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

Holoprosencefalia

Dr. Pablo Silva Labarca
Programa de especialización Medicina Materno Fetal
Facultad de Medicina
Universidad de Chile

Introducción

- Espectro de malformaciones del prosencéfalo caracterizado por una falla en la separación de ambos hemisferios cerebrales y estructuras diencefálicas.

- Frecuentemente se asocia a malformaciones craneofaciales.

Epidemiología

- Malformación cerebral mas común en humanos.

- Prevalencia en RNV 1 en 10.000.
- Prevalencia en abortos 1 en 250.

Embriología

- Posterior al periodo de neurulación (dia 25) el polo cefálico forma 3 vesículas primarias:
  - Prosencéfalo
  - Mesencéfalo
  - Rombencéfalo

- Prosencéfalo → Inducción ventral
  - Formación
  - División
  - Desarrollo de línea media

Embriología

Dia 49: Subdivisión en 5 vesículas.

- Prosencefalo
  - Telencefalo
  - Diencefalo
- Mesencéfalo
- Rombencéfalo
  - Metencéfalo
  - Mielencéfalo

HPE resulta de la falla en la división del prosencéfalo entre el dia 18 y 28 del periodo emrbionario

Embriología

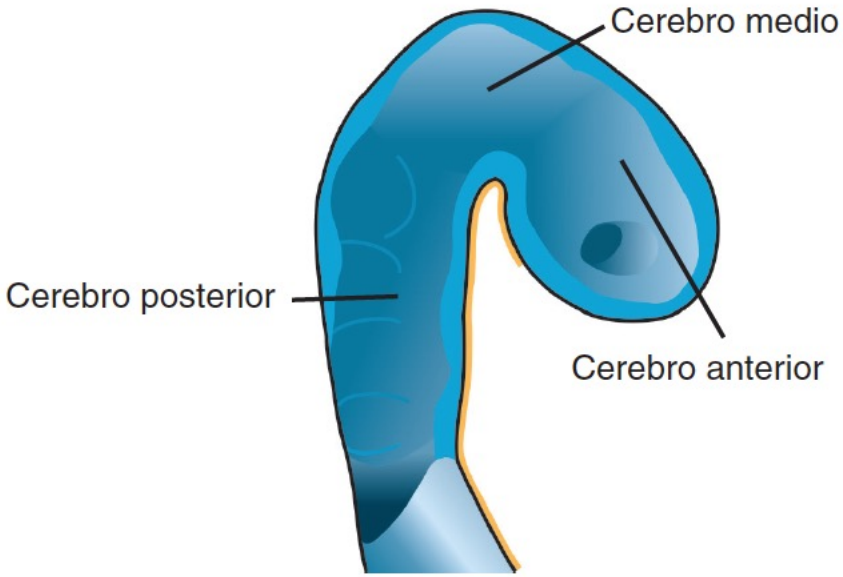

FIGURA 18.4 Sección sagital del cerebro aproximadamente a los 28 días del desarrollo humano. Las tres vesículas cerebrales representan el cerebro anterior, el cerebro medio y el cerebro posterior.

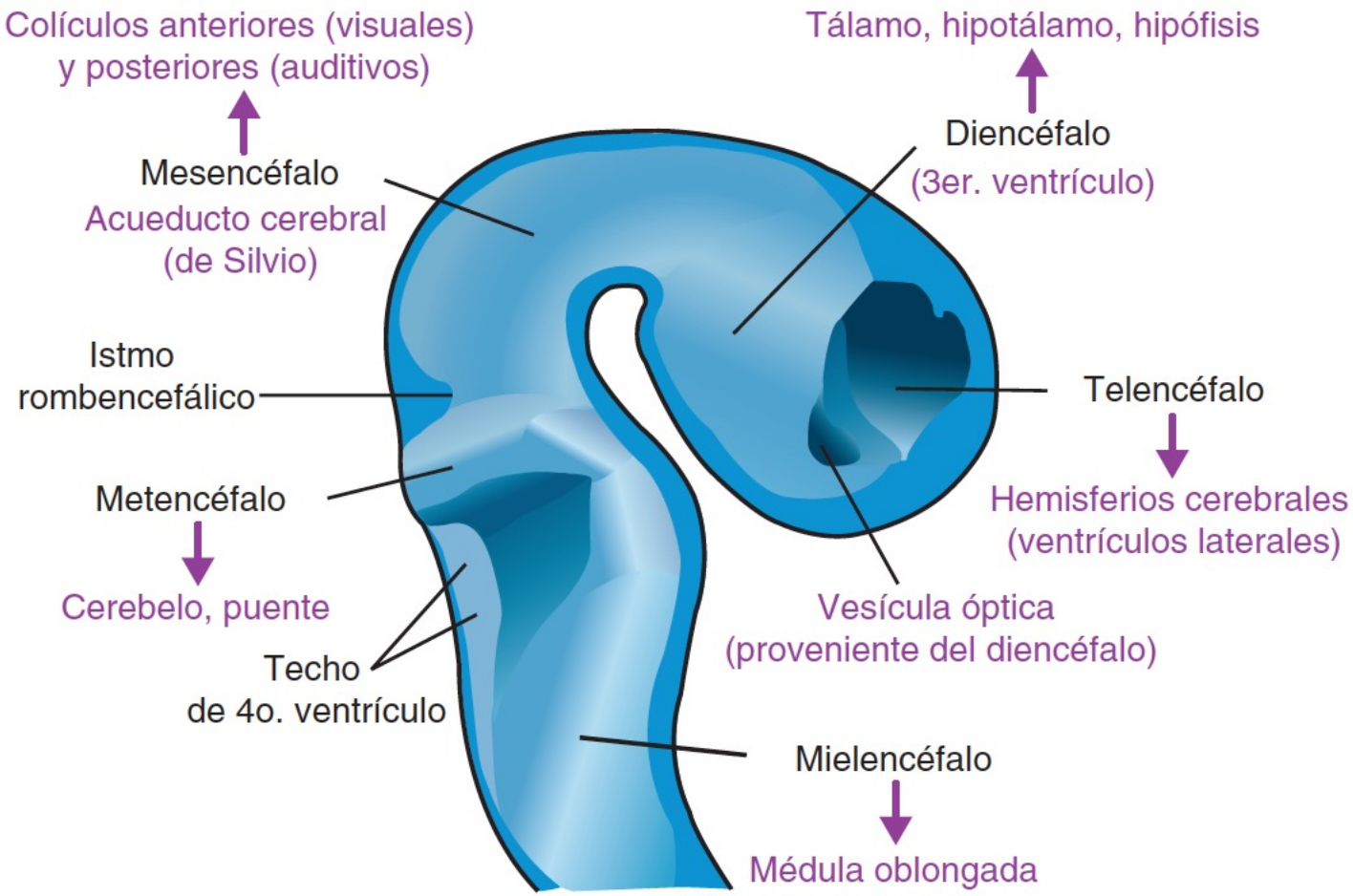

FIGURA 18.5 Sección sagital del cerebro aproximadamente a los 32 días del desarrollo humano. Las tres vesículas primitivas del cerebro fueron divididas en telencéfalo, diencéfalo, mesencéfalo, metencéfalo y mielencéfalo. También se muestran las principales estructuras derivadas de cada división.

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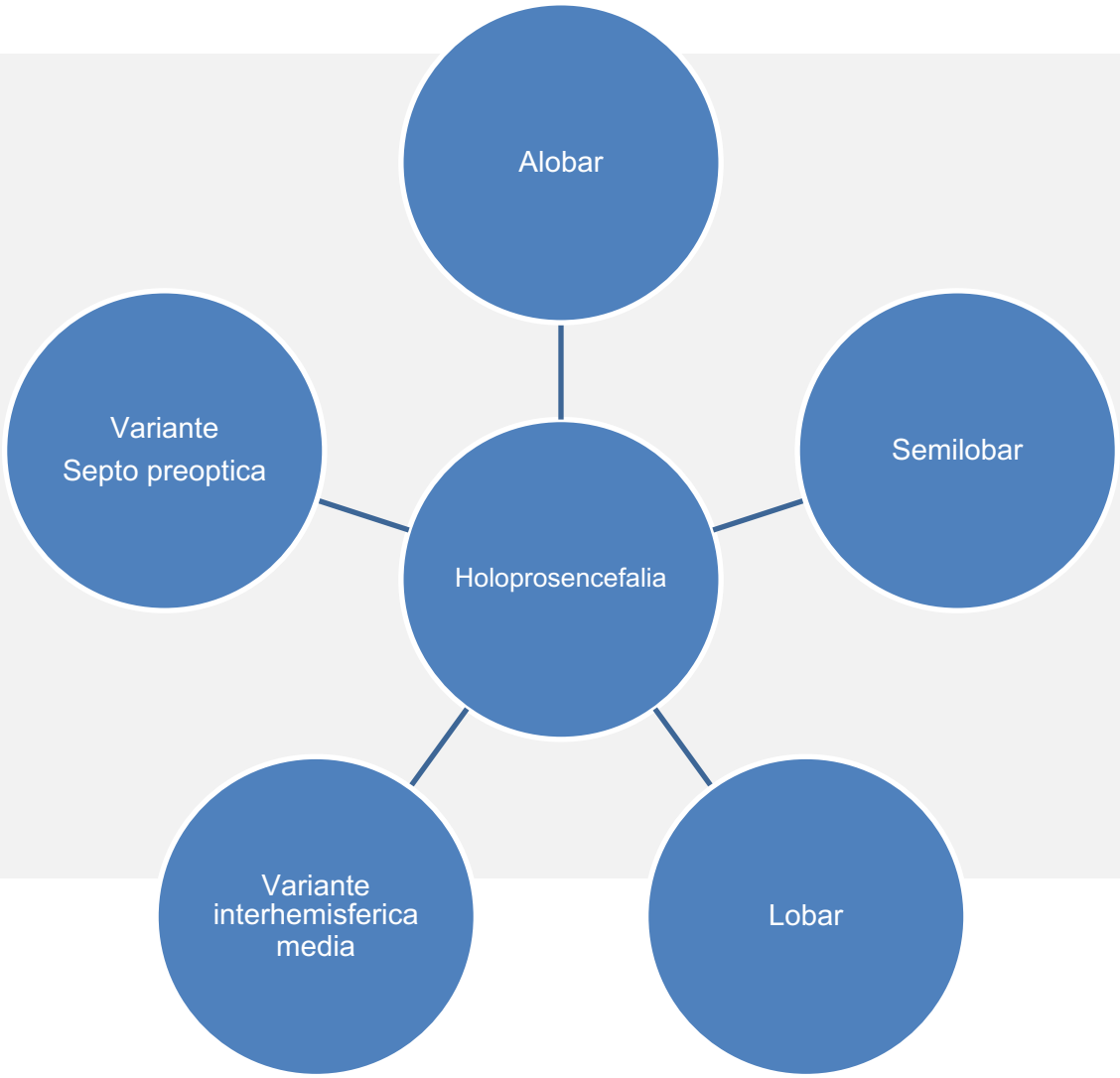
Table 6–1. ANOMALIES OF VENTRAL INDUCTION
Disorders of prosencephalic formation
Aprosencephaly
Atelencephaly
Disorders of prosencephalic cleavage
Holoprosencephaly
Holotelencephaly
Disorders of prosencephalic midline development
Agenesis of the corpus callosum, complete and partial
Agenesis of the septum pellucidum
Septo-optic dysplasia

Tipos


Alobar
Variante
Septo preoptica
Semilobar
Holoprosencefalia
Variante
interhemisferica
media
Lobar

HPE Alobar

- Es el tipo mas frecuente (40-75% de los casos).
- Prosencéfalo único en línea media con un único ventrículo primitivo.
- Quiste dorsal grande.
- 3 diferentes formas de las estructuras fusionadas:
  - Pancake-like
  - Cup-like
  - Ball-like (más común)
- Arteria cerebral anterior tiene su trayecto bajo el hueso frontal.
- Asociado a malformaciones craneofaciales severas.

HPE Semilobar

- La fisura interhemisférica y el falx cerebri pueden estar presentes posteriormente.
- Mas del 50% de los lóbulos frontales están fusionados.
- Cuerpo calloso conservado en su parte posterior (esplenio).
- Tálamo e hipotálamo pueden permanecer fusionados.
- Malformaciones faciales leves o ausentes.
- El único signo puede ser la ausencia de septum pellucidum.

HPE Lobar

- La fisura interhemisférica esta presente a lo largo de casi toda la línea media, excepto la parte mas inferior de los lóbulos frontales.
- La rodilla del cuerpo calloso es levemente hipoplasica o displasica.
- Fornix fusionado.
- Septum pellucidum ausente.
- Astas anteriores rudimentarias.

Variante interhemisférica media

- 2-15% de los casos. Subtipo leve.
- La parte posterior de los lóbulos frontales y los lóbulos parietales fallan en dividirse.
- Núcleo caudado y talamos están incompletamente separados.
- Esplenio y rodilla del cuerpo calloso están presentes pero el cuerpo está ausente.
- Cisura de Silvio orientada verticalmente y conectada por la línea media.

Variante Septo preoptica

- Forma leve de HPE.
- La no-separación esta restringida sólo a la corteza subcallosa y/o la región preoptica.
- El rostrum del cuerpo calloso puede estar ausente o hipoplasico. El cuerpo y el esplenio están presentes pero pueden estar engrosados y mas cortos.
- Tálamo e hipotálamo pueden aparecer fusionados.
- Anomalias craneofaciales leves.

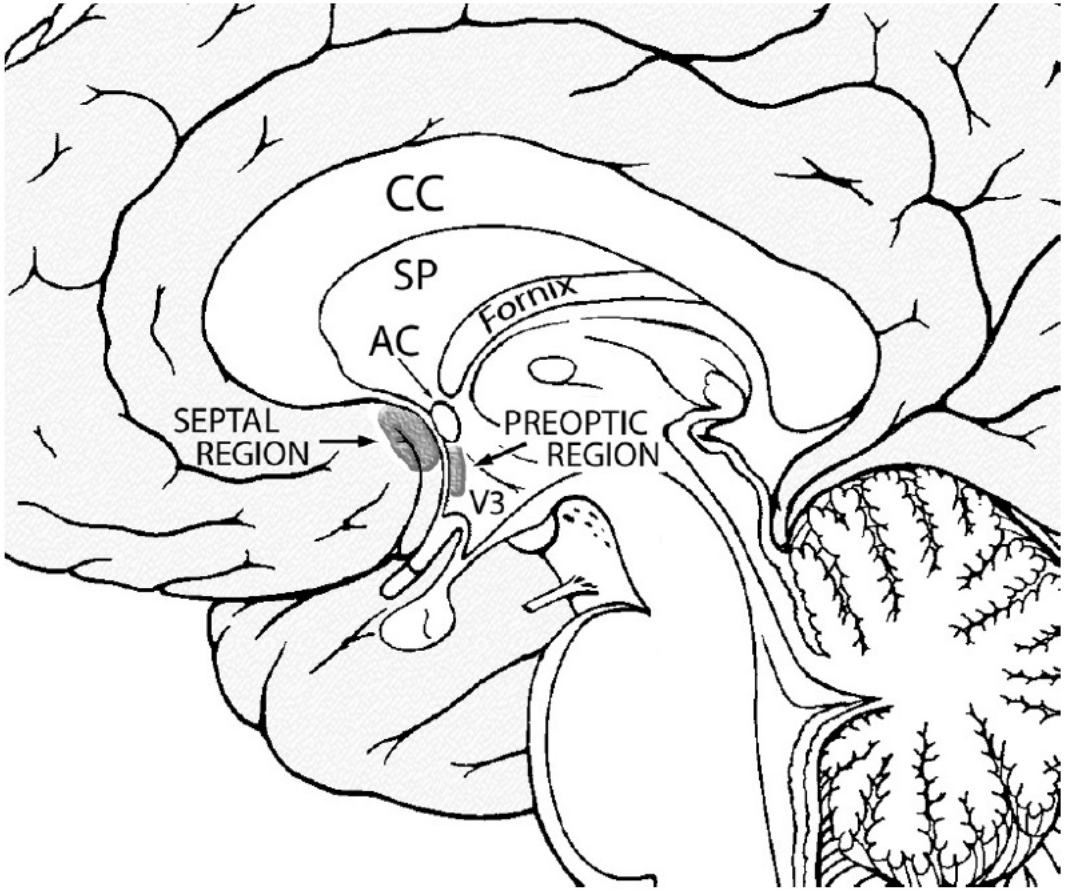


Fig 1. Diagram of the midsagittal view of the brain displaying the locations of the septal and preoptic regions. Modified from Martin J.[22]

PRENATAL DIAGNOSIS
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REVIEW

Disorders of prosencephalic development

P. Volpe*, G. Campobasso, V. De Robertis and G. Rembouskos
Fetal Medicine Unit, Di Venere and Sarcone Hospitals, Bari, Italy

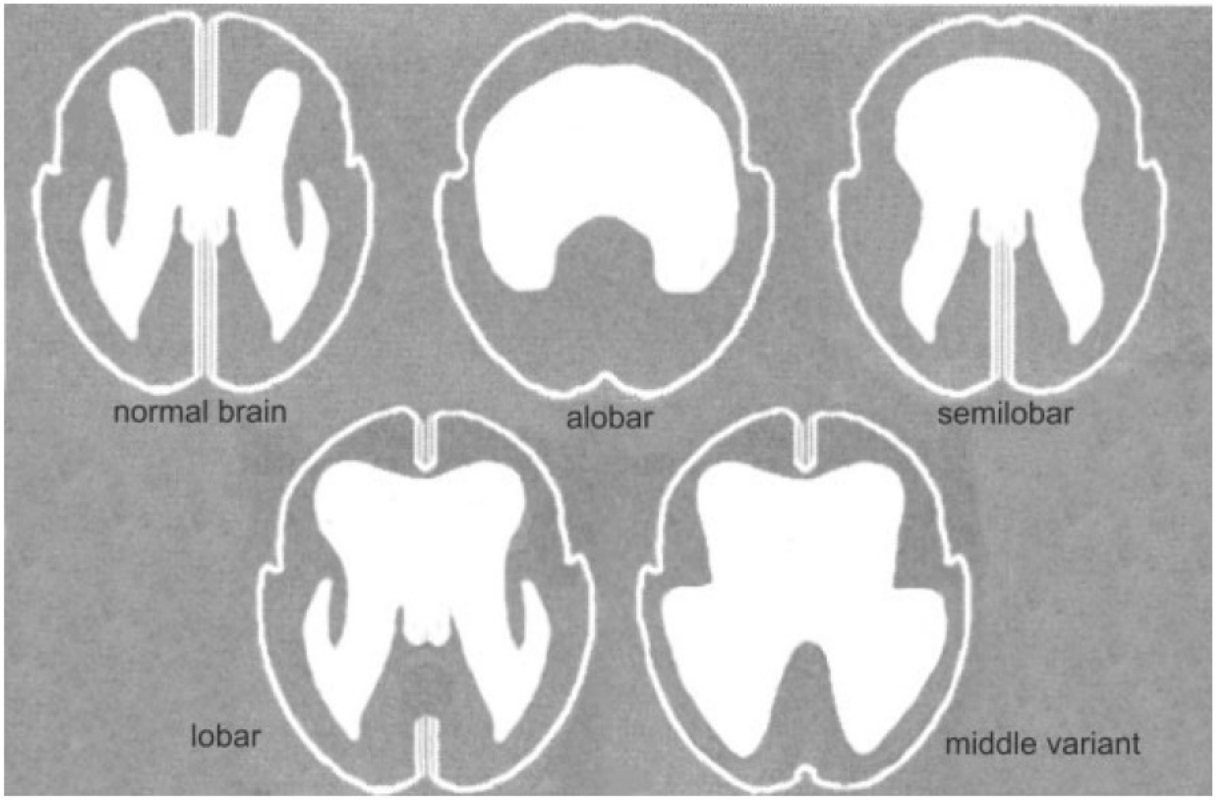

Figure 11—Variants of holoprosencephaly (HPE), compared with the normal brain

TABLE 1 Summary of HPE loci and their associated genes

MIM #	Chromosomal region	Gene	Replication status	Current status	Comment
236100	Chr21q22.3 (*HPE1*)	Unknown	N/A	N/A	Not *LSS*, not *SIM1*
157170	Chr2p21 (*HPE2*)	*SIX3*	Yes	Active (major gene)	Either de novo, or preferentially transmitted
142945	Chr7q36.3 (*HPE3*)	*SHH*	Yes	Active (major gene)	Either de novo, or preferentially transmitted
142946	Chr18p11.31 (*HPE4*)	*TGIF1*	Yes	Active (minor gene)	Either de novo, or preferentially transmitted
609637	Chr13q32.3 (*HPE5*)	*ZIC2*	Yes	Active (major gene)	Either de novo, or preferentially transmitted
605934	Chr2q37.1-q37.3 deletion syndrome	Unknown	N/A	N/A	N/A
610828	Chr9q22.3 (*HPE7*)	*PTCH1*	No	Likely modifier	Similar transmitted vs. nontransmitted
610829	Chr2q14.2 (*HPE9*)	*GLI2*	Yes	Syndromic HPE	Culler–Jones syndrome
615465	Chr8p11.23	*FGFR1 (FGF8)*	Yes	Syndromic HPE	Hartsfield syndrome
612702	Chr10q24.32	*FGF8*	Yes	Syndromic IHH; HPE	Kallmann syndrome
612530	Chr1q42 deletion syndrome *(HPE10)*	*DISP1*	Yes	Likely modifier	Similar transmitted vs. nontransmitted
608707	Chr11q24.2 (*HPE11*)	*CDON*	Yes	Active (minor gene)	Rare, preferentially transmitted
608708	Chr3	*BOC*	N/A	Likely modifier	Similar transmitted vs. nontransmitted
606582	Chr6q27	*DLL1*	No	Rare potential driver	Rare. Similar transmitted vs. nontransmitted
181590	Chr1p33	*STIL*	No	Rare autosomal recessive primary microcephaly 7	Very rare. Seen in consanguineous families

American Journal of Medical Genetics Part C (Seminars in Medical Genetics) 154C:133–141 (2010)

ARTICLE

Analysis of Genotype–Phenotype Correlations in Human Holoprosencephaly

BENJAMIN D. SOLOMON, SANDRA MERCIER, JORGE I. VÉLEZ, DANIEL E. PINEDA-ALVAREZ, ADRIAN WYLLIE, NAN ZHOU, CHRISTÈLE DUBOURG, VERONIQUE DAVID, SYLVIE ODENT, ERICH ROESSLER, AND MAXIMILIAN MUENKE*

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TABLE I. All Individuals With Identified Mutations in the Four Most Common HPE-Associated Genes in Whom the HPE Type (or Lack Thereof) is Known

	Brain anomalies				No structural brain anomalies		
HPE gene	A	S	L	M	Mic	Phenotypically normal[a]	Total
SHH	19	21	7	0	45	11	103
ZIC2	29	44	11	4	6	7	101
SIX3	27	22	9	1	13	20	92
TGIF	3	4	4	0	8	6	25
Total	78	91	31	5	72	44	321

A, alobar; S, semilobar; L, lobar; M, MIHV; Mic, microform.

Individuals presented in this table include 180 propositi and 141 relatives; note that full trio analysis was not available for all propositi. Individuals in whom clinical descriptions did not include HPE type or clinical characterization were not included in the analysis.

[a]Individuals are described as phenotypically normal here when no microform features are reported and in whom there was no clinical indication for neuroimaging. All phenotypically normal individuals were relatives of propositi (the vast majority of which were parents of severely affected patients).

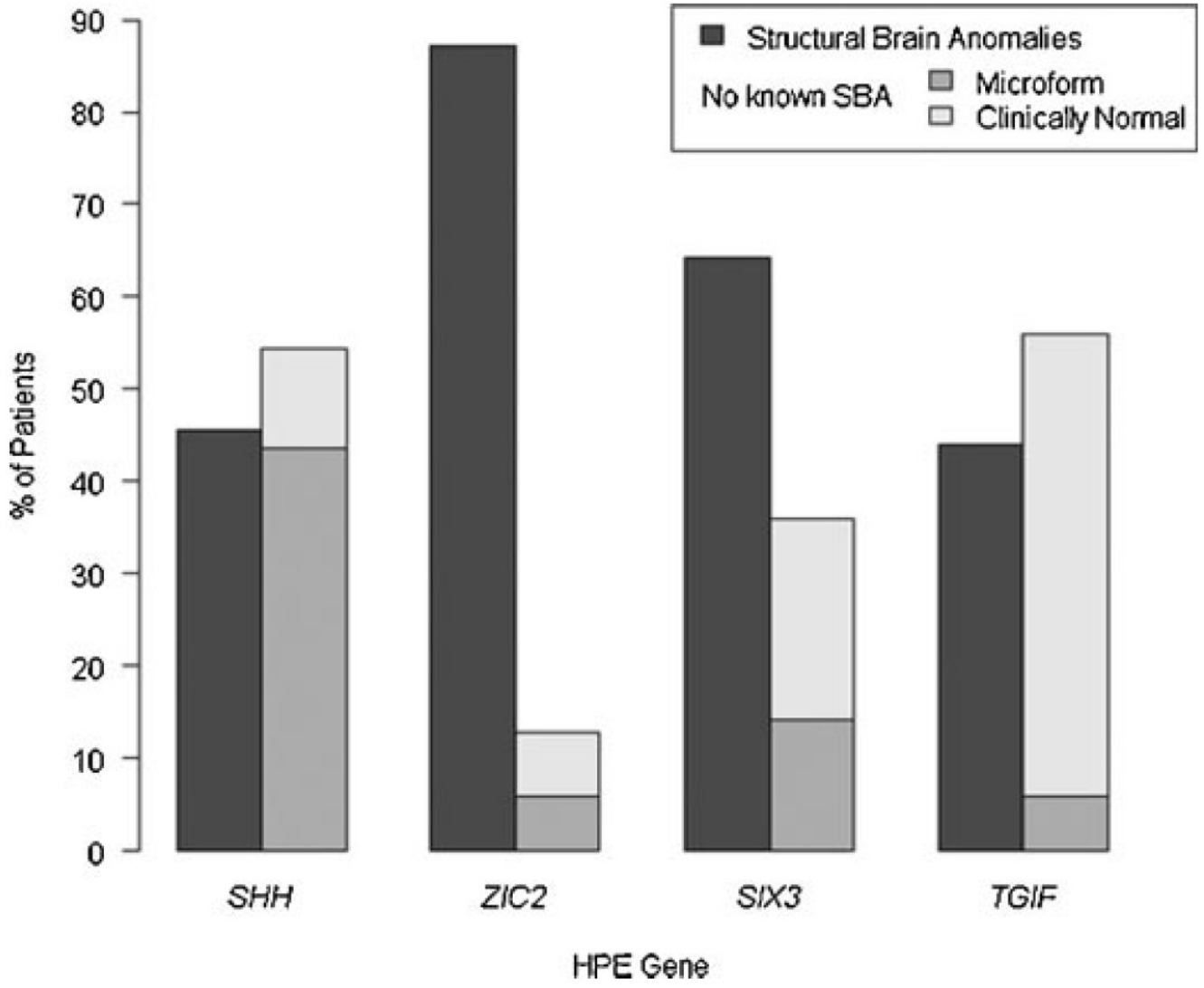

Figure 2. Proportion of HPE cases among all patients with mutations in the four classic HPE genes by the presence (dark bars) or absence of structural brain anomalies (SBA). Note the non-SBA group consists of individuals with mutations and either microform findings (gray bars) or who were apparently normal by standard clinical criteria yet also mutation positive (light bars). Note that the authors suspect that many individuals described as being clinically unaffected may have unappreciated microform features.

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Table 7—Genetic syndromes associated with HPE

Genetic syndrome		OMIM#	Locus	Gene	Other possile US features
Autosomal dominant	Dysgnathia complex	*%202 650*	*Unknown*		Mandibular hypoplasia or agenesis, skeletal and genitourinary, CHD, situs inversus, polyhydramnios
	Kallman s.	*#147 950*	*8p11.2-p11.1*	*PROKR2*	Midline facial cleft
	Pallister-Hall s.	*#146 510*	*7p13*	*GLI3*	Micrognathia, absent lung, CHD, renal abnormalities, and atresia, anomalies of the digits, mild IUGR
	Rubinstein-Taybi s.	*#180 849*	*16p13.3*	*REBBP*	CHD, spina bifida, 5h finger clinodactyly, overlapping toes, polihydramnios
	Steinfeld s.	*184 705*	*Unknown*		Radial/ulnar hypoplasia, absent thumbs, midline cleft lip and palate, CHD, renal abnormalities, absent gallbladder
	Thanatophoric dysplasia type II	*#187 601*		*FGFR3*	Straight and relatively normal femours but severe cloverleaf scull
Autosomal recessive	Spinocerebellar ataxia (Van Bogaert-Martin s.)	*%271 250*	*6p23-p21*		Commonly no prenatal US findings
	Ivemark s. (Heterotaxy and HPE)	*%208 530*	*Unknown*		Asplenia/polysplenia, situs ambiguus CHD,
	Hydrolethalus s.	*#236 680*	*11q24.2*	HYLS1	Hydrocephalus, abnormal gyrations, facial cleft, micrognathia, micropthalma, CHD, polydactyly, club foot, polyhydramnios
	Lambotte s.	*245 552*			Microcephaly, IUGR
	Meckel-Gruber s. type 1	*#249 000*	*17q22-q23*		Occipital cephalocele, cystic kidneys, polydactyly, oligohydramnios
	Pseudotrisomy 13 s.				Severe facial anomalies, postaxial polydactyly,
	Smith-Lemli-Opitz s.	*#270 400*	*11q12-q13*		Microcephaly, syndactyly, genital abnormalities, facial cleft
	XK aprosencephaly s.	*264 480*			Severe facial anomalies, postaxial polydactyly, CHD
X-linked	Aicardi s. (D)	*%304 050*	*Xp22*		Micro-ophtalmia, CPCs, CPP, D-W m, facial cleft
	Ectrodactyly (R)	*300 571*	*Unknown*		Ectrodactyly, facial cleft, hypertelorism, craniosynostosis, radial agenesis
	Fetal hypokinesia/akinesia (R)	*306 990*	*Unknown*		Microcephaly, IUGR

D/R, dominant/recessive; poly, polygenic pattern of inheritance; CPC, chorioid plexus cyst; CPP, chorioid plexus papilloma; D-W m, Dandy-Walker malformation.

Prenatal ultrasound findings of holoprosencephaly spectrum: Unusual associations

Sara H. El-Dessouky[1] | Mona M. Aboulghar[2] | Hassan M. Gaafar[2] | Rana M. Abdella[2] | Marwa F. Sharaf[2] | Mohamed I. Ateya[2] | Ahmed Ezz Elarab[2] | Walaa H. Zidan[2] | Rania M. Helal[2] | Samah M. Aboelsaud[2] | Maha M. Eid[3] | Ghada M.H. Abdel-Salam[4]

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TABLE 4 Brain ultrasound findings encountered for each subtype of HPE

	Alobar HPE	Semilobar HPE	Lobar HPE
Number of cases	17	7	1
Cortical hemispheres fusion	Complete fusion	No anterior separation but some posterior separation	No separation of the most ventral frontal cortex
Interhemispheric fissure	Absent	Present only posteriorly	Hypoplastic anteriorly and present posteriorly
Corpus callosum	Absent	Absent	Thin and hypoplastic
Cavum septum pellucidum	Absent	Absent	Absent
Lateral ventricles	Single midline monoventricle	Absent anterior horns of lateral ventricles	Partially fused anterior horns of lateral ventricles
Third ventricle	Absent	Absent	Present
Dorsal cyst	Present (three cases)	Present (one case)	Absent
Thalamus	Often fused	Partial fusion	Usually fully separated

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The wide spectrum of ultrasound diagnosis of holoprosencephaly

Cringu Antoniu Ionescu[1], Simona Vladareanu[2], Stefania Tudorache[3], Liana Ples[4], Catalin Gabriel Herghelegiu[5], Adrian Neacsu[4], Dan Navolan[6], Ioana Dragan[5], Daniela-Nuti Oprescu[5]

Table II. Brain ultrasound characteristics encountered for each subtype of HPE

	Alobar (n=6)	**Semilobar (n=3)**	**Lobar (n=7)**	**MIH (n=2)**
Cortical hemispheres fusion	complete	anterior half	basal frontal	posterior frontal and parietal
Interhemispheric fissure and falx cerebri	absent	present posteriorly only	hypoplastic anteriorly and present posteriorly	present in the anterior and posterior poles
Corpus callosum	absent	absent or thin and hypo-plastic	thin and hypoplastic	absent or thin and hypoplastic
Cavum septum pelu-cidum	absent	absent	absent or dysplastic	absent or dysplastic
Lateral ventricles	monoventricle	fusion of the anterior half of the lateral ventricles	hypoplastic and partially fused frontal horns	fused at their middle portion (body)
Third ventricle	absent	absent	visible	visible
Dorsal cyst	present (n=2)	absent	absent	absent
Deep grey nuclei	often completely fussed	incompletely separated	partially fused	normal
Doppler findings	-	-	"rete of vessels" branching from the internal carotids (n=1)	-
Head circumference	macrocephaly (n=1)	microcephaly (n=1)	no	no

n – number of cases

TABLE I. Neuroimaging Features of Various Types of HPE

	Alobar	Semilobar	Lobar	MIH
Cortical nonseparation	Diffuse (holosphere)	Frontal	Basal frontal	Posterior frontal and parietal
Corpus callosum	Absent	Rostrum, genu, and body absent. Splenium present	Rostrum and genu absent. Anterior body variably present. Splenium present	Body absent; genu variably present. Splenium present
IHF and Falx	Completely absent anteriorly and posteriorly	Present posteriorly only	Hypoplastic anteriorly and present posteriorly	Absent in the posterior frontal and parietal region
Ventricles	Monoventricle communicating widely with dorsal cyst	Anterior horns absent. Posterior horns present. Small third ventricle	Rudimentary anterior horns. Third ventricle formed	Normal or hypoplastic anterior horns. Third ventricle formed
Dorsal cyst	Usually present	Variably present	Absent	Present in 1/4
Septum pellucidum	Absent	Absent	Absent or dysplastic	Absent
Thalamus	Often fused	Partial fusion	Usually fully separated	Fused in 1/3 to 1/2
Basal ganglia	Often fused (may form single mass with thalami)	Partial fusion (especially head of caudate)	Variable degree of fusion	Separated
Hypothalamus	Always fused to some degree (100%)	Very often fused to some degree (98%)	Often fused to some degree (83%)	Separated
Sylvian fissure	Often absent	Anteriorly and medially displaced (wide sylvian fissure) with fused frontal lobe	Anteriorly and medially displaced (wide sylvian fissure) with small frontal lobes	Often abnormally connected across the midline over the vertex
Cortical dysplasia and heterotopic gray matter	Frequent presence of diffuse broad gyri with too few sulci	Occasional broad gyri with too few sulci	Rare midline subcortical heterotopias in frontal regions	Very common
Cerebral vasculature	Rete of vessels branching from the internal cerebral arteries	Azygous anterior cerebral artery	Azygous anterior cerebral artery	Azygous anterior cerebral artery

Table 1
Radiologic findings and correlated facial dysmorphisms for the four types of HPE

Type of HPE	Imaging Findings	Facial Dysmorphism
Alobar	Small monoventricle No interhemispheric division Absence of olfactory bulbs and tracts Absence of corpus callosum Fusion of deep gray nuclei	Cyclopia without proboscis Ethmocephaly Cebocephaly Closely spaced eyes Anophthalmia or microphthalmia Premaxillary agenesis with median cleft lip, closely spaced eyes, depressed nasal ridge Bilateral cleft lip Relatively normal facial appearance (especially in persons with pathogenic variants in *ZIC2*)
Semilobar	Rudimentary cerebral lobes Partially developed occipital and temporal horns Incomplete interhemispheric division (only posteriorly) Absence or hypoplasia of olfactory bulbs and tracts Absence of corpus callosum Varying nonseparation of deep gray nuclei (fusion of the thalami)	Closely spaced eyes Anophthalmia/microphthalmia Depressed nasal bridge Absent nasal septum Flat nasal tip Bilateral cleft lip with median process representing the philtrum-premaxilla anlage Midline cleft (lip and/or palate) Relatively normal facial appearance
Lobar	Fully developed cerebral lobes Distinct interhemispheric division Midline continuous frontal neocortex Callosal genu and splenium hypoplastic Fused fornix Septum pellucidum possibly absent	Bilateral cleft lip with median process Closely spaced eyes Depressed nasal ridge Relatively normal facial appearance
MIH	Failure of separation of the posterior frontal and parietal lobes Callosal genu and splenium normally formed Absence of corpus callosum Hypothalamus and lentiform nuclei normally separated Caudate nuclei and thalami partially fused Heterotopic gray matter Cerebellar anomalies	Closely spaced eyes Depressed nasal bridge Narrow nasal bridge Relatively normal facial appearance

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ORIGINAL ARTICLE

First trimester screening for holoprosencephaly with choroid plexus morphology ('butterfly' sign) and biparietal diameter

Waldo Sepulveda* and Amy E. Wong

Fetal Medicine Center, Department of Obstetrics and Gynecology, Clinica Las Condes, Santiago, Chile
*Correspondence to: Waldo Sepulveda. E-mail: fetalmed@yahoo.com

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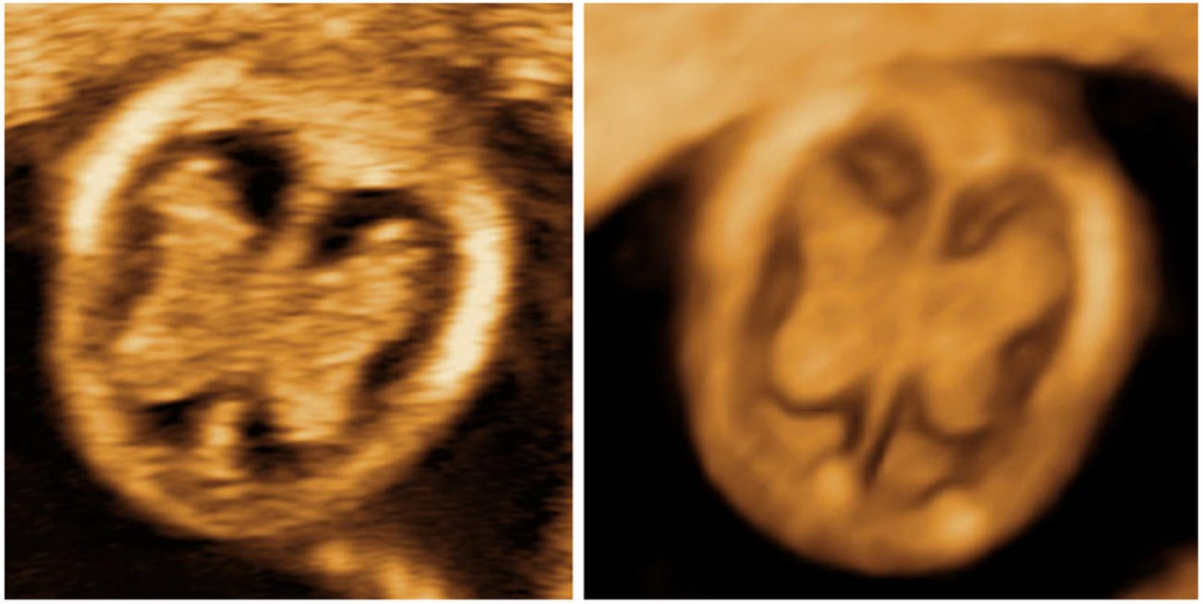


Figure 1 First trimester two-dimensional (left) and three-dimensional (right) sonograms display the axial view of the fetal head at the level of the choroid plexuses and show the 'butterfly' sign

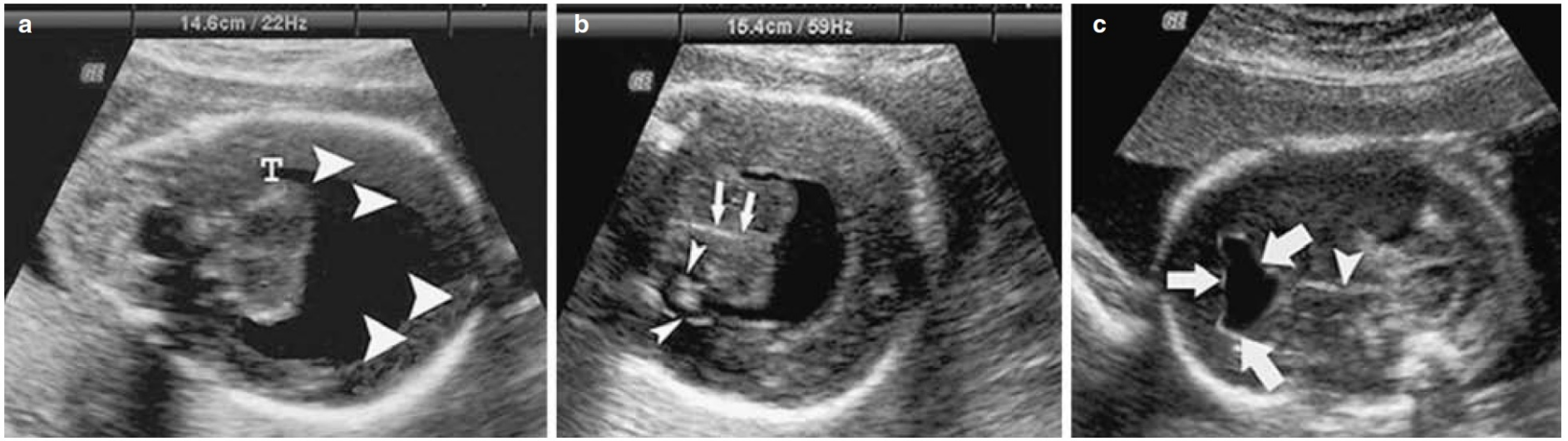
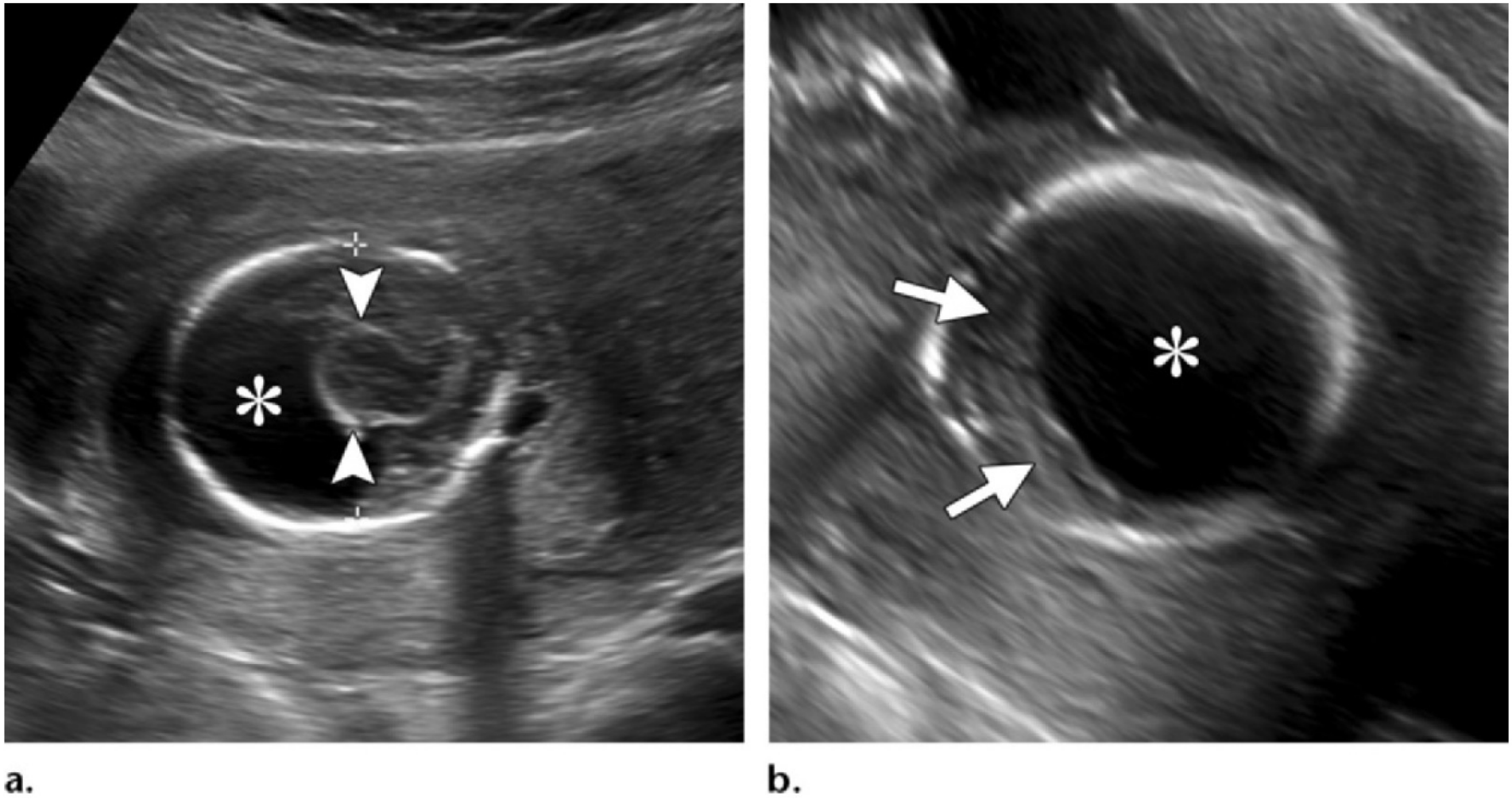


Figure 2.16 (a) Alobar holoprosencephaly: axial scan at the level of the thalami showing the single ventricle, absence of midline structures, and fused thalamus (T); the arrowheads indicate the rim of the cortex. (b) Semilobar holoprosencephaly: ultrasound image showing the two cerebral hemispheres partially separated posteriorly; the rudimentary lateral ventricles with sketchy posterior horns (arrowheads) and a more developed cortex are present. (c) Lobar holoprosencephaly: axial scan showing the brain almost completely divided into two distinct hemispheres, with the only exception being at the level of the frontal horns of the lateral ventricles (arrows); the interhemispheric fissure is evident (arrowhead).



a. b.

Figure 7. Alobar HPE. **(a)** Axial oblique US image obtained at 18 weeks shows fused thalami (arrowheads) and a monoventricle (*). **(b)** Axial oblique US scan obtained at a higher level shows the cuplike morphology of the noncleaved hemispheres (arrows) "cupping" the monoventricle (*).

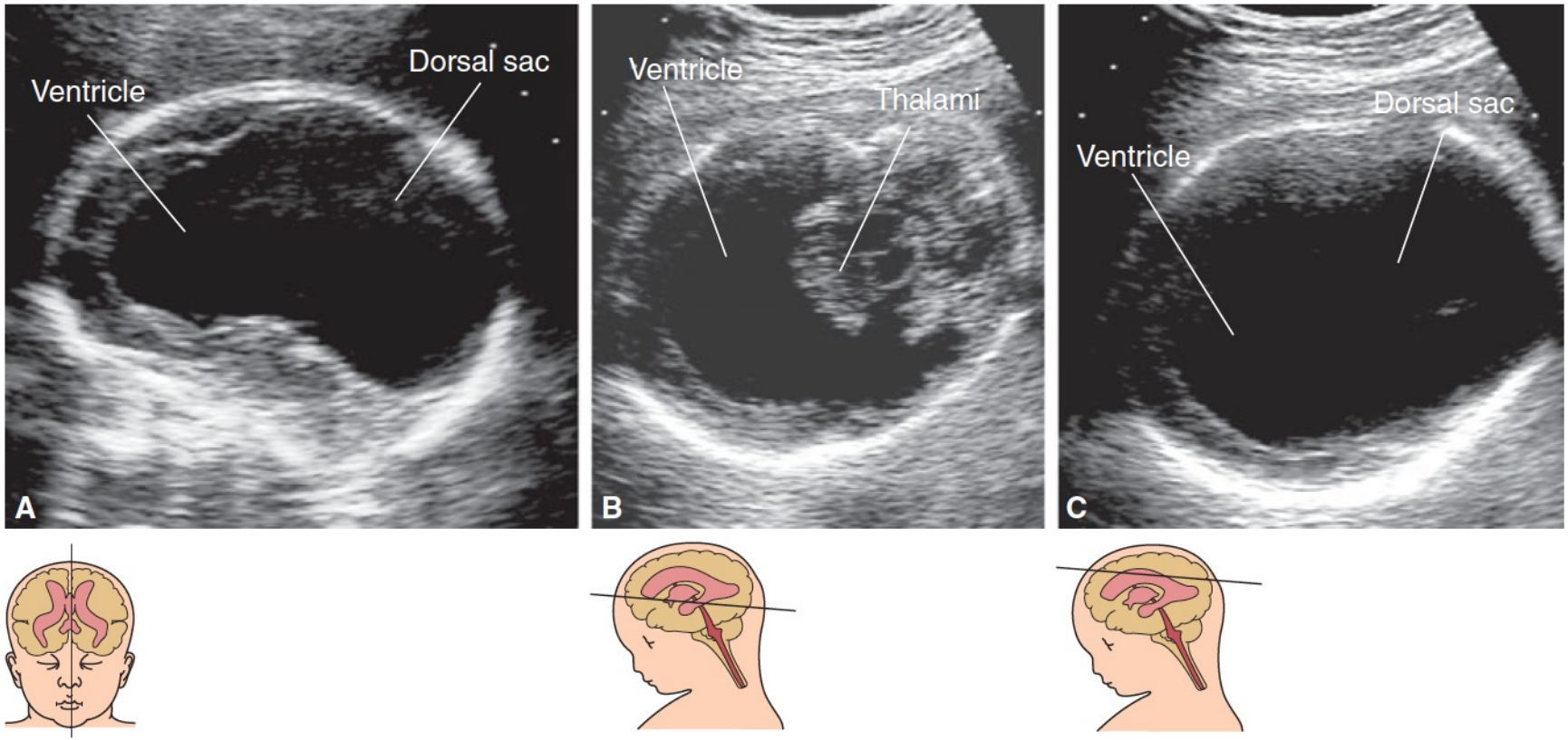


Figure 6–3. Multiplanar sonography of alobar holoprosencephaly in the midtrimester. (**A**) Median plane demonstrating the single ventricular cavity, which has a rim of cortex anteriorly and amply communicates posteriorly with a dorsal sac. (**B**) Axial scan at the level of the thalamus, demonstrating the crescent-shaped single ventricle and the absence of the midline in the anterior cortex. (**C**) In a slightly craniad axial plane than the previous one, the communication between the ventricular cavity and the dorsal sac is demonstrated. (Reproduced, with permission, from the *Visual Encyclopedia of Ultrasound in Obstetrics and Gynecology,* International Society of Ultrasound in Obstetrics and Gynecology, 2010, www.isuog.org.)

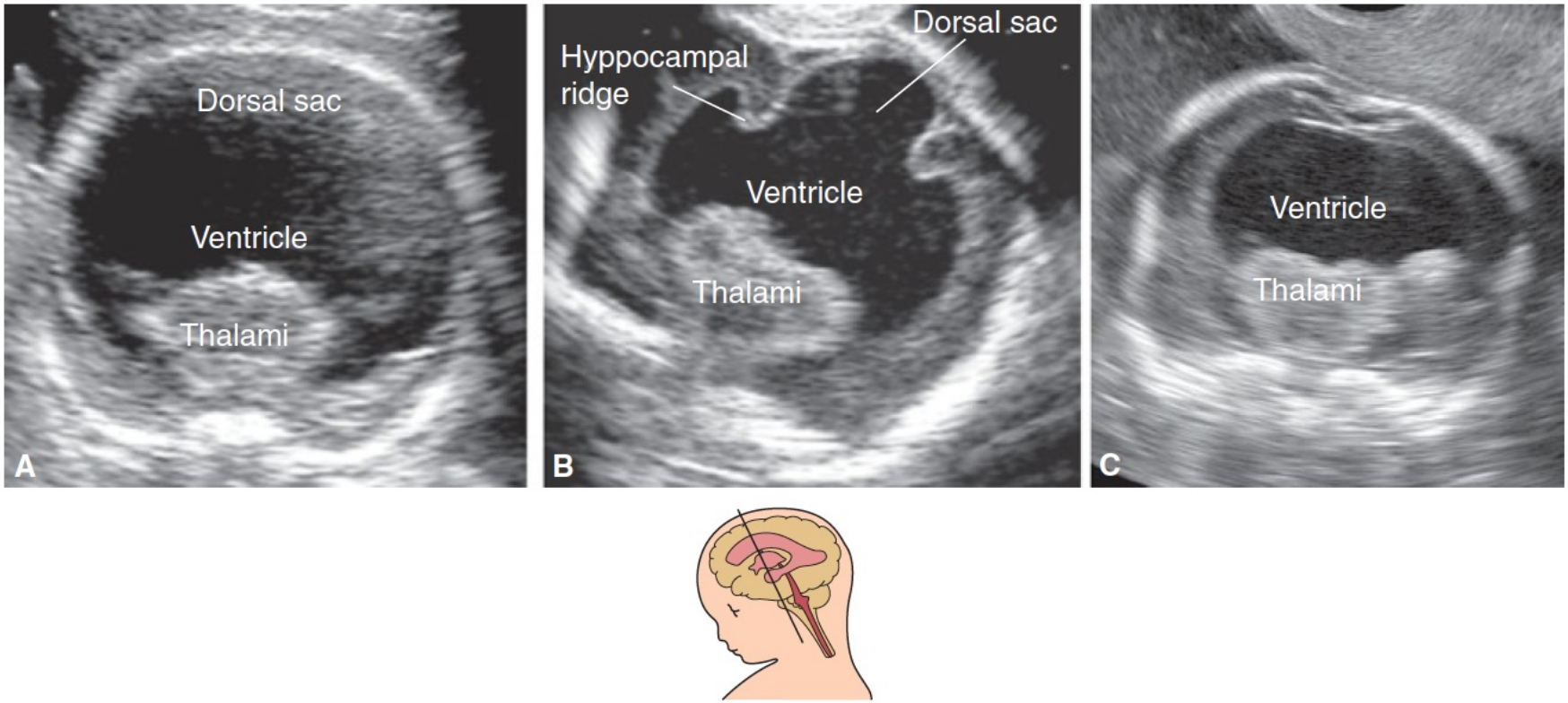


Figure 6–4. In alobal holoprosencephaly, a dorsal sac is frequently seen on top of the ventricular cavity; the degree of development of the cortex is variable. (**A**) In some cases, it forms a thin rim at the base of the ventricles (pancake). (**B**) In other cases, it is partially enfolded on top of the ventricular cavity. (**C**) In still other cases, the ventricle is completely covered, and there is no dorsal sac; frequently, these cases are pathologically diagnosed as belonging to the semilobar variety. (Reproduced, with permission, from the *Visual Encyclopedia of Ultrasound in Obstetrics and Gynecology,* International Society of Ultrasound in Obstetrics and Gynecology, 2010, www.isuog.org.)

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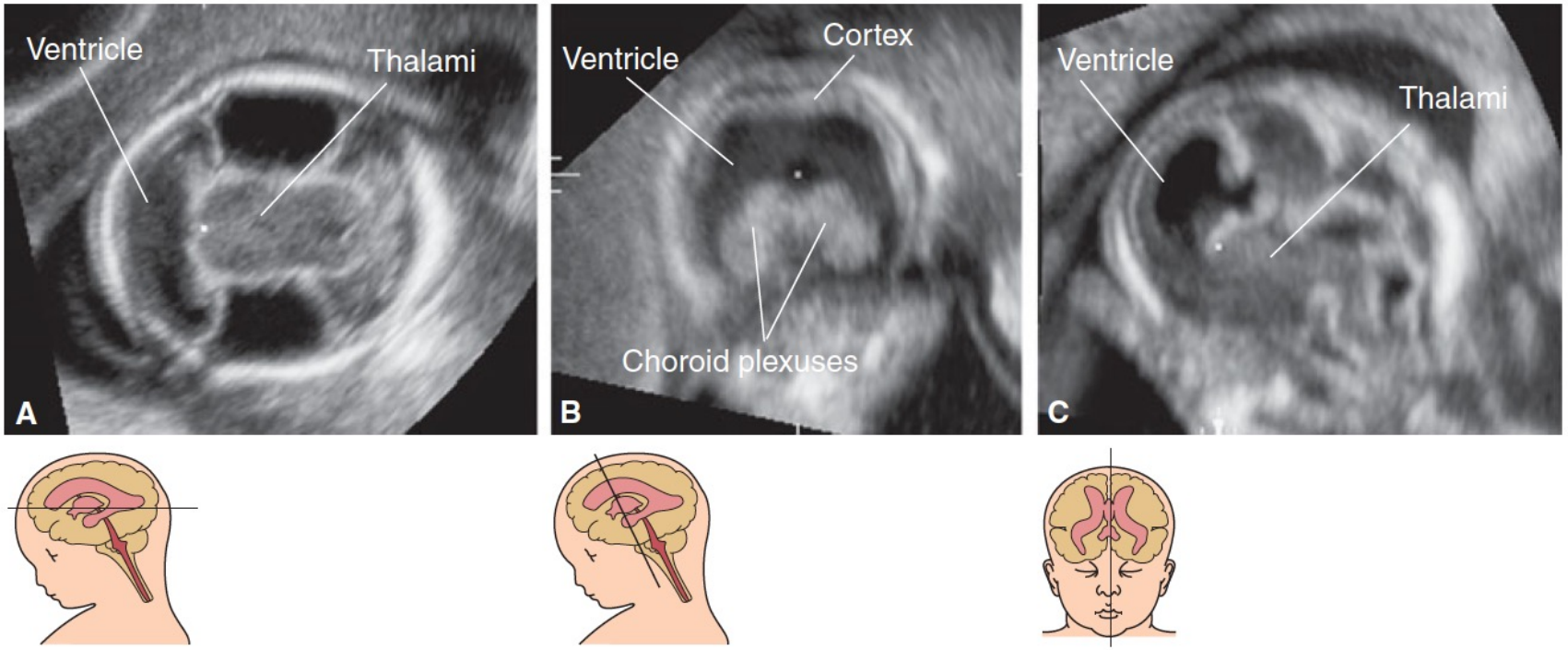
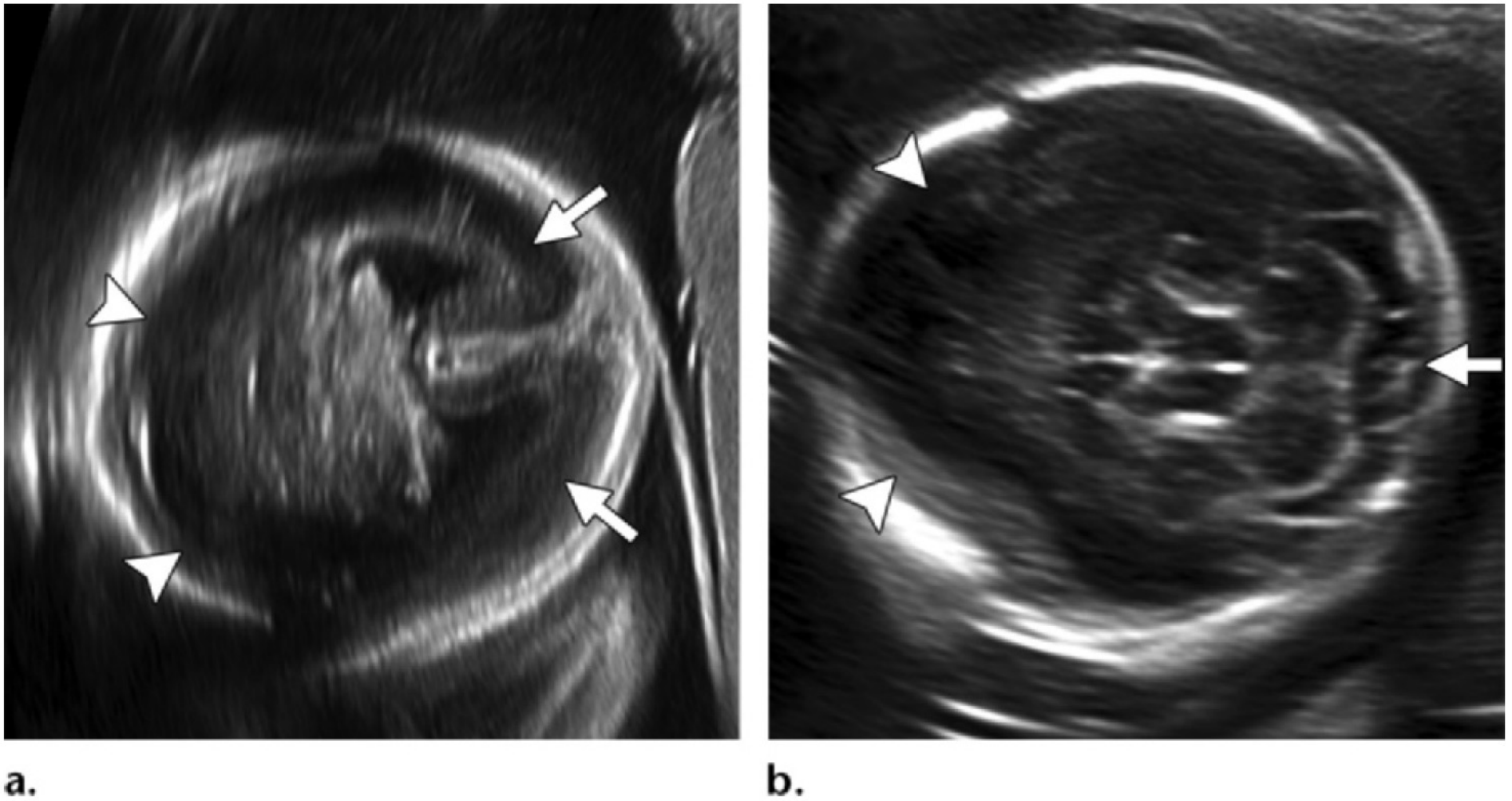
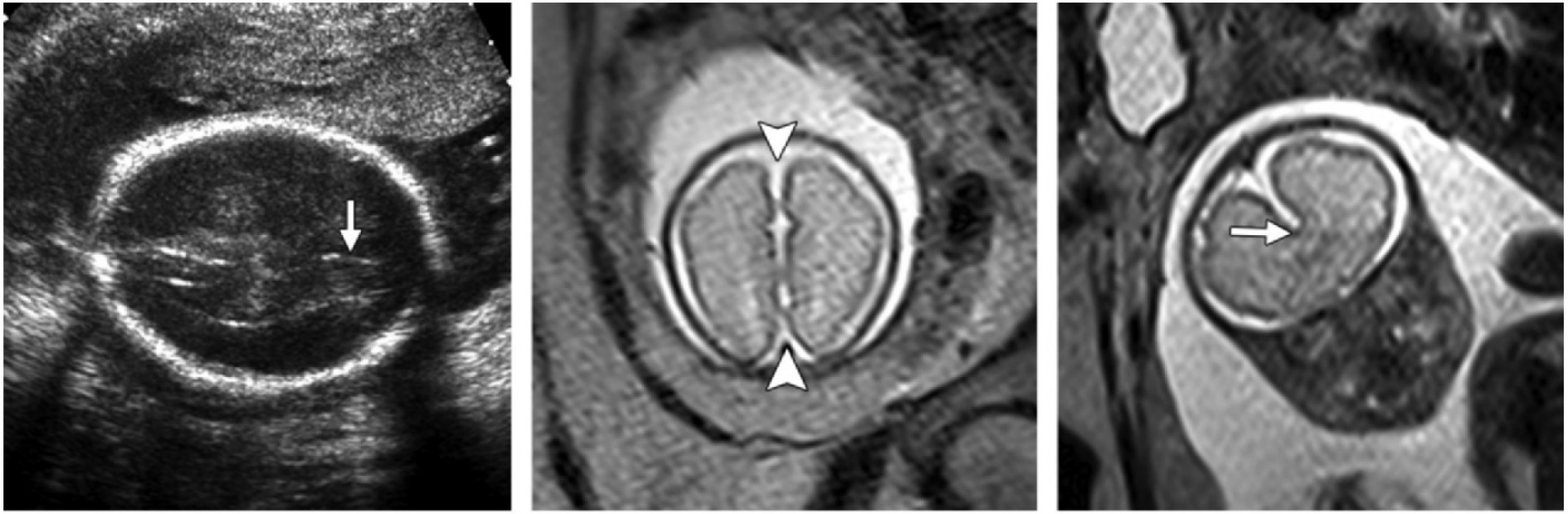


Figure 6–5. Alobar holoprosencephaly in a fetus at 13 postmenstrual weeks. The most striking findings, the absence of the midline echo and the presence of a single rudimentary ventricular cavity, are well demonstrated in a vaginal scan. (Reproduced, with permission, from Tutschek B, PiluG. Virtual reality ultrasound imaging of the normal and abnormal fetal central nervous system. *Ultrasound Obstet Gynecol.* 2009;34(3):259–267.)



a. b.

Figure 14. Semilobar HPE. **(a)** Axial oblique US image shows a continuous mantle of brain anteriorly (arrowheads) but posterior division into hemispheres (arrows). **(b)** More inferior axial US image in the same patient shows normal posterior fossa structures (arrow) below the tentorium but fused anterior supratentorial brain (arrowheads).



a. b. c.

Figure 18. Lobar HPE. **(a)** Axial US image shows a continuous midline echo anteriorly (arrow). We were not able to demonstrate the cavum septum pellucidum in any plane. **(b)** Axial fetal MR image shows apparent complete division of the cerebral hemispheres (arrowheads). **(c)** Coronal fetal MR image shows anterior inferior gyral continuity between the frontal lobes (arrow). This was not demonstrable at US; the index finding was inability to demonstrate a normal cavum septum pellucidum.

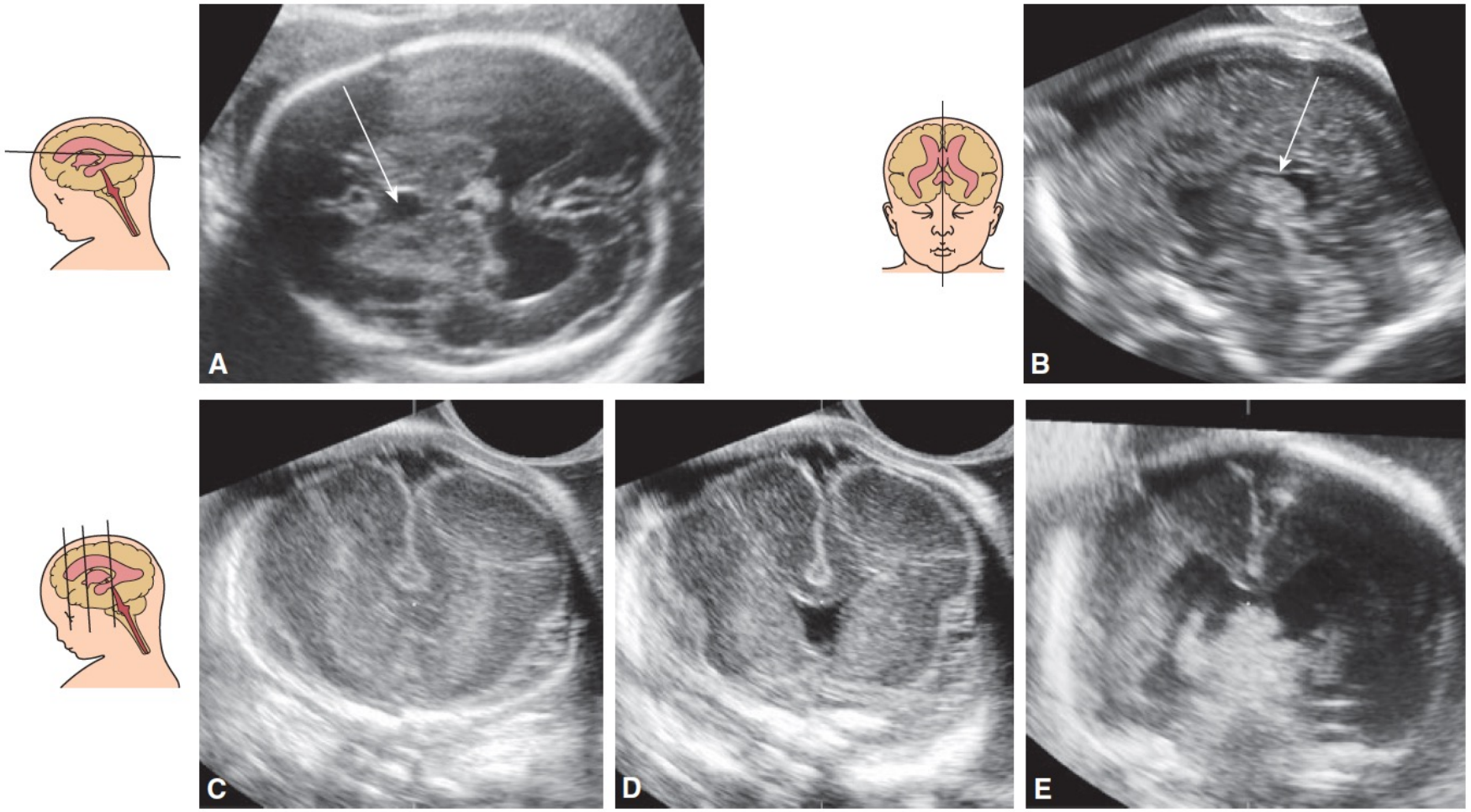


Figure 6–7. Lobar holoprosencephaly. (**A**) The cavum septi pellucidi is absent, and the lateral ventricles appear significantly dysmorphic and fused from the level of the frontal horns to the bodies. (**B**) In the sagittal plane, the corpus callosum is not clearly visible, and only an irregular ridge of tissue is seen bridging between the hemispheres posteriorly (*arrow*). (**C–E**) Coronal sections are most useful for the diagnosis in that they demonstrate inferior fusion of the frontal lobes, poorly developed fused frontal horns, and communication between the bodies of the lateral ventricles. (Reproduced, with permission, from the *Visual Encyclopedia of Ultrasound in Obstetrics and Gynecology,* International Society of Ultrasound in Obstetrics and Gynecology, 2010, www.isuog.org.)

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REVIEW

Disorders of prosencephalic development

P. Volpe*, G. Campobasso, V. De Robertis and G. Rembouskos
Fetal Medicine Unit, Di Venere and Sarcone Hospitals, Bari, Italy

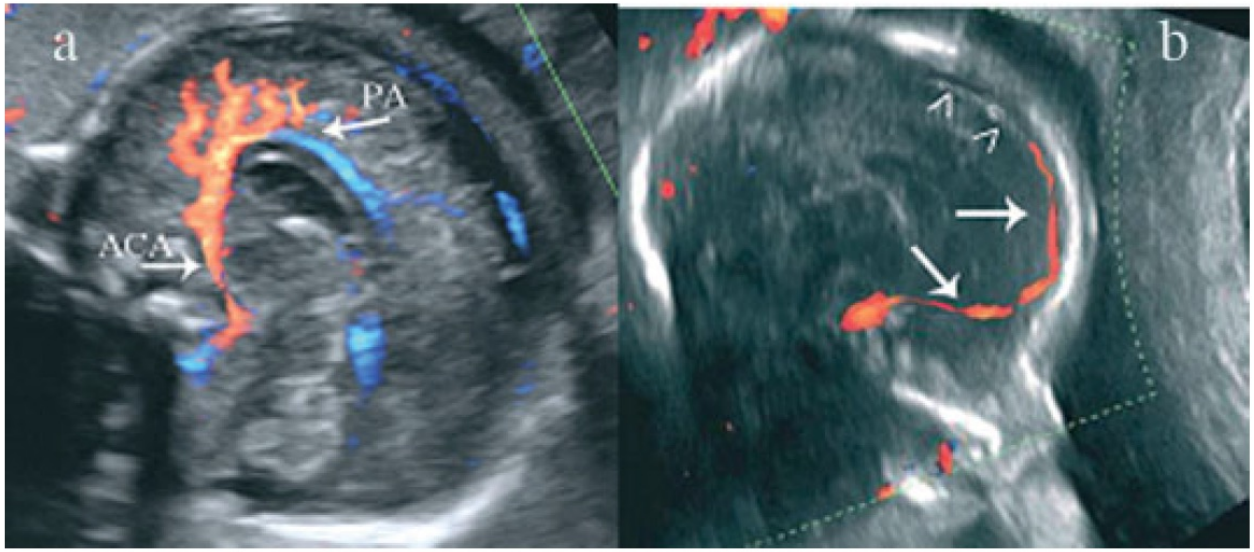


Figure 13—(a) Color Doppler demonstration of anterior cerebral artery (ACA) branching in a 24-week normal fetus and giving rise to the pericallosal artery (PA). (b) Lobar holoprosencephaly in a 25-week fetus. The anterior cerebral artery branching (arrows) is pushed externally alongside the frontal bone (sign of a 'snake under the skull') by the abnormal bridge of cortical tissue between the two frontal gyri (arrowheads)

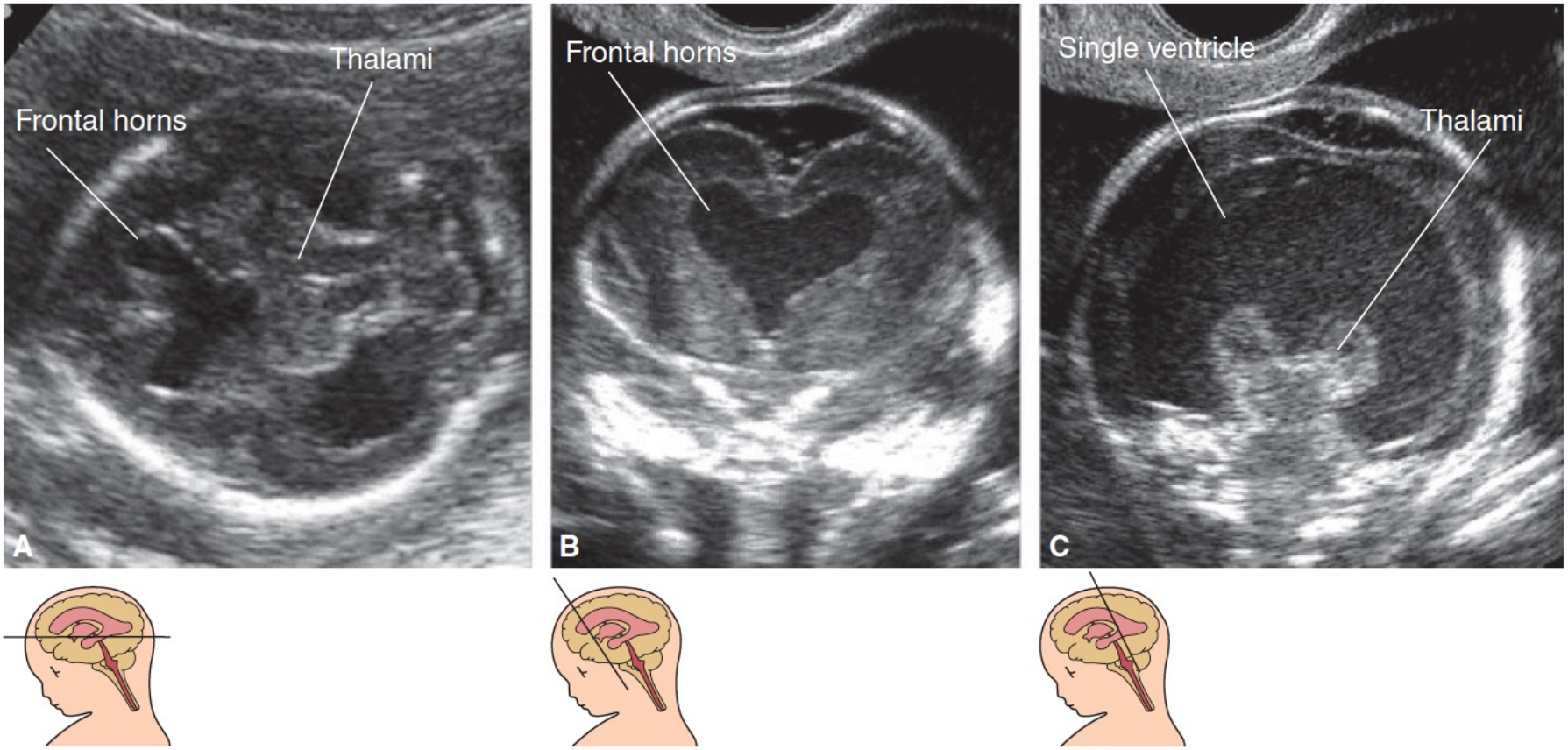


Figure 6–8. Middle interhemispheric variant of holoprosencephaly in the axial (**A**), anterior coronal (**B**), and midcoronal plane (**C**). The frontal horns are well developed, and there is a partial formation of the interhemispheric fissure. However, the midcoronal plane reveals a common ventricular cavity with hypoplastic undivided thalami.

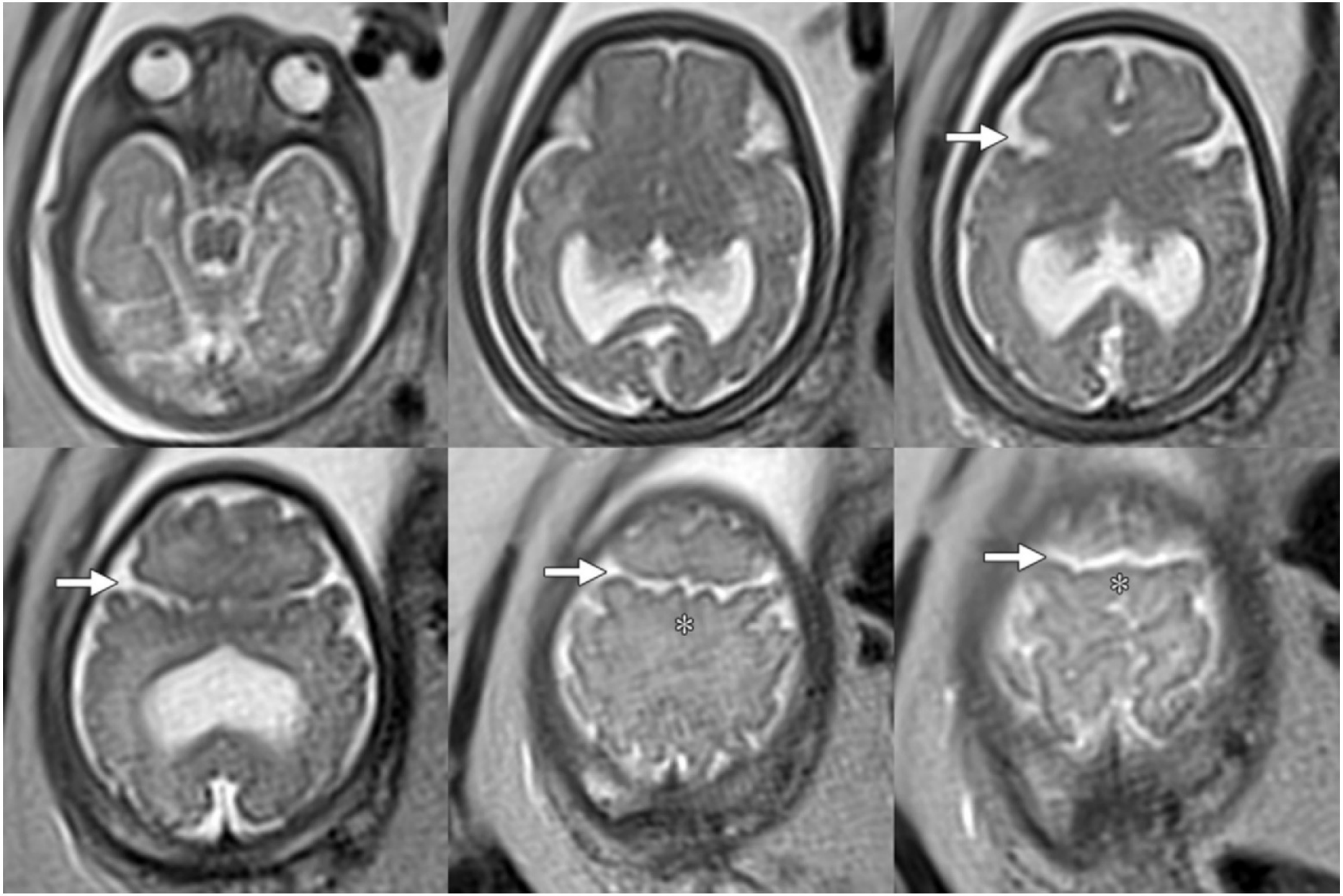
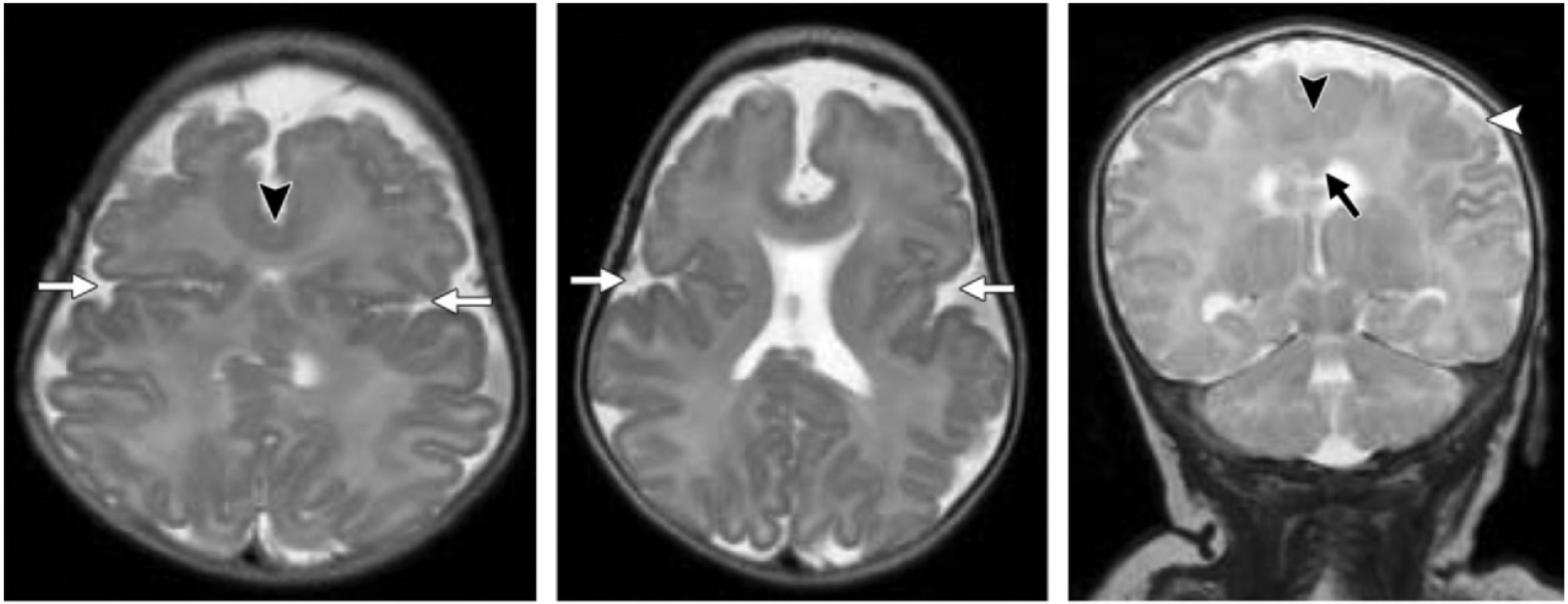


Figure 20. MIH. Axial T2-weighted half-Fourier RARE MR images obtained at 33 weeks estimated gestational age. Note the lack of midline separation in the posterior frontal and parietal areas (*), while rostral and posterior regions of the cerebrum are cleaved normally, and the orbits are spaced normally. Also, note the vertically oriented sylvian fissures (arrows), which abnormally connect across the vertex.



a. b. c.

Figure 21. MIH. Axial **(a, b)** and coronal **(c)** T2-weighted MR images in a neonate diagnosed prenatally with MIH show a lack of separation in the posterior frontal lobes (black arrowhead). Also note the abnormal appearance of the vertically oriented sylvian fissures (arrows in **a** and **b**), which extend more toward the midline than expected, and the cortical dysplasia (white arrowhead in **c**) and gray matter heterotopia (arrow in **c**).

Variante Septo preoptica

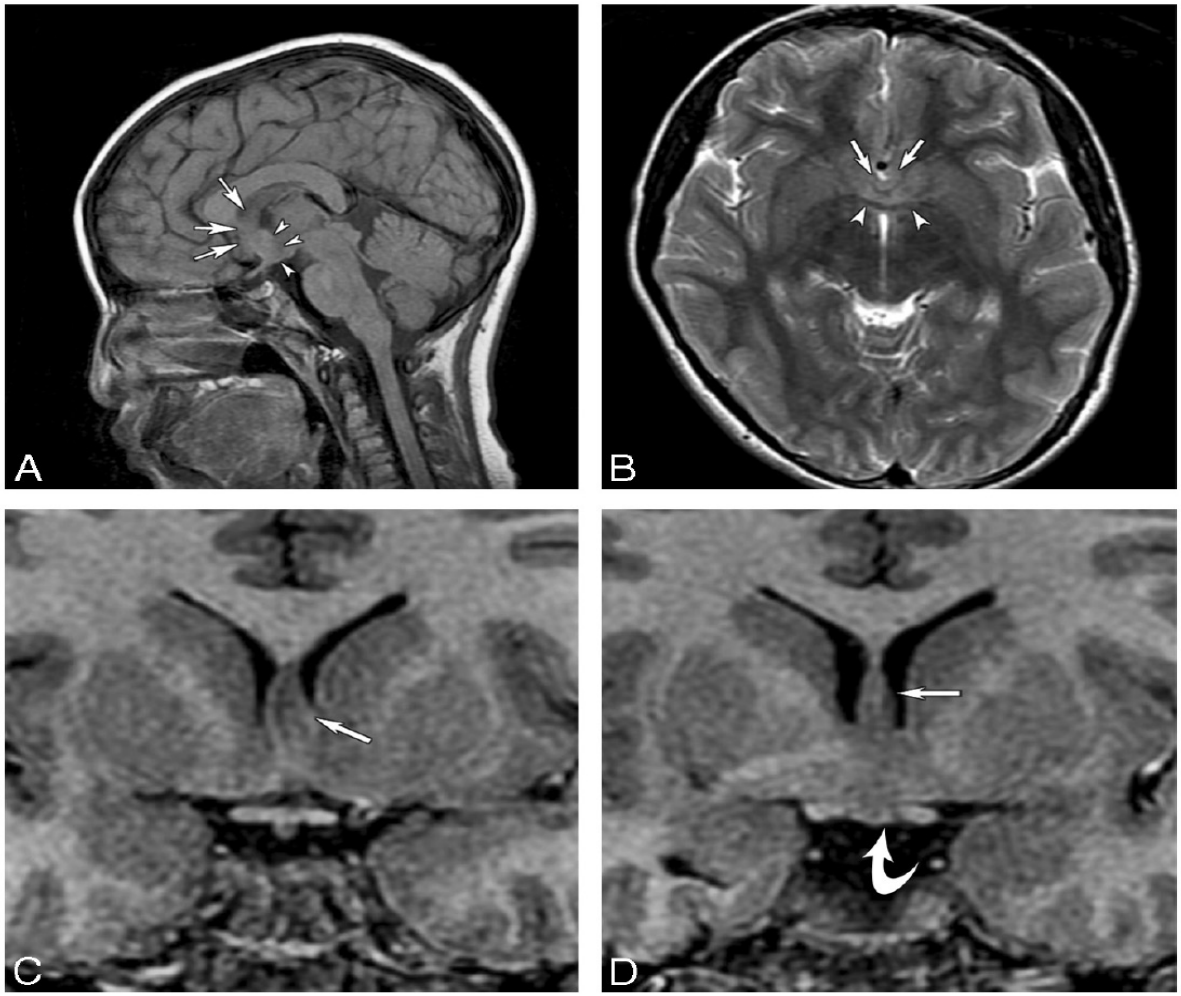


Fig 2. MR imaging of a 10-year-old boy with learning disabilities, a SMMCI, CNPAS, precocious puberty, and other endocrinopathies. *A*, T1-weighted midsagittal image shows hypoplasia of the rostrum of the CC and a rectangular area of abnormality in the subcallosal region, anterior to the hypothalamic region (*arrowheads*). The dysplastic-appearing fornix is anterior to this region (*arrows*). *B*, Axial T2-weighted image shows well-developed anterior and posterior interhemispheric fissures and an azygous ACA flow void in the anterior interhemispheric fissure. There is an area of midline fusion just anterior to the AC, which appears as a dark bowlike band (*arrowheads*). Further anterior to this region are the dysplastic fornix (*arrows*) and cortical gray matter that is continuous in the middle. *C*, Coronal SPGR image anterior to the AC shows an area of fusion of the septal region (*arrow*). *D*, Coronal SPGR image at the level to the AC shows dysplastic thickened fornices (*arrow*) traveling below the SP and inferiorly an area of midline fusion in the preoptic region and basal structures (*curved arrow*).

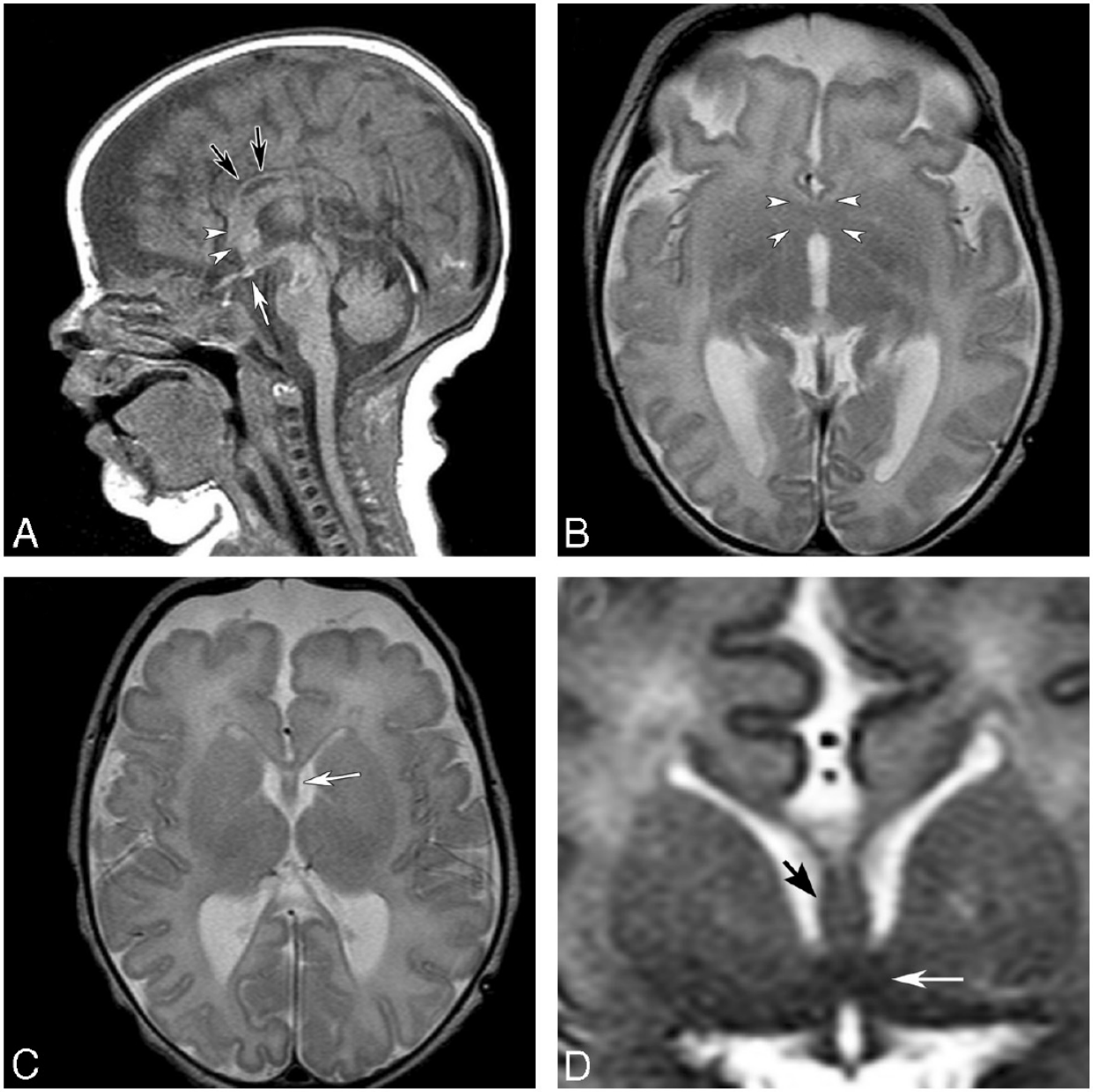


Fig 3. MR imaging of an 8-day-old term neonate with atrial and ventricular septal defects and SMMCI. *A*, Sagittal T1-weighted image shows a thin CC (*black arrows*), a thickened fornix, and dysplastic subcallosal areas (*arrowheads*). A small ectopic pituitary gland is noted near the chiasm (*white arrow*). *B*, Axial T2-weighted image shows an area of fusion in the septal and preoptic regions (*arrowheads*). *C*, An azygous ACA is present in the anterior IHF. Axial T2-weighted image slightly superior shows the presence of the SP (*white arrow*) and a thin genu of the CC. *D*, Coronal T2-weighted image at the level of the AC shows fusion of the midline region (*white arrow*) below the fornices (*black arrow*).

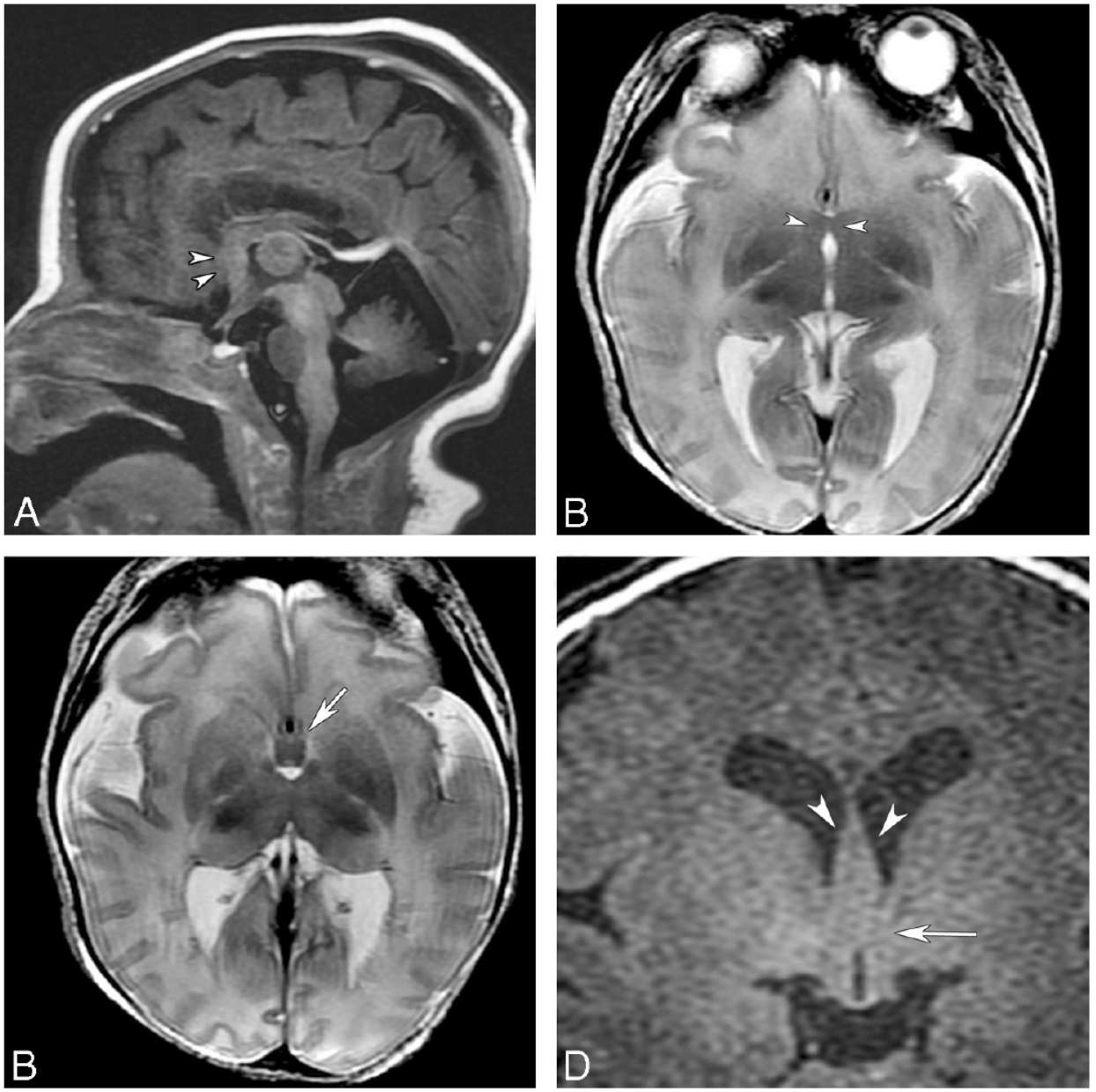


Fig 4. MR imaging of a 6-day-old term neonate initially diagnosed as having choanal atresia, vertebral anomalies, and coactation of aorta. *A*, Sagittal FSPGR image shows an area of fusion in the subcallosal region (*arrowheads*). *B*, Axial T2-weighted image shows the abnormal fusion in the same region (*arrowheads*). An azygous ACA is present in the anterior IHF. *C*, Axial T2-weighted image slightly superior shows thickened fornices (*arrow*) and partial fusion of the thalami. *D*, Coronal FSPGR image shows thickened fornices (*arrowheads*) and an area of fusion in the preoptic area (*arrow*).

HPE Lobar vs Septo preoptica

CERPO

Neuroimaging features comparing lobar versus septopreoptic HPE		
	Lobar	Septopreoptic
Cortical nonseparation	Basal frontal	Septal and preoptic regions
CC	Rostrum and genu absent; anterior body variably present; splenium present	Rostrum absent or hypoplastic; genu hypoplastic; body and splenium present
Anterior interhemispheric fissure and falx	Hypoplastic anteriorly	Fairly deep IHF
Ventricles	Rudimentary frontal horns; third ventricle formed	Normal or small frontal horns; third ventricle formed
Dorsal cyst	Absent	Absent
SP	Absent	Present or dysplastic, rarely absent
Hypothalamus	Often fused to some degree (83%)	Anterior hypothalamus often fused
Cerebral vasculature	Azygous anterior cerebral artery (more anteriorly displaced)	Azygous anterior cerebral artery (more posteriorly placed)

Anomalías asociadas

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Table 6–2. FACIAL DEFECTS IN HOLOPROSENCEPHALY	
Cyclopia	Single eye or single orbit Arrhinia with prosboscis
Ethmocephaly	Extreme hypotelorism Arrhinia with prosboscis
Cebocephaly	Orbital hypotelorism Prosboscis-like nose, no cleft
Median cleft	Orbital hypotelorism Flat nose
Agnathia-astomia	Hypoplasia or absence of the mandible Small or absent mouth Abnormal position of the ears

Diagnostico diferencial

- Hidranencefalia
- Hidrocefalia severa
- Esquizencefalia
- Quiste aracnoideo
- Ausencia de septum pellucidum
- Displasia septo-óptica

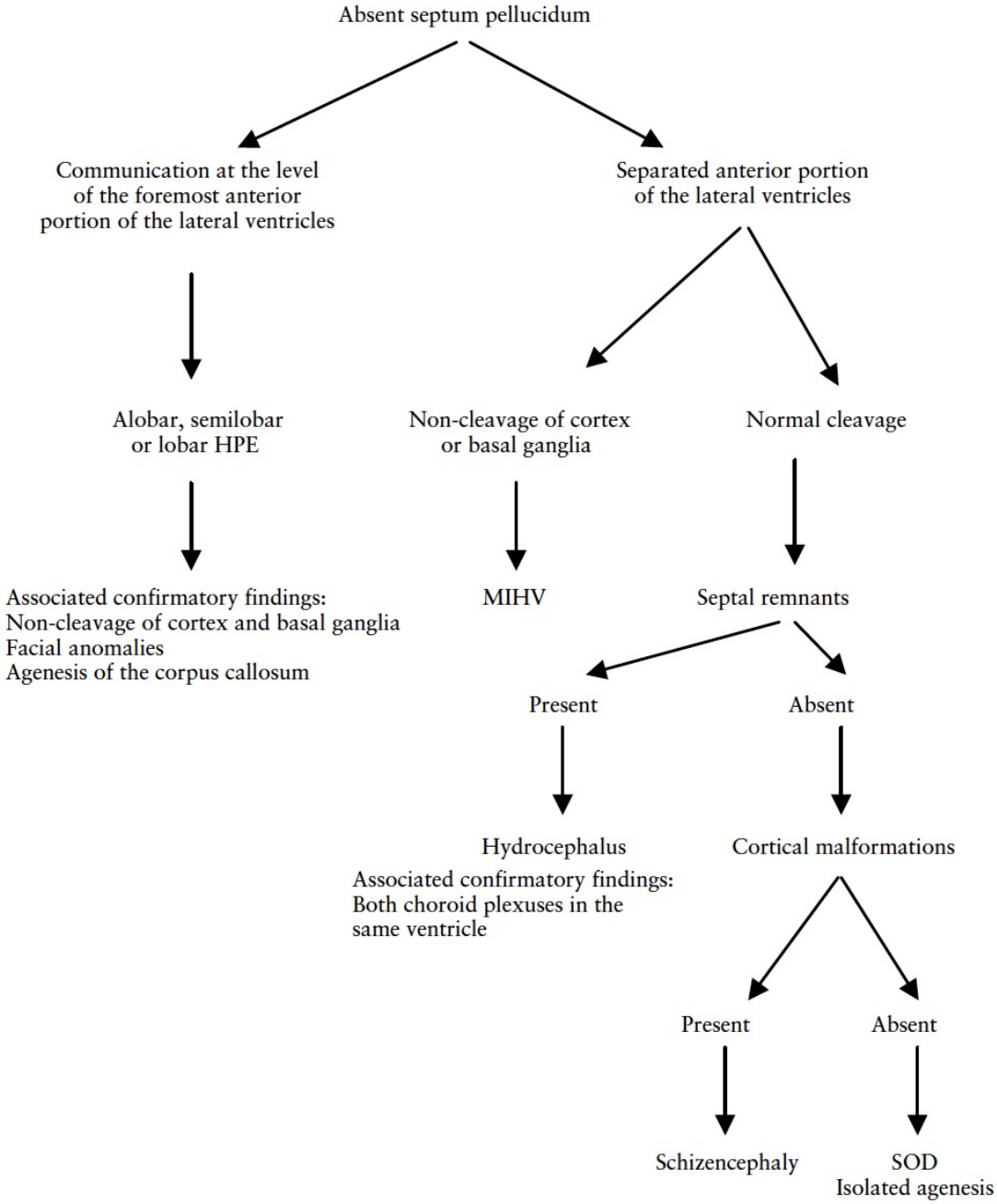

Figure 2 Flowchart used in the differential diagnosis in fetuses with absent septum pellucidum. HPE, holoprosencephaly; MIHV, middle interhemispheric variant; SOD, septo-optic dysplasia.

Manejo

CERPO

- Evaluación anatómica (evaluación dirigida anomalías faciales).
- Neurosonografía
- Ecocardiografía fetal
- Considerar RNM

- Estudio genético (Cariotipo / CMA)

- Evaluación multidisciplinaria (Neonatología, Neurología pediátrica, Genética).

- Ofrecer interrupción del embarazo.

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

Holoprosencefalia

Dr. Pablo Silva Labarca
Becado Medicina Materno Fetal
Universidad de Chile