

Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

e-Table 1: Baseline Clinical Features.

Case	History of prenatal ultrasound abnormalities	Gestational age at birth	Birth weight for gestational age	Birth head circumference (HC) in cm	Z-score HC at birth	Microcephaly	Maternal rash	Craniofacial disproportion at birth	Prominence of occipital bone at birth	Redundant scalp skin at birth	Irritability during first months of life	Hyperexcitability	Arthrogryposis
1	yes (30 wks)	35 wks	appropriate	25cm	-4,36	yes, severe	5 mo	yes	no	yes	yes	yes	no
2	yes (32 wks)	39 wks	appropriate	29cm	-3,76	yes, severe	none	yes	yes	yes	no	no	yes
3	yes (28 wks)	37 wks	small	27cm	-4,23	yes, severe	3 mo	yes	yes	yes	yes	yes	no
4	yes (37 wks)	41 wks	appropriate	29cm	-4,06	yes, severe	none	yes	yes	yes	no	no	no
5	yes (32 wks)	40 wks	appropriate	27cm	-4,82	yes, severe	2 mo	yes	yes	yes	yes	yes	no
6	yes (31 wks)	37 wks	appropriate	29,5cm	-3,07	yes	3 mo	yes	yes	yes	yes	yes	yes
7	yes (29 wks)	39 wks	appropriate	28cm	-4,11	yes, severe	3 mo	yes	yes	yes	yes	yes	no
8	yes (32 wks)	41 wks	appropriate	27cm	-5,30	yes, severe	none	yes	yes	yes	yes	yes	no

9	yes (30 wks)	40 wks	small	29cm	-3,82	yes, severe	none	yes	yes	yes	yes	yes	yes
10	yes (36 wks)	39 wks	appropriate	30cm	-2,89	yes	3 mo	yes	no	no	no	yes	yes
11	yes (32 wks)	35 wks	appropriate	27cm	-3,52	yes	3 mo	yes	yes	yes	yes	yes	no
12	no	37 wks	small	28cm	-3,52	yes, severe	none	yes	yes	yes	yes	yes	yes
13	no	37 wks	small	26cm	-4,71	yes, severe	4 mo	yes	yes	yes	no	yes	yes
14	yes (27 wks)	40 wks	appropriate	24cm	-5,89	yes, severe	4 mo	yes	yes	yes	yes	yes	no
15	yes (20 wks)	40 wks	small	27cm	-4,82	yes, severe	3 mo	yes	yes	yes	no	yes	no
16	no	39 wks	appropriate	27cm	-4,81	yes, severe	no	yes	yes	yes	yes	yes	no
17	yes (37 wks)	40 wks	appropriate	29cm	-3,82	yes	7 mo	yes	no	yes	no	yes	no
18	yes (30 wks)	39 wks	small	27cm	-4,60	yes, severe	6 mo	yes	yes	yes	no	yes	no

19	no	31 wks	small	23cm	-3,56	yes, severe	3 mo	yes	no	no	no	no	no
20	no	40 wks	appropriate	27cm	-5,06	yes, severe	none	yes	yes	yes	no	no	no
21	no	termo	appropriate	29cm	-3,82	yes, severe	none	yes	yes	no	no	yes	no
22	yes	39 wks	small	27cm	-4,81	yes, severe	none	yes	no	yes	yes	yes	no
23	no	41 wks	appropriate	28cm	-4,85	yes, severe	yes	yes	no	yes	yes	yes	yes
24	yes	40 wks	appropriate	27cm	-4,82	yes, severe	yes	yes	no	no	yes	yes	no

Cm = centimeters, wk = weeks

e-Table 2: Clinical features at the time of hydrocephalus diagnosis.

Case	Age of diagnosis of hydrocephaly	Corrected age	Head circumference at the diagnosis of hydrocephaly	Z score of hc at the time of hydrocephalus diagnosis	Symptoms suggestive of hydrocephaly	Clinical findings at the time of diagnosis of hydrocephaly						
						Hypertonia*	Primitive reflex	Dysphagia	Abnormal ocular movement	Visual fixation and pursuit	Milestones achieved (head control, sitting without support, voluntary grasp)	Epilepsy
1	12 mo	11 months	34 cm	-7.82	Vomiting, irritability and worsening of seizures	Yes	Present	Yes, feeding tube	Strabismus, nystagmus	No	Neither	Yes
2	11 mo	Not applied	39,5 cm	-5.29	Drowsiness	Yes	Present	Yes	Nystagmus	No	Neither	Yes
3	3 mo	Not applied	33 cm	-6.36	Irritability and sutures disjunction	Yes	Present	Yes	Nystagmus	No	Neither	Yes
4	12 mo	Not applied	42,7 cm	-2.13	Hypoactivity and increased hc	Yes	Present	Yes	Strabismus	No	Neither	Yes
5	11 mo	Not applied	40,5 cm	-3.39	Increased hc, with no other symptoms, with 11 m	Yes	Present	Yes	Nystagmus	No	Neither	Yes
6	10 mo	Not applied	41,5 cm	-3.48	Irritability, worsening of seizures, increased hc and sutures disjunction	Yes	Present	Yes	Strabismus	No	Neither	Yes
7	11 mo	Not applied	37,4 cm	-5.61	Worsening of dysphagia and seizures	Yes	Present	Yes, feeding tube	Strabismus	No	Neither	Yes

					with vomiting.							
8	4 mo	Not applied	41 cm	-0.53	Irritability and increased hc	Yes	Present	Yes	Nystagmus	No	Neither	Yes
9	13 mo	Not applied	36,8 cm	-6.73	None	Yes	Present	Yes	Nystagmus	No	Neither	No
10	11 mo	Not applied	42 cm	-1.91	Increased hc, vomiting and worsening of seizures	Yes	Present	Yes	No	No	Neither	Yes
11	11 mo	10 months	39 cm	-5.29	Irritability , vomiting and uncontrolled seizures	Yes	Present	Yes, gastrostomy	Nystagmus	No	Neither	Yes
12	12 mo	Not applied	38 cm	-5.07	Worsening of the seizures at 9 months, worsening of dysphagia and respiratory symptoms.	Yes	Present	Yes	Nystagmus	No	Neither	Yes
13	14 mo	Not applied	36 cm	-8.14	Vomiting	Yes	Present	Yes	Nystagmus	No	Neither	Yes
14	14 mo	Not applied	37 cm	-6.16	Worsening of seizures, hypertension.	Yes	Present	Yes	Nystagmus	No	Neither	Yes
15	14 mo	Not applied	38 cm	-5.43	Vomiting; irritability; worsening of dysphagia	Yes	Present	Yes	No	No	Neither	Yes

16	14 mo	Not applied	34 cm	-9.68	Vomiting; worsening of dysphagia; seizures	Yes	Present	Yes	Nystagmus	No	Neither	Yes
17	18 mo	Not applied	40,5 cm	-416	None	Yes	Present	Yes	No	No	Neither	Yes
18	15 mo	Not applied	37,2 cm	-6.16	Vomiting and worsening of seizures	Yes	Present	Yes	Strabismus	No	Neither	Yes
19	16 mo	14 mo	35 cm	-8.91	Worsening of seizures	Yes	Present	Yes	Strabismus, nystagmus	No	Neither	Yes
20	12 mo	Not applied	34 cm	-9.39	Worsening of seizures	Yes	Present	Yes	Tendencia a olhar p esquerda	No	Neither	Yes
21	18 mo	Not applied	39,2cm	-524	Worsening of seizures; sleep disorders	Yes	Present	Yes	No	No	Neither	Yes
22	9 months	Not applied	40	-3,91	Increased seizures; drowsiness	Yes	Present	Yes	No	No	Neither	Yes
23	9 months	Not applied	37	-6,42	Drowsiness and vertical gaze palsy	Yes	Present	Yes	Exotropia, nystagmus, up beat	No	Neither	Yes
24	13 months	Not applied	Not analysed	Not analysed	Vomiting; irritability	Yes	Present	Yes	No	Yes	Neither	Yes

*abnormalities include arthrogryposis with mixture of hypotonia and hypertonia (case 2, 6, 9, 10, 12, 13, 23)

e-Table 3: Main findings in CSF analysis.

Case	CSF routine		Proteins electrophoretic separation					
	cel count (/mm3)	proteins (mg/dl)	Prealbumin (%)	Albumin (%)	Alfa 1 globulin (%)	Alfa 2 globulin (%)	Beta globulin (%)	Gama globulin (%)
1	na	65 (hemolyzed)	3	53	4	6	202	12
2	na	17	3	57	4	7	19	10
3	na	na	na	na	na	na	na	na
4	na	48	4	52	6	7	19	12
5	na	55	2	47	4	5	28	14
6	na	10	10	47	4	5	26	8
7	na	37	2	61	3	4	20	10
8	na	na	na	na	na	na	na	na
9	na	26	2	55	5	7	21	10
10	na	18	5	55	3	6	19	12
11	na	52	na	na	na	na	na	na
12	na	13	3	46	6	8	27	10
13	na	35	3	45	6	10	26	10
14	na	12	3	59	4	7	17	10
15	na	65 (hemolyzed)	5	42	4	7	27	15
16	1	23	na	na	na	na	na	na
17	4	52	3	55	3	6	20	11
18	1	20	3	54	5	7	18	13

19	na	na	na	na	na	na	na	na
20	na	na	na	na	na	na	na	na
21	1	45	13	48	5	6	16	12

eFigure. Representative brain image near birth and at diagnosis of hydrocephalus in patients with CZS. (A-H) Follow-up images illustrate worsening cerebral volume loss and increased ventricular dilation consistent with hydrocephalus (at birth on top and at the diagnosis of hydrocephalus on bottom).

