

	Hunt et al (2014)	Lalani et al (2014)	Tanaka et al (2015)	Okamoto et al (2017)
	N = 4	N = 11	N = 6	N = 1
Gender	4x Female	4x Male, 7x Female	2x Male, 4x Female	1x Male
Age of examination (range)	4 years - 14 years	6 months - 15 years	6 months - 15 years	10 years
Pregnancy/delivery				
Complicated pregnancy	0/4	Not reported	Not reported	0/1
Excessive hiccups in utero	Not reported	Not reported	Not reported	Not reported
Complicated delivery	1/4 (Caesarian section)	Not reported	Not reported	0/1
Gestational age > 41 weeks	3/4	Not reported	Not reported	0/1
Abnormal birth weight	0/4	Not reported	Not reported	0/1
Neonatal problems				
Hyptonia	3/4	11/11	Not reported	1/1
Feeding difficulties	3/4	11/11	1/6	1/1
Requiring tube feeding	3/3	3/11	Not reported	Not reported
Gastro-oesophageal reflux	Not reported	Not reported	1/6	Not reported
Requiring medical treatment	Not reported	Not reported	Not reported	Not reported
Requiring surgery	Not reported	Not reported	Not reported	Not reported
Breathing problems	3/4	10/10	1/6	1/1
Requiring mechanical ventilation	0/3	Not reported	Not reported	Not reported
Hypersomnolence	Not reported	Not reported	Not reported	Not reported
Temperature instability	1/4	Not reported	Not reported	Not reported
Other	None	None	Bradycardia (1/6)	None
Growth				
Short stature	1/4	1/11	0/6	1/1
Low weight	1/4	2/11	0/6	0/1
Aberrant OFC	Microcephaly (1/4)	Macrocephaly (1/11)	Macrocephaly (1/6)	0/1
Development				
Intellectual disability	4/4	11/11	6/6	1/1
Mild/Moderate/Severe	Not reported	Not reported	Not reported	Not reported
IQ level	Not reported	Not reported	Not reported	Not reported
Language delay	4/4	11/11	6/6	1/1
Age of first words (range)	11 months - not achieved	8/8 Non-verbal	4/5 Non-verbal	Non-verbal
Receptive > Expressive	1/4	Not reported	Not reported	Not reported
Motor delay	4/4	11/11	6/6	1/1
Age of sitting unsupported (range)	12 months - not achieved	10 months - not achieved	1 year - 5 years	1 years
Age of first steps (range)	22 months - not achieved	3.5 years	3 years - not achieved	7 years
Regression since onset of seizures	Not reported	Not reported	0/6	Not reported
Neurological				
Behavior problems	Anxiety (2/4)	Autism (1/11)	Not reported	Not reported
Use of psychiatric drugs	Not reported	Not reported	Not reported	Not reported
Stereotypic hand movements	Not reported	Not reported	Not reported	Not reported
Hypotonia	3/4	Not reported	Not reported	1/1
Epilepsy	3/4	9/11	1/6	0/1
Type	Not reported	Myoclonic jerks (6/9); Generalized tonic-clonic (5/9); Lennox Gastaut (2/9); Atonic (1/9)	Infantile spasms	Not applicable
Age of onset (range)	7 months - 3 years	3 weeks - 4 years	Not reported	Not applicable
EEG abnormality	2/3	7/7	1/1	1/1 (diffuse small spikes)
Movement disorder	Dystonia and choreoathetoid limb movements (1/4)	Not reported	Seizure-like movements (2/6)	Not reported
Gait	Broad-based (1/4); Non-ambulatory (3/4)	Non-ambulatory (7/8), Scissoring gait, ataxic (1/8)	Not reported	Waddling (1/1)
Nystagmus	Not reported	4/11	Not reported	Not reported
Exaggerated startle response	2/4	2/11	Not reported	Not reported
Other	Dysconjugate gaze (2/4)	No	No	None
Brain MRI abnormalities				
Delayed myelination	2/4	2/10	1/6	0/1
Corpus callosum	Normal (4/4)	Normal (9/10); slightly ascending (1/10)	Volume loss (1/6)	Normal
Perivascular spaces	Normal (4/4)	Normal (9/10); increased (1/10)	0/6	Normal
Other	Possible cerebral atrophy (1/4) and excessive extra-axial fluid spaces (1/4)	Absent septum pellucidum (1/10), intraventricular hemorrhage (1/10)	White matter changes (1/6); Periventricular leukomalacia (1/6)	0/1
Cardiac abnormalities				
	Not reported	Bicuspid aortic valve (1/8); ASD (1/8)	Not reported	Not reported
Gastrointestinal abnormalities				
Swallow problems/drooling	Not reported	5/6	Not reported	Not reported
Constipation	Not reported	Not reported	3/6	Not reported
Respiratory abnormalities				
Apnoeas > 1 year	1/4	3/11	Not reported	Not reported
Requiring mechanical ventilation	Not reported	1/3	Not reported	Not reported
Other	No	No	No	No
Urogenital abnormalities				
	Not reported	Duplex left kidney, hydronephrosis (1/11)	Not reported	Not reported
Ophthalmologic abnormalities				
Refraction abnormality	Not reported	Myopia (1/11); Severe hypermetropia (1/11)	Myopia (1/6)	Not reported
Strabismus	Not reported	4/11	2/6	Not reported
Cortical visual impairment	1/4	0/11	1/6	Not reported
Other	No	Esotropia (1/11); Exotropia (1/11)	Optic nerve pallor (1/6); Esotropia (2/6); Exotropia (1/6)	No
Musculoskeletal abnormalities				
Scoliosis	Not reported	2/11	Not reported	Not reported
Age of onset	Not reported	Not reported	Not reported	Not reported
Requiring surgery	Not reported	Not reported	Not reported	Not reported
Hip dysplasia	Not reported	0/11	Not reported	Not reported
Age of onset	Not reported	Not reported	Not reported	Not reported
Requiring surgery	Not reported	Not reported	Not reported	Not reported
Low bone mineralization	Not reported	3/11	1/6	Not reported
Other	No	Pectus carinatum (1/11)	No	No
Endocrine abnormalities				
Abnormal vitamin D levels	1/4	Not reported	Not reported	Not reported
Abnormal iron levels	0/4	Not reported	Not reported	Not reported
Abnormal hemoglobin levels	0/4	Not reported	Not reported	Not reported
Abnormal sex hormone levels	1/4	Not reported	Not reported	Not reported
Abnormal cortisol reponse	1/4	Not reported	Not reported	Not reported
Abnormal thyroid hormone levels	0/4	Not reported	Not reported	Not reported
Other	Elevated prolactin levels (1/4)	No	No	No
Physical examination				
Extremities				
Small hands	Not reported	0/11	Not reported	Not reported
Small feet	Not reported	0/11	Not reported	Not reported
Puffy hands	Not reported	1/11	Not reported	Not reported
Puffy feet	Not reported	2/11	Not reported	Not reported
Pes planus	Not reported	Not reported	Not reported	Not reported
Hyperlaxity	Not reported	1/11	Not reported	Not reported
Tapering fingers	Not reported	Not reported	Not reported	Not reported
Abnormal creases	Not reported	Not reported	Not reported	Not reported
Other	No	No	No	Not reported
Other clinical features				
Thether cord	Not reported	Not reported	Not reported	No
Laryngeal cleft	Not reported	Not reported	Not reported	No
Soft skin	Not reported	Not reported	Not reported	Not reported
Other skin abnormalities	Not reported	Hypertrichosis (1/1)	Not reported	Not reported
Other	No	No	No	No
Tests performed in past				
Karyotyping	Not reported	Not reported	Not reported	Not reported
Array	Not reported	10/11	Not reported	Not reported

Single gene tests	Not reported	Angelman Syndrome (3/11); CDG (2/11); myotonic dystrophy (4/11); Prader Willi Syndrome (8/11); Rett Syndrome (3/11); SMA (4/11); PHOX2B (1/11); PTEN (1/11); POLG1 (2/11); Mito-DNA (2/11); ARX (2/11); ATRX (1/11)	Not reported	Not reported
Metabolic testing	Not reported	Not reported	Not reported	Not reported
Muscle biopsy	Not reported	Not reported	Not reported	Not reported
Lumbar puncture	Normal (1/4); Elevated di-hydrobiopterin levels	Not reported	Not reported	Not reported
Peripheral nerve testing	Not reported	Not reported	Not reported	Not reported
Other	No	No	No	Not reported
Current medical treatment				
<i>Please complete</i>	Not reported	Not reported	Not reported	Not reported
Medical treatment used in the past				
<i>Please complete</i>	Not reported	Not reported	Not reported	Not reported