Table 1: Clinical features of the five subjects with pathogenic *ARF3* missense mutations.

General information	S1	S2	S3	S4	S5
Gene	*ARF3*	*ARF3*	*ARF3*	*ARF3*	*ARF3*
cDNA change (NM_001659.2)	c.379A>G	c.34C>G and c.200A>T	c.139C>T	c.277G>A	c.95C>A
Amino acid change	p.Lys127Glu	p.Leu12Val and p.Asp67Val	p.Pro47Ser	p.Asp93Asn	p.Thr32Asn
Mode of inheritance	sporadic, *de novo*	sporadic, *de novo*	sporadic, *de novo*	sporadic, *de novo*	sporadic, *de novo*
Gender	F	M	F	F	M
Age at last examination	3 years	18 months	3 years, 10 months	7 years	13 years, 5 months
Nationality	Italian	French	Italian	Italian	Italian
Birth					
Gestational age (weeks)	39	38	41	39	40
Birth weight (grams/SD)	2700 g (-1.42 SD)	2800 g (-1.24 SD)	3240 g (-0.73 SD)	3600 g (+0.73 SD)	3500 g (-0.21 SD)
Birth length (cm/SD)	46 cm (-2.05 SD)	46.5 cm (-1.73 SD)	not available	50.5 cm (+0.42 SD)	not available
Head circumference at birth (cm/SD)	33.5 cm (-1.11 SD)	31.5 cm (-2.33 SD)	not available	33 cm (-0.99 SD)	not available
Growth					
Height at last exam (cm/SD, age)	52 cm (-6.6 SD, 5m)	59 cm (-8.21 SD, 16 m)	101 cm (-0.29 SD, 3 y, 10 m)	126 cm (+0.80 SD, 7 y)	169.2 cm (+1.24 SD, 13 y 5 m)
Weight at last exam (kg/SD, age)	3.77 kg (-5.95 SD, 5 m)	9.7 kg (-1.42 SD, 16 m)	not available	23.5 Kg (+0.20 SD, 7 y)	58.1 Kg (+0.94 SD, 13 y 5 m)
Head circumference at last exam (cm/SD, age)	37 cm (-4.56 SD, 5 m)	40 cm (-5.12 SD,11 m)	49.4 cm (-1.01 SD, 3 y 10 m)	47.5 cm (-3 SD, 7 y)	56 cm (+1.5 SD, 13 y 5 m)
Neurological abnormalities					
Developmental delay/Intellectual disability	yes /profound	yes /profound	yes	yes / severe	yes
Walking age	not acquired	not acquired	3 y 9 m	24 m	34 m
Age at first words	not acquired	not acquired	not acquired	7 y (two words-sentence)	36 m
Speech/language development	absent	absent	delayed	delayed	severe delayed
Seizures	yes	no	yes, seizure-free since age 2 y	no	no
Age at first seizure	5 m	not applicable	8 m	not applicable	not applicable
EEG anomalies	yes, diffuse multifocal epileptic discharges	no	no	not performed	not applicable
Antiseizure medication	gardenal (5 mg/Kg/die), baclofen	not applicable	acute intrarectal diazepam (5 mg)	not applicable	not applicable

	(0.6 mg/Kg/die), lorazepam (2 mg/Kg/die), morphine and clonidine				
Muscle tone	hypotonia	dystonia	no	hypotonia	no
Brain MRI (age)	yes (multiple, 1 m to 3 y)	yes (multiple, 3 m and 14 m)	yes (17 m)	yes (1 y)	yes (3 y 9 m)
Brain MRI abnormalities	diffuse severe cortical atrophy, diminished cerebral white matter, progressive pontocerebellar hypoplasia, hypoplasia of corpus callosum, cerebellar vermis hypoplasia	diffuse severe cortical atrophy, progressive pontocerebellar hypoplasia, reduced white matter	mild frontal lobe hypoplasia, cavum septum pellucidum, thin corpus callosum, under-rotated hippocampi	microcephaly, frontal lobe hypoplasia, thin corpus callosum	corpus callosum hypoplasia in the median and posterior part, mild white matter hyperintensity
Behavioural anomalies	not applicable	not applicable	no	no	no
Additional neurologic findings	pyramidal signs	pyramidal signs	none	none	none
Other abnormalities					
Eye anomalies	no	no	no	no	no
Facial dysmorphism	bitemporal narrowing, hypotelorism, long eyelashes and flat nasal bridge with small nose	no	no	brachycephaly, deep-set eyes, epicanthal folds, short philtrum, anteverted ears	no
Palate anomalies (e.g. High p., cleft)	no	no	no	no	no
Cardiac anomalies	pulmonary anomalous venous return, interatrial defect	none	none (echocardiography at 3 y 10 m)	echocardiography not performed	no
Gastrointestinal problems	gastrostomy tube	gastrostomy tube	none	none	none
Urogenital/kidney anomalies	unilateral pyelectasy, moderate	none	none	none	none
Skeletal anomalies	11 pairs of ribs, scoliosis	11 pairs of ribs, scoliosis	none	X-ray not performed	none
Other findings	inguinal hernia	none	neonatal jaundice	pectus excavatum (mild), cafe-au-lait spot (1, leg)	thoracic gibbus