Septooptic Dysplasia

**TERMINOLOGY**
- Septooptic dysplasia (SOD)
- De Morsier syndrome

**IMAGING**
- Absent septum pellucidum, small optic chiasm
- Optic nerves, pituitary gland, septum pellucidum
- Coronal imaging shows
  - Flat-roofed ventricles
  - Downward pointing anterior horns
- 3 orthogonal planes crucial to identify all findings
  - Absent septum pellucidum, flat roof of frontal horns, small optic chiasm

**CLINICAL ISSUES**
- Newborns: Hypoglycemic seizures, apnea, cyanosis, hypotonia, prolonged conjugated jaundice, and (in boys) microphallus
- Abnormal endocrine function (60%): Look for multiple pituitary deficiencies
- Normal endocrine function (40%): Often have schizencephaly, seizures
- Child with short stature, endocrine dysfunction
- Normal or color blindness, visual loss, nystagmus, strabismus
- ± mental retardation, spasticity, microcephaly, anosmia
- 75-90% have brain abnormalities; 45% have pituitary insufficiency
- Bilateral optic nerve hypoplasia (70%)

**DIAGNOSTIC CHECKLIST**
- SOD in small stature pediatric patient with absent septum pellucidum
- Small optic nerves, with ectopic posterior pituitary lobe, with absent septum pellucidum

(Left) Coronal graphic depicts flat-roofed anterior horns and the absence of a midline septum pellucidum. The anterior horns are draped inferiorly around the fornices and the optic chiasm is small. (Right) Sagittal T1WI MR shows absent septum pellucidum (note the low-lying fornices) and the ectopic posterior lobe of the pituitary gland at the median eminence. Note that the pituitary gland is small for an adolescent, and the infundibulum is not seen.

(Left) Coronal T2WI FSE MR shows the absence of septum pellucidum and pointing of the inferior margins of the frontal horns, drapped over fornices. Note that the optic chiasm is normal in size, as is often the case in septooptic dysplasia (SOD). (Right) Coronal T2WI FSE MR in the same patient at the level of the intraorbital optic nerves shows unilateral optic nerve hypoplasia. The right optic nerve is tiny, running through a small optic nerve sheath. The left optic nerve is normal.
**Septooptic Dysplasia**

**TERMINOLOGY**

**Abbreviations**
- Septooptic dysplasia (SOD)

**Synonyms**
- De Morsier syndrome
- Kaplan-Grumbach-Hoyt syndrome
- Suprasellar dysgenesis
- Septooptic-pituitary dysgenesis

**Definitions**
- Heterogeneous association characterized by optic nerve hypoplasia (ONH), absent septum pellucidum, hypothalamic-pituitary dysfunction
  - De Morsier (1956): Described 7 patients with SOD
  - Hoyt (1978): Described association of SOD with hypopituitarism
- Some authors consider SOD and lobar holoprosencephaly to overlap
- SOD plus: Abnormal optic nerves/chiasm, septum pellucidum, pituitary gland, plus cortical dysplasias

**IMAGING**

**General Features**
- Best diagnostic clue
  - Absent septum pellucidum, small optic chiasm
- Location
  - Optic nerves, pituitary gland, septum pellucidum
- Size
  - Small optic nerves
  - Small pituitary gland with ectopic posterior lobe
  - Absent septum pellucidum
- Morphology
  - Coronal imaging shows
    - Flat-roofed ventricles
    - Downward-pointing anterior horns

**CT Findings**
- NECT
  - Absent septum pellucidum
  - Large lateral ventricles
  - Small bony optic foramina on axial and coronal imaging

**MR Findings**
- T1WI
  - 3 orthogonal planes crucial to identify all findings
    - Absent septum pellucidum (remnants may be present)
    - Flat roof of frontal horns, pointed inferior aspect of frontal horns
    - Small optic chiasm/nerves (fat saturation aides visualization of optic nerves)
    - ± thin pituitary stalk, small anterior lobe of pituitary
    - ± posterior pituitary ectopia
    - Callosal-forniceal continuation or fused midline fornices
    - Thin corpus callosum
    - Vertical hippocampi
    - ± hypoplastic/absent olfactory nerves
    - ± schizencephaly
  - T2WI
    - Deficient falk (especially anteriorly) ± hypomyelination
  - T1WI C+
    - ± ectopic posterior pituitary lobe
    - Delayed enhancement of anterior pituitary lobe on dynamic MR

**DIFFERENTIAL DIAGNOSIS**

**Syndromes Overlapping With Septooptic Dysplasia**
- Optic-infundibular dysplasia, normal septum
- Schizencephaly with absent septum

**Kallmann Syndrome**
- Absent olfactory nerves
- ± visual, septal, pituitary abnormalities

**Holoprosencephaly**
- Similar to SOD
  - Many consider it same disorder as SOD

**Isolated Ectopic Posterior Pituitary Lobe**
- Normal chiasm/nerves, septum pellucidum

**PATHOLOGY**

**General Features**
- Etiology
  - Theories
    - Midline heritable defect (mild holoprosencephaly variant)
    - Or secondary degeneration of optic nerve fibers due to cerebral lesion
    - Or vascular disruption (field defect) during brain development
    - Damage to cerebral and optic nerve around 6th week gestation
    - Teratogens: Cytomegalovirus, antiepileptic drugs, alcohol, maternal diabetes
- Genetics
  - Most are sporadic
  - Some are autosomal dominant or recessive
  - Some cases have mutations in HESX1 gene
    - Homozygous mutations = full syndrome
    - Heterozygous mutations = milder pituitary phenotypes
Septooptic Dysplasia

- Inactivation of HESX1 (3p21.2-3p21.1) by Arg53Cys substitution leads to deficient anterior pituitary lobe (does not occur in sporadic SOD)
- Mutations of FGFR1, PROKR2 also described
- Associated abnormalities
  - Frequently associated with other cerebral anomalies
    - Most common = schizencephaly
    - Perisylvian polymicrogyria
    - Midline malformations (callosal dysgenesis, etc.)
    - Ocular anomalies (coloboma, anophthalmia, microphthalmia)
    - Olfactory tract/bulb hypoplasia
    - Incomplete hippocampal rotation
  - Overlapping syndromes with optic, septal, frontal lobe, midline, olfactory deficiencies

Staging, Grading, & Classification
- Isolated ONH: Visual defect only; intelligence and growth normal
- ONH and septal deficiency: Same as isolated
- ONH and septal and pituitary deficiency: May have developmental delay
- Complete septal agenesis: Worse developmental prognosis

Gross Pathologic & Surgical Features
- Small optic chiasm/nerves
- Small or absent geniculate nucleus
- Deficient/absent septum pellucidum
- Fornicial columns (± fused) → run along roof of 3rd ventricle
- Common: Hypoplasia pituitary, olfactory lobes

Microscopic Features
- Optic nerves, chiasm have sparse or absent myelinated fibers
- Geniculate nucleus (if found): Disorganized layering of small neurons

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Newborns: Hypoglycemic seizures, apnea, cyanosis, hypotonia, prolonged conjugated jaundice, and (in boys) microphallus
  - Abnormal endocrine function (60%): Look for multiple pituitary deficiencies
  - Normal endocrine function (40%): Often have schizencephaly, seizures
- Clinical profile
  - Child with short stature, endocrine dysfunction
  - Normal or color blindness, visual loss, nystagmus, strabismus
  - 2 mental retardation, spasticity, microcephaly, anosmia

Demographics
- Age
  - Generally detected in infants
- More common among younger mothers and 1st born child
- Gender
  - M = F
- Epidemiology
  - 1 in 50,000 worldwide
  - Optic nerve hypoplasia
    - 60% have brain abnormalities (not just schizencephaly); 62-88% have pituitary insufficiency
    - 30% have both
    - 25-50% have absent septum pellucidum
  - Septooptic dysplasia
    - 75-90% have brain abnormalities; 45% have pituitary insufficiency
    - Bilateral optic nerve hypoplasia (70%)

Natural History & Prognosis
- Hypothalamic and pituitary crises; sudden death (hypocortisolism)
- Depends upon severity of associated brain and pituitary malformations

Treatment
- Hormonal replacement therapy

DIAGNOSTIC CHECKLIST

Consider
- SOD in small stature pediatric patient with absent septum pellucidum

SELECTED REFERENCES