Table 1. Clinical findings and genetic test results in 23 patients with ID and MCA selected for targeted sequencing, chromosomal microarray (CMA) and/or exome sequencing (ES)

Case no.	Gender, age (years)‡	Neurological features	Growth and head features	Facial features	Extremities	Genitals/ reproductive problems	Others	Suspected diagnosis	Diagnostic test(s)	Molecular diagnosis and conclusion
P1	M, 25	Moderate ID	Dolichocephaly	Asymmetry, long face, macrognathia	-	-	Scoliosis	22q deletion syndrome	CMA	arr[GRCh37] 16p13.3(3609444_5325700)x3 interstitial gain of 1.72 Mb; Chromosome 16p duplication syndrome
P2	M, 21	Moderate ID	Short stature	Upslanting palpebral fissures, telecanthus	Short fingers and toes, proximal implantation of the thumbs	-	-	16p13 duplication syndrome	CMA	arr[GRCh37] 18q21.32q23(57536587_78014124)x1 Terminal loss of 20.48 Mb Chromosome 18q deletion syndrome
P3	F, 23	Moderate ID	Microcephaly	Prominent ears, downslanted palpebral fissures, bulbous nose	-	-	-	22q11.2 distal microdeletion syndrome	CMA	No aberration found
P4	F, 26	Moderate ID	Macrocephaly, overgrowth	Midface dysplasia	-	-	Strabismus, scoliosis	Microdeletion syndrome (not specified)	CMA Segregation analysis	[NM_001271043.2(NFIX):c.718C>T (p.(Gln240*))]; Malan syndrome (OMIM: 614753)
P5	F, 22	Moderate ID	Macrocephaly	Midface dysplasia	-	-	Strabismus, scoliosis	Microdeletion syndrome (not specified)	CMA Segregation analysis	[NM_001271043.2(NFIX):c.718C>T (p.(Gln240*))]; Malan syndrome (OMIM: 614753)
P6	F, 22	Severe ID, seizure	Macrocephaly	Midface dysplasia	-	-	Strabismus, scoliosis	Microdeletion syndrome (not specified)	CMA ES	[NM_001271043.2(NFIX):c.718C>T (p.(Gln240*))]; Malan syndrome (OMIM: 614753)
P7	M, 3 months	N/A	Left hemihypertrophy, macrocephaly	Macroglossia	-	-	ASD, Lymphedema, umbilical hernia	Beckwith-Wiedemann syndrome (BWS)	CMA	arr[GRCh37] 11p15.5p11.2(198510_44006144)x2 homozygous Region of homozygosity on chromosome 11p15, known as imprinting region of BWS
P8	M, 10	Moderate ID, speech delay	Microcephaly	Microtia, oligodontia	-	-	Scoliosis	9p deletion syndrome	CMA	arr[GRCh37] 9p24.3p22.2(203862_16917927)x1 -terminal loss of 16.71 Mb; Chromosome 9p deletion
P9	M, 3 months	N/A	Hydrocephalus	-	-	-	Spina bifida, oesophageal and anal atresia	Confirming cytogenetic results 46,XY, t(1;2)(q43;q10)	CMA	No aberration found
P10	F, 2 months	N/A	Right hemihypertrophy	Macroglossia, ear crease	-	-	-	Beckwith-Wiedemann syndrome	CMA	arr(1-22,X)x2 with of ~9.5 Mb homozygous stretch around chromosome 11 centromere – indicating upd(11)
P11	F, 5 months	N/A	Microcephaly, hypotonia	hypertelorism, flat nasal bridge, low set ears, high arched palate, micrognathia	Bilateral split hands and feet	-	-	Split-hand foot malformation	CMA	arr(18)x3 Trisomy 18
P12	F, 14	Moderate ID	Microcephaly	Sparse hair	-	Primary amenorrhea	Strabismus	Microdeletion syndrome	CMA	arr(1-22)x2 with large homozygous regions (144 Mb of autosomal genome, ~4.8%)
P13	F, 8	GDD	Short stature, microcephaly	Broad forehead, sparse eyebrows, epicanthus, thin upper vermilion	-	-	-	Angelman syndrome/ other microdeletion/ duplication syndromes	CMA	arr[GRCh37] 1q31.3q41(198099838_216201262)x3 interstitial gain of 18,10 Mb Chromosome 1q duplication syndrome
P14	F, 3	GDD, seizures, hypotonia	Short stature, microcephaly	Broad forehead, sparse eyebrows, epicanthus, thin upper vermilion	-	-	Hypothyroidism	Angelman syndrome/ other microdeletion/ duplication syndromes	ES	seq[GRCh37] dup(1)(q31.3q41) Chr1:g.(198231767_198233254)_ (216219934_216221875)dup; (heterozygous) interstitial gain of 18,10 Mb Chromosome 1q duplication syndrome
P15	F, 24	Moderate ID	-	Low anterior hairline, coarse face, synophrys	-	-	-	Coffin-Siris syndrome	ES	No causative pathogenic variants were detected
P16	M, 2	GDD	Brachycephaly	Protruding eyes, downturned mouth, prominent ears	Brachydactyly, tapering fingers, upper extremities contracture	-	Scoliosis, pectus excavatum-carinatum	Robinow syndrome, Pfeiffer syndrome, Antley-Bixler syndrome	ES	*FLNA*; ChrX(GRCh37): g.153588738T>A; NM_001456.3: c.3425A>T (p(Asp1142Val)); hemizygous, de novo. Causative of frontometaphyseal dysplasia (FMD1, OMIM #305620)
P17	F, 6 months	GDD	Craniosynostosis (brachycephaly)	Exophthalmia, ptosis	CTEV	-	ASD	Crouzon syndrome	ES	*FGFR2*; Chr10(GRCh37): g.123256215T>G; NM_000141.4: c.1694A>C; p.(Glu565Ala); heterozygous, de novo Pfeiffer syndrome (OMIM #101600)
P18	M, 11	Bilateral spastic hemiparesis, cranial nerve palsy (CN IX, CN X, and CN XXI)	-	-	-	-	Abnormal MRI results: symmetric lesion on bilateral putamen and caudate nucleus	Leigh disease Wilson disease	ES	*TTC19*; Chr17(GRCh37): g.15903283C>T; NM_017775.3:c.121C>T; p.(Gln41*), heterozygous, maternal; *TTC19*; Chr17(GRCh37): g.15907539del; NM_017775.3:c.544del; p.(Ser182fs), heterozygous, paternal Mitochondrial complex III deficiency, nuclear type 2 (OMIM #615157)
P19	F, 6 months	GDD	Craniosynostosis	High palate, ankyloglossia	-	-	Abnormal frontoparietal lobes (CT scan results), multiple kidney cysts	Syndrome related to craniosynostosis and GDD (not specified)	ES	No causative pathogenic variants were detected
P20	M, 25	Mild ID	-	Microphthalmia	-	Cryptorchidism	-	Lenz microphthalmia	Targeted sequencing:	No causative pathogenic variants were detected

									NAA10, *BCOR* genes	
P21	F, 24	Moderate ID	Short stature	Hypertelorism, epicanthus, macrognathia, microphthalmia	Hairy elbow, hands and feet	-	-	Wiedemann-Steiner syndrome	Targeted sequencing: *KMT2A* gene	No causative pathogenic variants were detected
P22	F, 1	GDD	Microcephaly	Hypertelorism, low set ear, long philtrum, micrognathia, cleft palate	-	-	Pectus excavatum, mild hearing impairment	Stickler syndrome	Targeted gene panel sequencing for Stickler syndrome	*COL11A1* (NM_080629.3) c.3204+1G>T p.(?); heterozygous Stickler syndrome type II (STL2, OMIM #604841)
P23	F, 4 months	GDD	Microcephaly	Hypertelorism, epicanthus, flat nasal bridge, deep philtrum, high palate, low set ears, micrognathia	-	-	Umbilical hernia, HCOM, mild pulmonary valve stenosis	Noonan syndrome	Targeted gene panel sequencing for Noonan syndrome	*RIT1* (NM_001256821.1) c.297T>G (p.Phe99Leu)) Noonan syndrome 8 (NS8, OMIM #615355)

[‡]Unless otherwise specified
Abbreviation: ASD: atrial septal defect CMA: chromosomal microarray CN: cranial nerve CTEV: congenital talipes equinovarus ES: exome sequencing GDD: global developmental delay HCOM: hypertrophic cardiomyopathy ID: intellectual disability N/A: not applicable/not available