Hipoplasia pontocerebelosa.

A propósito de un caso.

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Hipoplasia pontocerebelosa

Paciente de 20 años, primigesta y sin antecedentes de interés.

Acude en semana 28 para segunda opinión por diagnóstico de hipoplasia cerebelosa asociada a anomalía cortical.

06/05 Neurosonografía semana 28+6:
Perímetro cefálico en percentil alto p95 con cerebelo de morfología normal con diámetro transverso de 30'7mm (Sherer et al. p5) , hemisferios cerebelosos simétricos.

12/05 RMN fetal :
Disminución de los hemisferios cerebelosos. Protuberancia 8'2/bulbo, con disminución de tamaño de la primera.

OD: Hipoplasia de los hemisferios cerebelosos y protuberancia. Vermis en rango normal.

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25/05 Estudio genético:

- **QF-PCR XY normal**
- **Arrays:**
  arr[GRCh37]12p13.33p13.2(204547_12058394)x3, 18q22.1q23(61714793_77982126)

El análisis de la muestra ha identificado una trisomía segmentaria y una monosomía segmentaria, las dos de grandes dimensiones (11'85 Mb i 16'26 Mb respectivamente), en los cromosomas 12 y 18.

Ambas alteraciones se han asociado previamente en la literatura con discapacidad intelectual y alteraciones fenotípicas (patológicas).

Deciden continuar con gestación.

Control ecográfico y RMN sin cambios.

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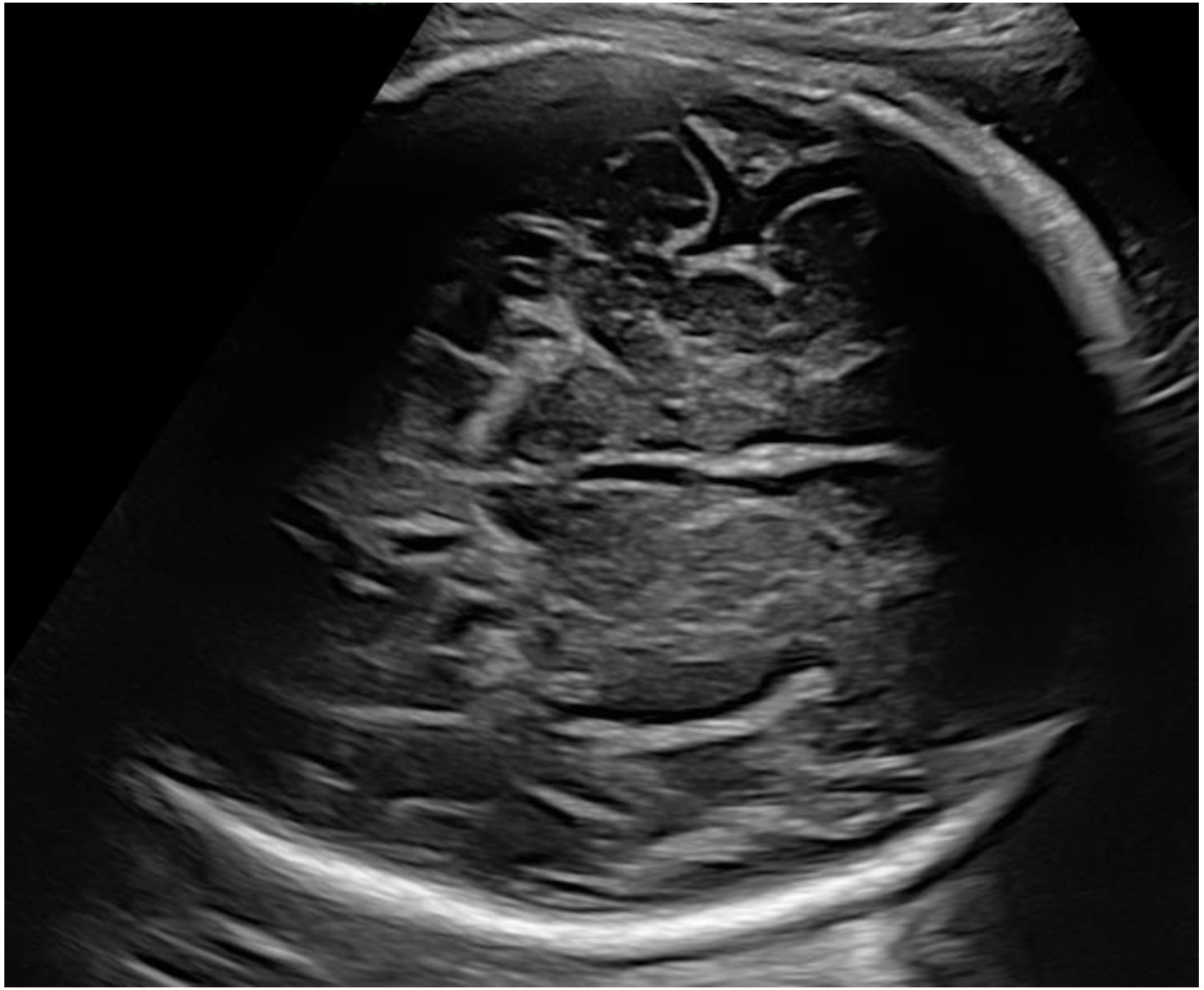

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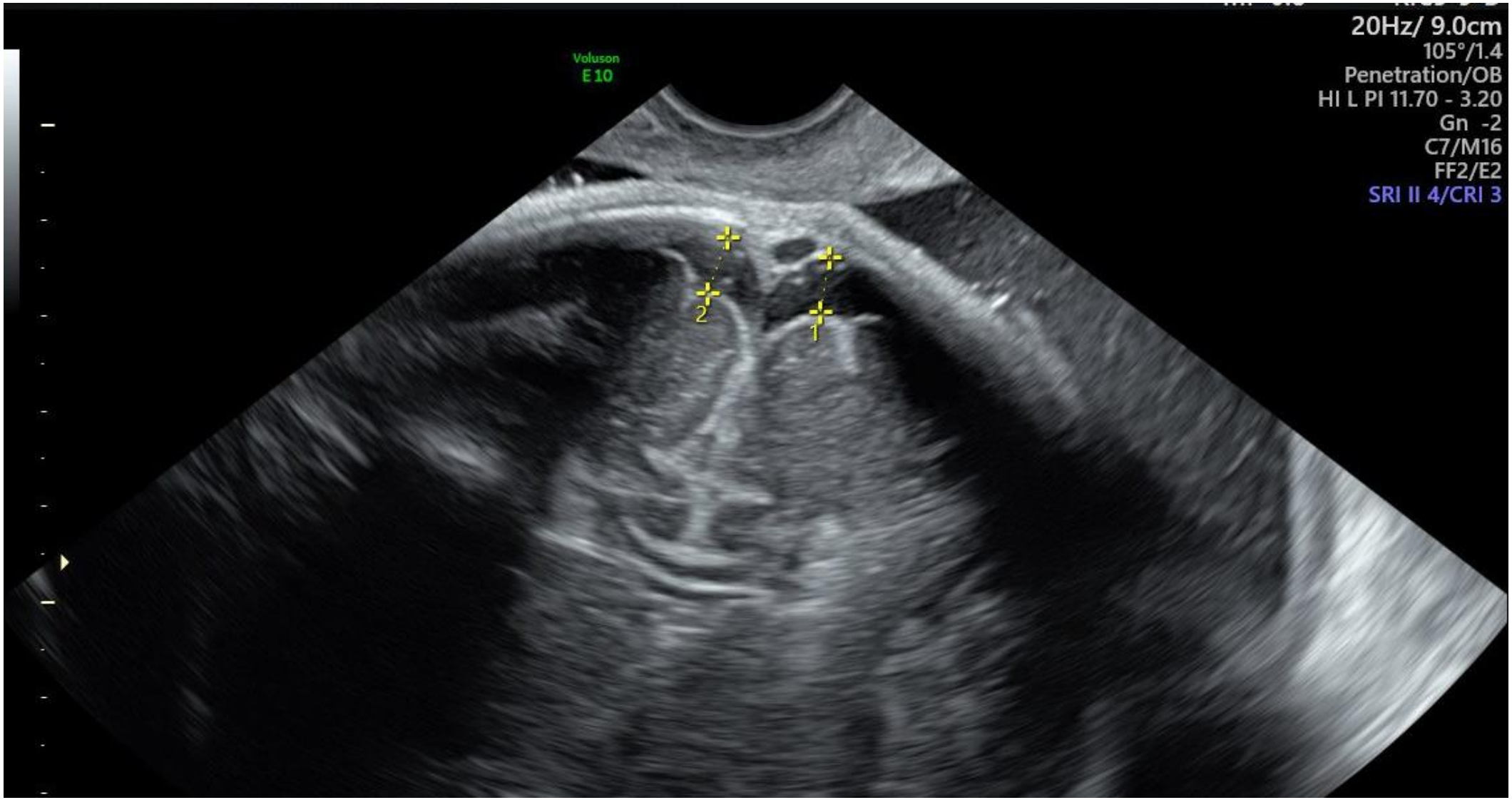

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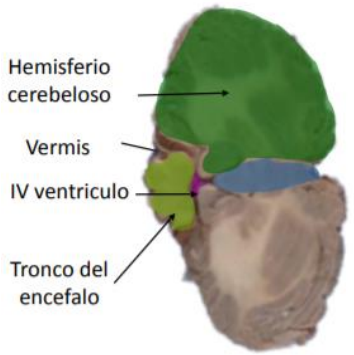

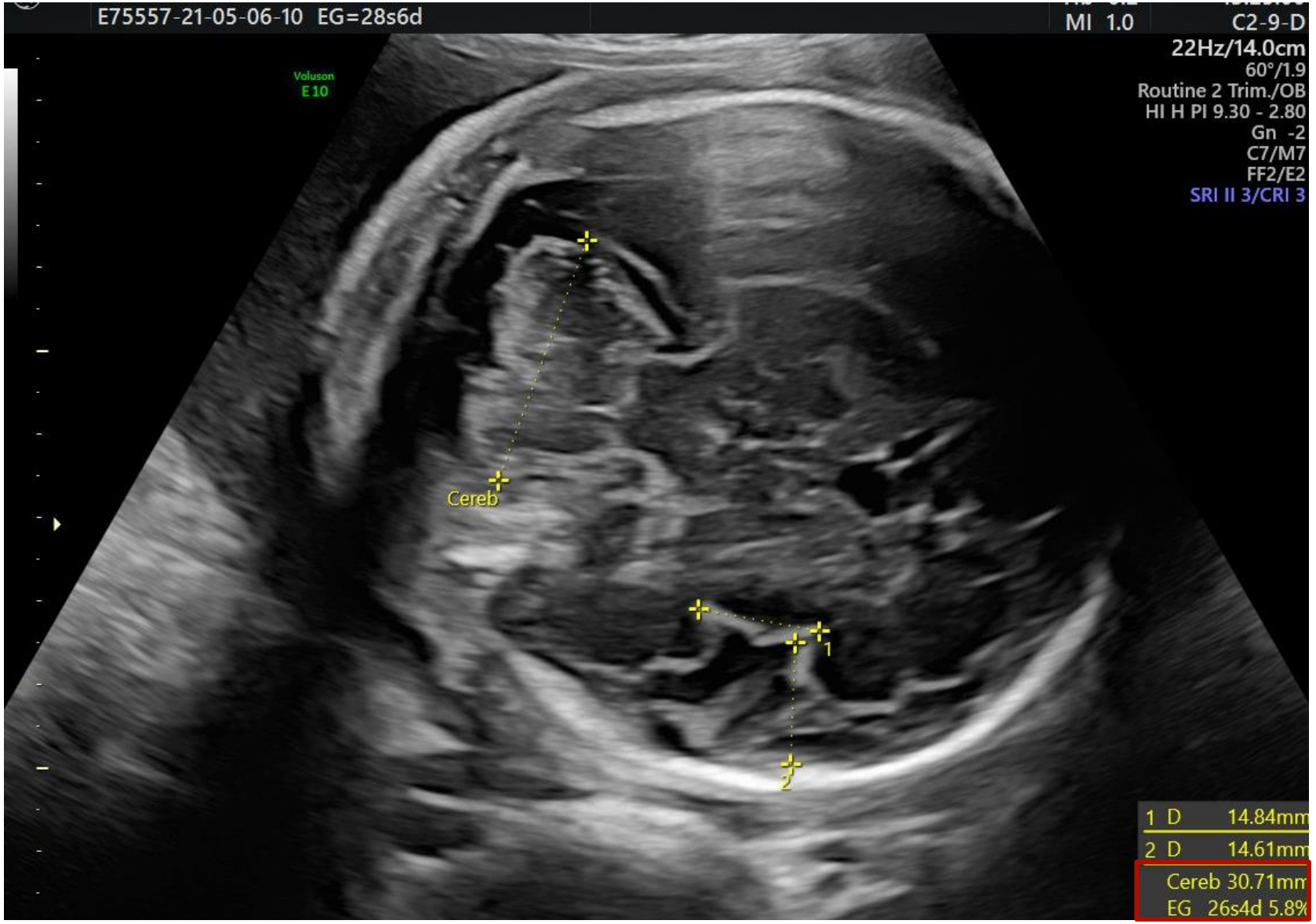

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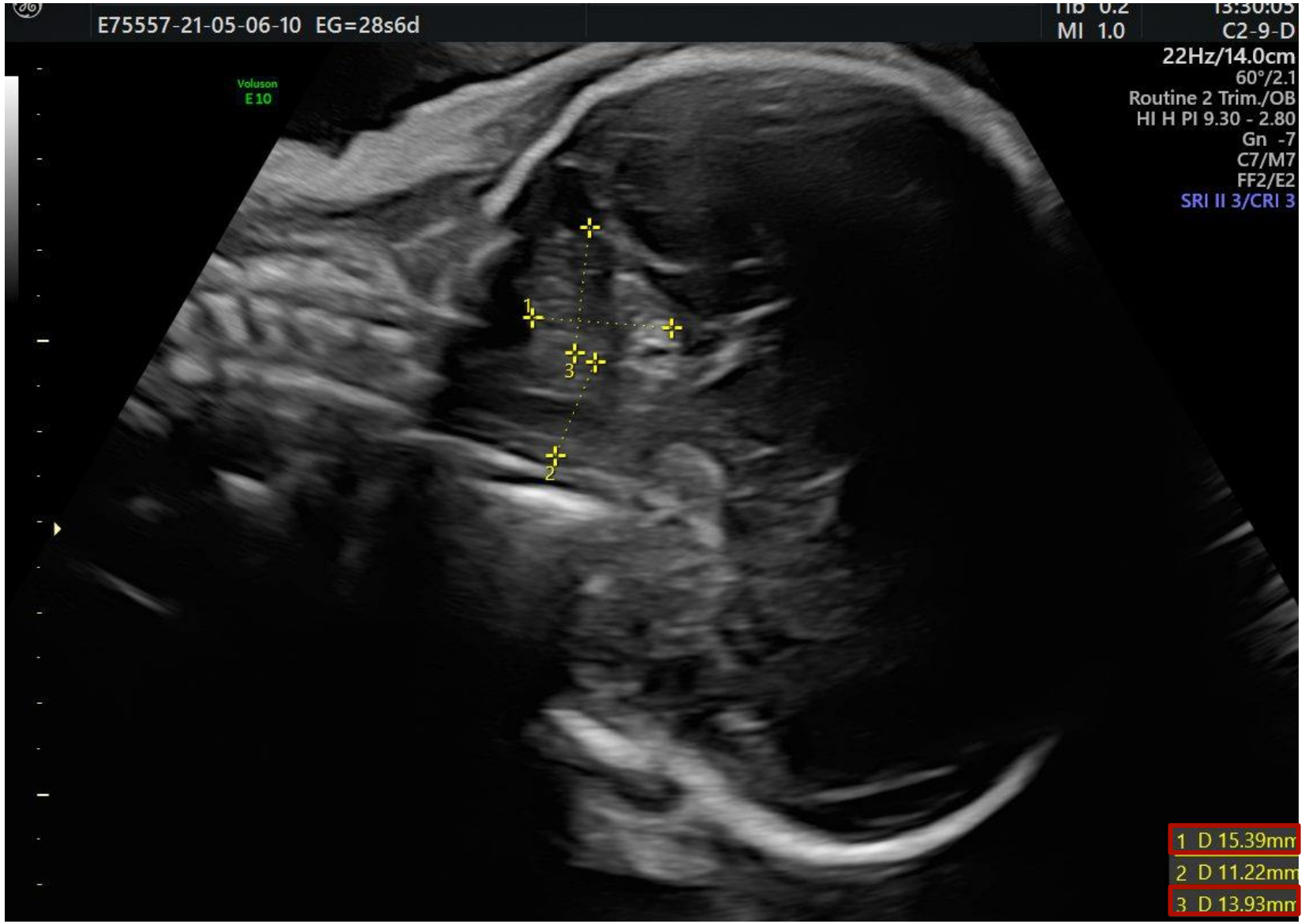

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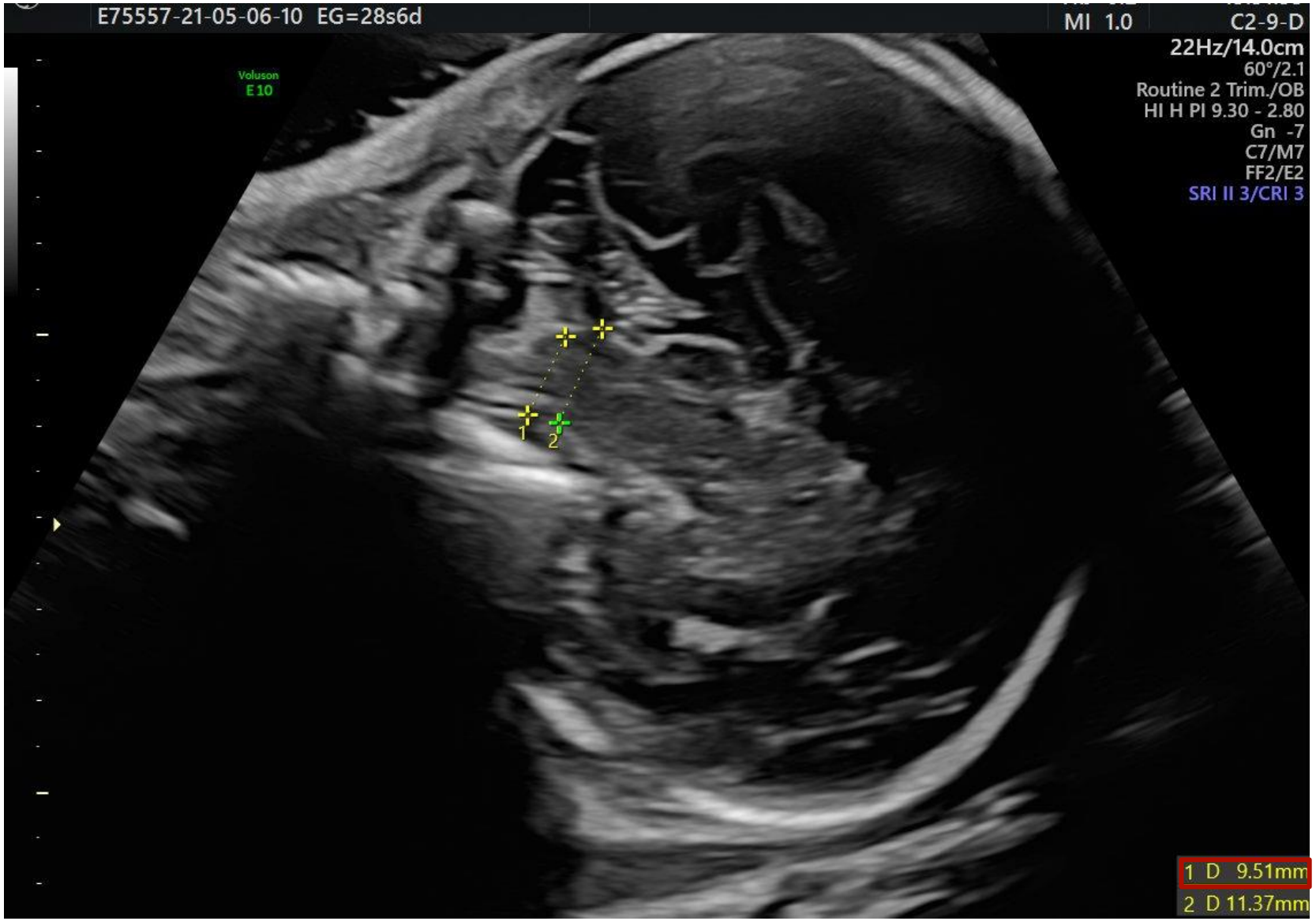

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Table 1. Reference intervals for the cerebellar vermis, basilar pons, and the brain stem.

		Vermis									Pons								
		Sagittal CC (mm)			Sagittal AP (mm)			Sagittal Surface area (cm^2)			Sagittal CC (mm)			Sagittal AP (mm)			Sagittal surface area (cm^2)		
GA (weeks)	Patients (n)	5%	50%	95%	5%	50%	95%	5%	50%	95%	5%	50%	95%	5%	50%	95%	5%	50%	95%
18–19	21	8.4	9.2	11.3	7.8	8.8	10.6	0.61	0.65	0.80	4.5	5.5	6.8	3.4	4.2	4.7	0.13	0.22	0.28
20–21	16	10.0	12.2	14.0	8.3	10.0	13.2	0.80	1.06	1.34	4.8	6.7	8.4	4.3	5.2	6.7	0.22	0.30	0.39
22–23	20	11.3	13.4	15.1	11.2	12.6	15.5	1.07	1.25	1.56	5.8	7.1	9.3	3.6	5.2	6.5	0.30	0.40	0.56
24–25	17	14.6	15.7	17.3	13.3	14.7	16.9	1.32	1.63	1.87	7.4	8.6	10.9	5.4	6.3	8.0	0.41	0.48	0.54
26–27	19	15.6	17.3	18.6	13.7	16.2	18.7	1.9	2.20	2.50	6.4	9.1	10.9	4.7	5.9	7.7	0.40	0.69	0.86
28–29	19	16.4	18.5	22.2	16.1	18.6	20.6	1.73	2.48	2.97	9.3	10.1	14.1	5.8	7.6	9.5	0.50	0.69	0.78
30–31	14	19.1	20.3	22.8	16.5	19.1	22.8	2.59	3.12	3.52	10.0	12.3	13.9	6.7	7.9	9.9	0.62	0.83	0.98
32–33	15	19.6	22.3	23.5	18.3	20.2	22.4	2.84	3.27	3.90	11.2	13.1	15.7	7.9	8.9	10.5	0.75	0.99	1.23
34–35	19	20.6	22.1	25.4	18.6	22.0	23.6	3.12	3.81	4.38	11.5	13.5	15.1	7.6	8.6	10.3	0.92	1.11	1.37
36–37	9	22.0	24.7	27.1	20.5	24.7	26.0	3.71	4.00	4.78	12.1	13.7	14.4	6.8	8.9	10.1	1.00	1.28	1.35
38–39	4	24.3	26.5	28.2	18.8	22.7	25.8	4.30	4.64	5.02	12.5	13.4	14.0	9.3	9.4	10.1	1.20	1.51	1.67
r			0.957			0.937			0.968			0.907			0.856			0.943	
p			<0.0001			<0.0001			<0.0001			<0.0001			<0.0001			<0.0001	

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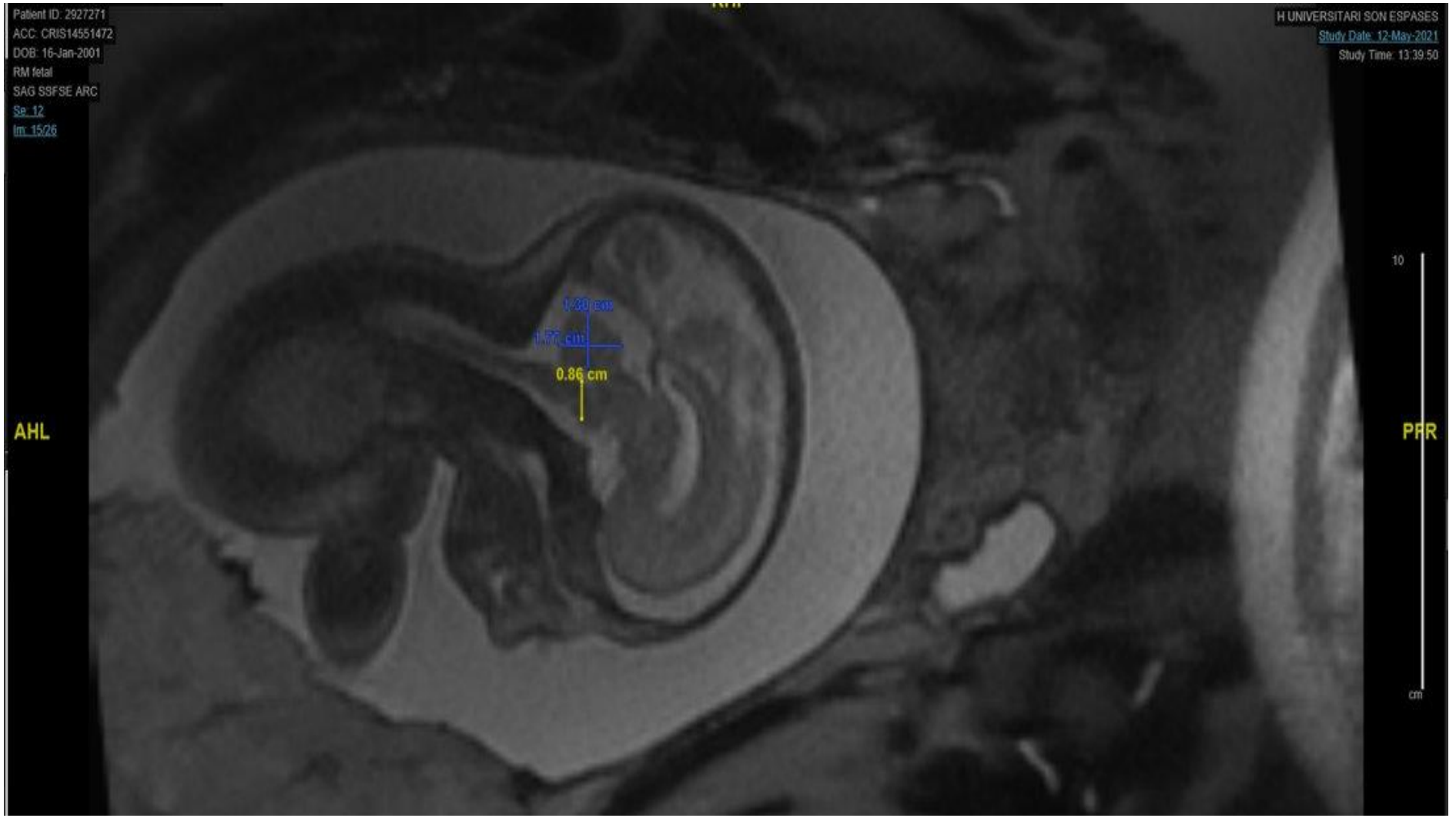

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Table 1
Classification scheme for malformations of mid-hindbrain development

- *Malformations of both midbrain and hindbrain*
  - Brainstem-cerebellar hypoplasia-dysplasia
  - Chiari II malformations
  - Cobblestone LIS with mid-hindbrain malformation
  - **Molar tooth sign associated malformations**
    - **Joubert syndrome**
    - **JSRD, including Senior–Löken and COACH**
  - Rhombencephalosynapsis
- *Malformations affecting predominantly the midbrain*
- *Malformations affecting predominantly the cerebellum and derivatives (Rh1)*
  - Focal cerebellar hypoplasia (focal or hemispheric)
  - Paleocerebellar hypoplasia (vermis predominantly affected, brainstem often mildly hypoplastic)
    - **Dandy–Walker malformation**
    - **Cerebellar vermis hypoplasia, isolated**
    - CVH with periventricular nodular heterotopia
    - CVH with cortical malformations (LIS, PMG)
  - Neocerebellar hypoplasia (hemispheres and vermis affected, predominantly granule cell hypoplasia)
- *Malformations affecting predominantly the lower hindbrain (Rh2-Rh8)*
  - Chiari I malformations
  - Cranial nerve and nuclear aplasias
    - Möbius syndrome
    - Duane retraction syndrome
- *Posterior fossa abnormalities*
  - Abnormal fluid collections
    - Arachnoid cyst
    - Blake's pouch cyst
    - Mega-cisterna magna
  - Abnormal bone and brain structure
- *Malformations associated with prenatal onset degeneration*
  - **Ponto-cerebellar hypoplasia (hypoplasia and prenatal onset atrophy)**
    - **PCH type 1, PCH type 2, PCH type 3**
  - Congenital disorders of glycosylation (CDG)

Conditions that are in bold indicate those featured in this review.

CDG, congenital disorders of glycosylation; COACH, Cerebellar vermis hypoplasia, Oligophrenia, Ataxia, Coloboma, and Hepatic fibrosis; CVH, cerebellar vermis hypoplasia; JSRD, Joubert syndrome and related disorders; LIS, lissencephaly; PCH, pontocerebellar hypoplasia; PMG, polymicrogyria; Rh, rhombomere.

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Neuroimaging Pattern	Malformations
Predominantly cerebellar involvement	
Predominantly vermian	DWM and other cystic lesions of the posterior fossa, including Blake pouch cyst, mega cisterna magna, and arachnoid cysts; isolated vermian hypoplasia; rhombencephalosynapsis
Global cerebellar	Malformations of cortical development: lissencephaly (*RELN*, *VLDRL*, tubulin genes), polymicrogyria (tubulin genes, *GPR56*), periventricular nodular heterotopia (*FLNA*), and primary microcephaly; macrocerebellum; cerebellar dysplasia, including Chudley-McCullough syndrome; global cerebellar hypoplasia in multiple genetic syndromes (eg, Ritschcer-Schinzel syndrome, CHARGE syndrome, Delleman syndrome); congenital CMV infection
Unilateral cerebellar	Isolated unilateral cerebellar hypoplasia, PHACES syndrome, *COL4A1* mutations, cerebellar cleft
Cerebellar and brainstem involvement	PCH type 1–10; glycosylation type 1a congenital disorder; *CASK* mutations; Joubert syndrome; cerebellar agenesis caused by a disruptive lesion or representing a malformation due to *PTF1A* mutations; congenital muscular dystrophies due to defective dystroglycan *O*-glycosylation; vanishing cerebellum in Chiari 2 malformation; cerebellar disruption secondary to prematurity
Predominantly brainstem involvement	Pontine tegmental cap dysplasia; horizontal gaze palsy and progressive scoliosis (*ROBO3* mutations)
Predominantly midbrain involvement	Dysplasia of the diencephalic-mesencephalic junction

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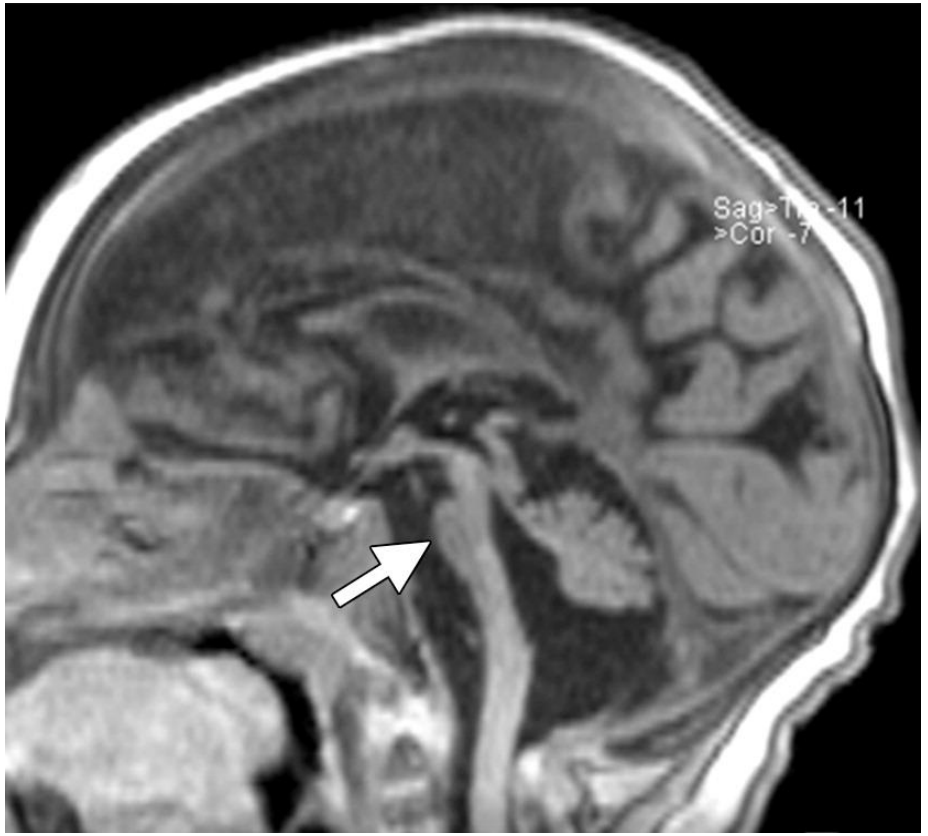
Subtype	Main Features	Genotype
1	Involvement of the anterior horn cells	*VRK1*, *TSEN54*, *RARS2*, *EXOSC3*
2	Chorea/dystonia; rarely, spasticity only	*TSEN54* (vast majority of cases); *TSEN2*, *TSEN34*
3	Optic atrophy, nonprogressive course	Locus on 7q11–21
4	Severe neonatal course with hypertonia and hypoventilation, absent inferior olivary prominence at autopsy	*TSEN54*
5	Lethal course with neonatal death, more pronounced involvement of the vermis than of the hemispheres	*TSEN54*
6	Lactic acidemia, high lactate level in CSF	*RARS2*
7	Micropenis with no palpable gonads	Unknown
8	Proportionate involvement of the vermis and hemispheres, nonprogressive course	*CHMP1A*
9	Dysgenesis of the corpus callosum	*AMPD2*
10	Dysmorphic features and axonal sensorimotor neuropathy (inconsistent)	*CLP1*



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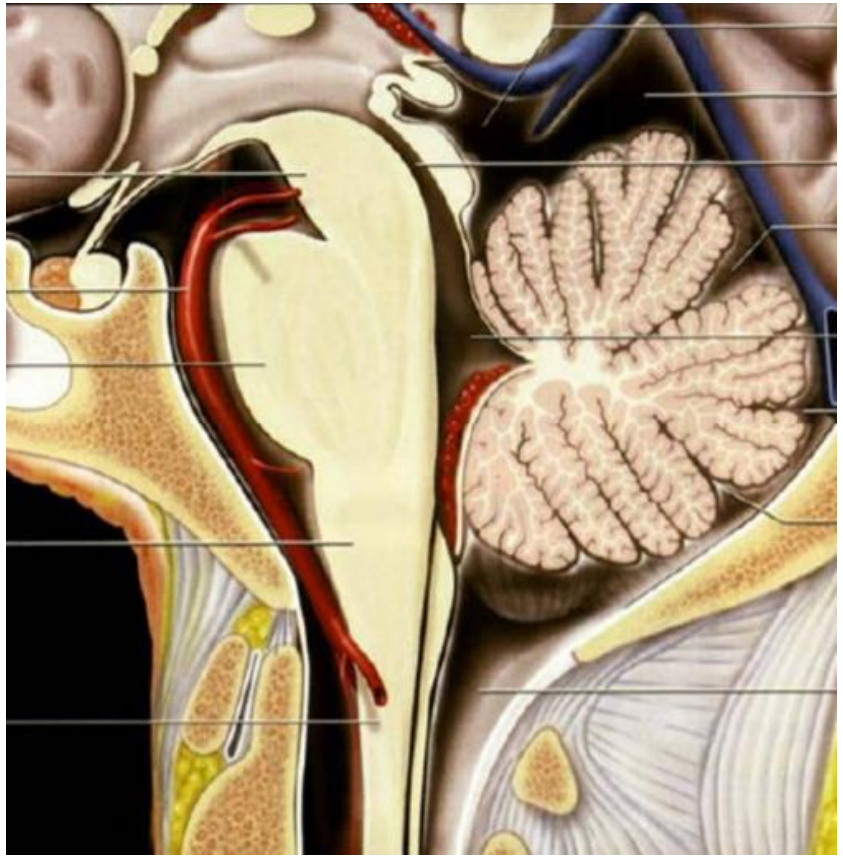
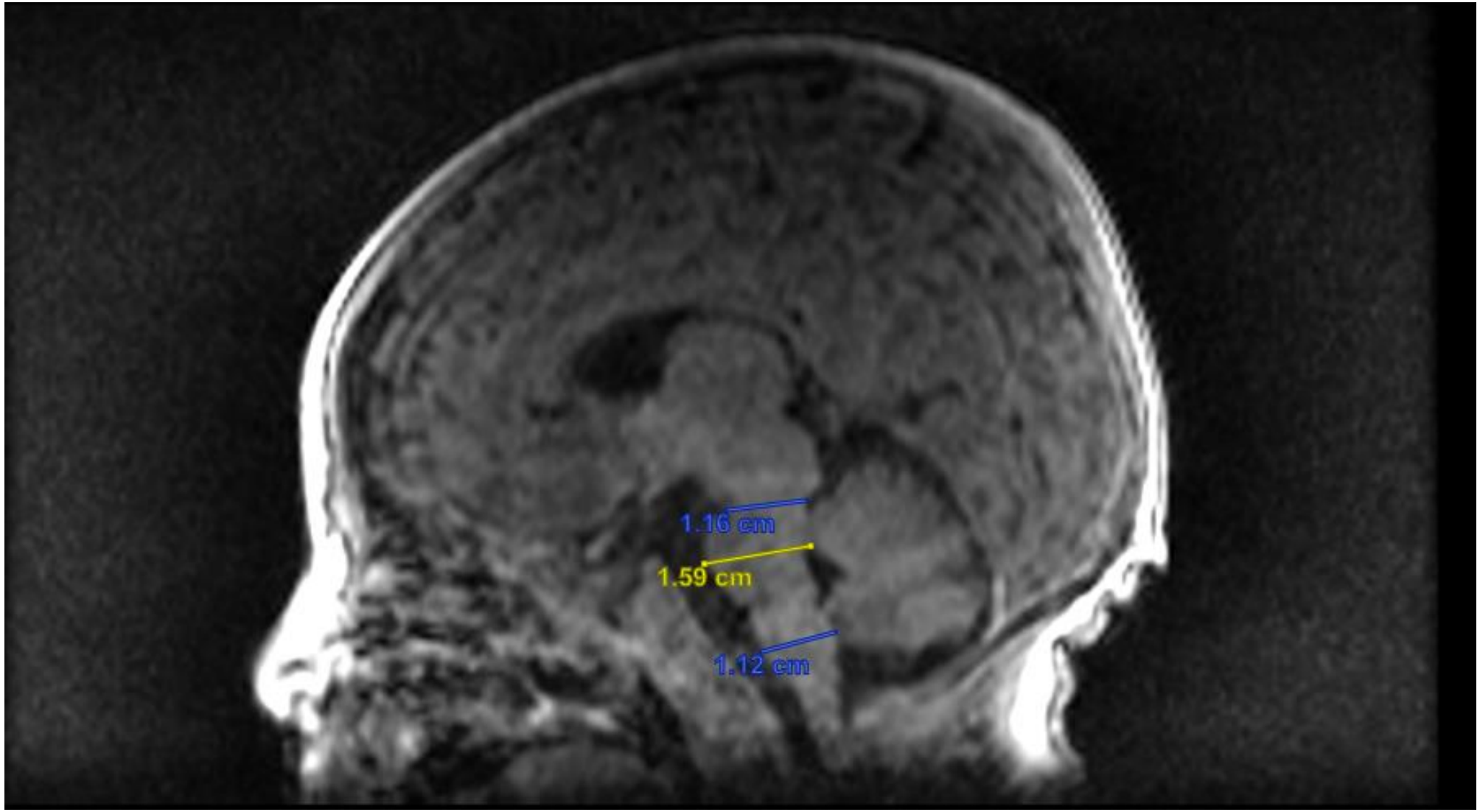
Hipoplasia cerebelosa difusa: alteraciones de severidad variable (motoras, cognitivas, lenguaje, afectividad)

Cognición: aproximadamente 74% retraso mental.

Evolución: mejoría progresiva pero con retraso mental leve-moderado.





En el momento actual, 6 meses de edad, con diagnóstico de hipoplasia pontocerebelosa, fisura palatina, pie talo por astrágalo vertical congénito bilateral, subluxación de muñecas, displasia leve-moderada de cadera izquierda, hipotiroidismo subclínico, foramen oval permeable e insuficiencia mitral leve.

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