, Rebecca Rakow-Penner, MD, PhD, Neda Ghassemi, BS, Paritosh C. Khanna, MD, Shira L. Robbins, MD, Andrew Hull, BMBS, Jeffrey Gold, MD, PhD, Dolores H. Pretorius, MD

CERPO

Serie retro (2020). 11 pacientes con SOD o sospecha

Sospecha Prenatal: 6/11

- SOD, obs. HPE, fusión asta anterior, ventriculomegalia.
- 2/10 casos TOP (Ausencia CSM y VM)

Posnatal

- 5 casos de panhipopituitarismo
- HNO uni o bilateral 100%, sólo 2 ceguera completa.
- 2/9 NV neurodesarrollo normal

Table 3. Concordance of Prenatal Suspicion With Postnatal Diagnosis of SOD

Case	Prenatal Suspected SOD?	Prenatal Findings: Complete or Partial Absence of CSP[a]	Postnatal Diagnosis?	Postnatal Findings: Complete or Partial Absence of CSP
1	No	Reported normal, however retrospective review of fetal MRI showed partial absence	Yes	Partial absence
2	Yes, by US only at 20 and 26 wk	Partial absence on US but fetal MRI reported normal Patient counseled about discordant imaging results	Yes	Complete absence
3	Yes, by US only at 19 wk	Reported normal, however retrospective review of fetal MRI showed partial absence	Yes	Complete absence
4	Yes, by follow-up US and fetal MRI	Complete absence	Yes	Complete absence
5	No	Assumed normal	Yes	Partial absence
6	Yes, by follow-up US and fetal MRI	Partial absence by US and fetal MRI	Yes	Complete absence
7	No	Limited	Yes	Partial absence
8	No	Assumed normal	Yes	Complete absence
9	No	Assumed normal	Yes	Normal
10	Yes, highly suspected	Complete absence with enlarged LVs and FHs	Terminated	NA
11	Yes, highly suspected	Complete absence with borderline LVs	Terminated	NA

[a]Assumed normal means that prenatal US images were reported as normal and no further advanced or follow-up imaging targeting the CSP was performed.

Long-term postnatal outcome of fetuses with prenatally suspected septo-optic dysplasia

S. SHINAR[1], S. BLASER[2], D. CHITAYAT[3,4], T. SELVANATHAN[5], V. CHAU[5], P. SHANNON[6], S. AGRAWAL[1], G. RYAN[1], V. PRUTHI[1], S. P. MILLER[5], P. KRISHNAN[2] and T. VAN MIEGHEM[1]

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2020. 214 fetos con ausencia de CSP.

18 casos (8.4%) sospecha de SOD prenatal

12 RNV → 5 displasia septo-ópticas confirmadas.

- 2 alteraciones visuales
- 4 endocrinológicas
- 80% de aquellos retraso dllo. (mayoría severo)
- VM leve

RN sin alteraciones visuales ni endocrinológicas, neurodesarrollo normal

Table 1 Suspected prenatal diagnosis in 214 fetuses with absent cavum septi pellucidi

Suspected diagnosis	n *(%)*
Septo-optic dysplasia	18 (8.4)
Anomaly of corpus callosum*	84 (39.3)
Severe ventriculomegaly†	33 (15.4)
Aqueductal stenosis	32 (15.0)
Holoprosencephaly	21 (9.8)
Neural tube defect‡	16 (7.5)
Porencephalic cyst	4 (1.9)
Cortical malformation§	3 (1.4)
Syntelencephaly	3 (1.4)
Hydranencephaly	1 (0.5)
Intraventricular hemorrhage without severe ventriculomegaly	1 (0.5)

*Included agenesis, partial agenesis, hypoplasia and dysplasia. †Defined as atrial width of lateral ventricles ≥ 15 mm. ‡Two fetuses also had agenesis of corpus callosum. §Included schizencephaly, lissencephaly and polymicrogyria.

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Table 3 Prenatal and postnatal imaging findings in 12 neonates with prenatally suspected septo-optic dysplasia

Imaging finding	*Value*
Ultrasound	12 (100)
Absent cavum septi pellucidi	12 (100)
Mild ventriculomegaly*	6 (50.0)
Moderate ventriculomegaly†	1 (8.3)
Additional findings	5 (41.6)
Echogenic cardiac focus	1 (8.3)
Oligohydramnios‡	2 (16.7)
Hypoplastic nasal bone	1 (8.3)
Retromicrognathia	1 (8.3)
Prenatal MRI	11 (91.7)
Septal remnants	11/11 (100)
Forniceal fusion	11/11 (100)
Thinned corpus callosum	4/11 (36.4)
Squared anterior horns	8/11 (72.7)
Dysplastic temporal horns	8/11 (72.7)
Olfactory bulbs present	11/11 (100)
Hypoplastic optic chiasm	0/11 (0)
Hypoplastic optic nerves	1/11 (9.1)
Unilateral microphthalmia	1/11 (9.1)
Abnormal pituitary gland	1/11 (9.1)
Mild-to-moderate ventriculomegaly	7/11 (63.6)
Postnatal ultrasound/MRI	10 (83.3)
Age at scan (days)	3.5 ± 1.7
Concordant findings pre- and postnatally	6/10 (60.0)
Non-concordant or additional findings	4/10 (40.0)

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Table 5 Summary of case series reporting outcome of fetuses with prenatally suspected septo-optic dysplasia (SOD), according to whether diagnosis was confirmed

			Non-SOD		*Confirmed SOD*					
Study	*Prenatally suspected SOD*	*No additional major brain anomalies*	*Cases*	*Abnormal neuro-development*	*Cases*	*Abnormal ophthalmologic exam*	*Pituitary dysfunction*	*Abnormal neuro-development*	*Follow-up length (years)*	*Lost to follow-up*
Lepinard (2005)[20]	2	2	1	0	1	1	1	1	2.1 (1.2–3.1)	0
Malinger (2005)[11]	2	0	1	0	0	0	0	0	0.5	0
Damaj (2010)[7]	17	17	13	4	3	2	1	0	3 (1.8–3.8)	1
Pilliod (2018)[18]	15	13	6	2	2	2	1	0	2.5 (2–3)	7
Vawter-Lee (2018)[19]	8	8	6	1	2	1	1	0	0.7 (0.7–0.8)	0
Present study	18	18	5	0	5	2	4	4	2.5 (2.5–7)	2
Total	62	58 (93.5)	32 (51.6)	7 (21.9)	13 (21.0)	8 (61.5)	8 (61.5)	5 (38.5)	—	10 (16.1)

Only first author of each study is given. Data are given as *n*, *n* (%) or median (interquartile range). Case reports not included. Total number of cases of confirmed SOD and non-SOD may not equal number of cases of prenatally suspected SOD due to patients lost to follow-up and termination of pregnancy.

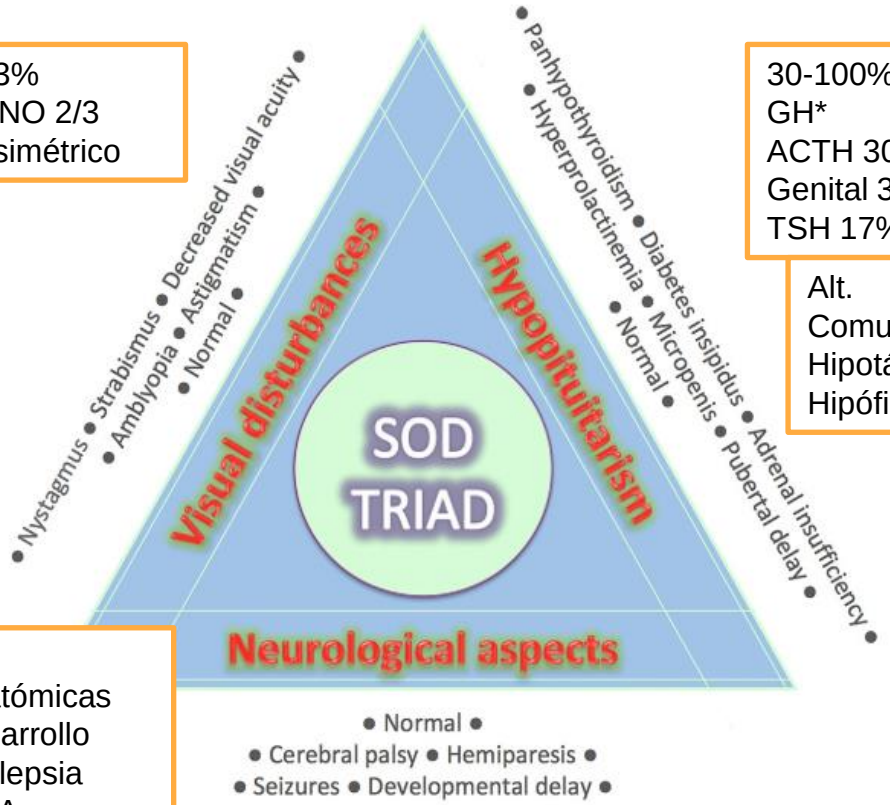
Pronóstico: Espectro

- >60% parto a término
- AEG y Apgar normal

- Neonatal precoz
  - Hipoglicemia
  - Hiperbilirrubinemia

- Anomalías faciales
  - Hipertelorismo
  - Frontal prominente
  - Puente nasal deprimido
  - Sindactilia o braquidactilia

23%
HNO 2/3
asimétrico



30-100%
GH*
ACTH 30-60%
Genital 30-50%
TSH 17%

Alt.
Comunicación
Hipotálamo-
Hipófisis

70%
- Anatómicas
- Desarrollo

30% epilepsia
30% TEA

Conclusiones

- Ausencia completa o parcial de CSP se asocia a múltiples diagnósticos
- Se debe realizar examen NSG detallado buscando realizar el diagnóstico diferencial
- Ausencia de septos del CSP, fusión fórnix, hipoplasia NO pueden orientar al diagnóstico
- Aproximadamente 25% de los casos sospechados de SOD se confirman posnatalmente
- La consejería prenatal es desafiante, pero debe hacerse hincapié en que el diagnóstico se confirma posnatalmente
- Se debe explicar que el pronóstico tiene un espectro amplio
- Sus manifestaciones incluyen: trastornos neurológicos, alteración visual y trastornos hipofisiaros.

CERPO
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