Supplementary Table 1. Demographic and clinical information of the patients

Patient	Age	Sex	Growth parameters at birth	Growth parameters	Skeletal findings	Laboratory and radiological findings	Other findings	Parental consanguinity	Family history
P1	2 y	F	-**Birth week**: 35 -**Height**: 40 cm (<3p) -**Weight**: 2.1 kg (10-50p) -**Head circumference**: N/A	At 1 y 9 m; -Height: 71.5 cm (-3.75 SD) -Weight: 9.3 kg (-2.19 SD) -Head circumference: 49.5 cm (65p)	-Disproportionate short stature -Rhizomelic limb shortening -Brachydactyly in hands and feet -Broad and prominent forehead -Hypertelorism -Upslanted palpebral fissure -Broad and depressed nasal bridge -Midface hypoplasia -Trident hand -Redundant skin folds on long bones	-**Echocardiography** (3 y 4 m): Normal -**Wrist radiograph** (1 y 7 m): Trident hand, cupping and irregularity of the metaphyses at the distal ends of the radius and ulna **Bilateral lower limb and pelvic radiograph** (1 year 7 months): The iliac wings are squared, the pelvic cavity has a champagne-glass configuration, the sacrosciatic notches are narrow and pointed, and the long bones of the lower limbs show universal shortening, predominantly rhizomelic, with medial bowing, the distal metaphyses demonstrate deep cupping and irregular undulation, and there is a ball-and-socket appearance at the epiphyseal-metaphyseal junctions -**Bone age**: Normal	-Motor development delay -Respiratory distress -Sleep apnea	No	Father has achondroplasia
P2	1.5 y	M	-**Birth week**: 36 -**Height**: 43 cm (-3.18 SD) -**Weight**: 2.5 kg (10-50p) -**Head circumference**: N/A	At 1 y 4 m; -**Height**: 67 cm (-4.12 SD) -**Weight**: 8 kg (-2.64 SD) -**Head circumference**: 53.5 cm (>99p)	-Disproportionate short stature -Rhizomelic limb shortening -Brachydactyly in hands and feet -Broad forehead -Wide anterior fontanel -Glabellar hemangioma -Prominent forehead -Hypertelorism -Broad and depressed nasal bridge -Anteverted nostril -Midface hypoplasia -Trident hand --Redundant skin folds on long bones	-**Echocardiography** (8 m): Patent foramen ovale (PFO) and prominent trabeculations of the left ventricular myocardium	-Short extremities, macrocephaly and polyhydramnios noted in intrauterine period -Bronchitis in newborn period -Delay in motor and language development -Axial hypotonia	No	Father has short stature
P3	12 y	F	**Birth week**: Term -**Height**: N/A -**Weight**: 2.5 kg (10-50p) -**Head circumference**: N/A	At 12 y; -**Height**: 93 cm (-9.35 SD) -**Weight**: 20 kg (-4.41 SD) -**Head circumference**: 51 (-2.12 SD)	-Disproportionate short stature -Rhizomelic limb shortening -Brachydactyly in hands and feet -Pronounced kyphoscoliosis -Facial asymmetry -Midface hypoplasia - Prominent forehead -Broad and depressed nasal bridge -Anteverted nostril -Prominent ears -Uplifted earlobe -Long chin -Dental crowding -Trident hand -Extension limitation in the elbows and knees -Overlapped fingers in feet	-**Cranial CT** (6 m): External hydrocephalus -**Abdominal Ultrasound** (4 y 5 m): Normal - **Skeletal survey** (12 y): Bowing deformities of the radius and left tibia, short distal end of the left ulna, and bilaterally shortened femoral necks, bilateral distal femoral metaphyseal widening, and medial widening of the bilateral hip joint spaces, thoracic scoliosis with convexity to the left - **Spine MRI** (12 y): Spinal canal narrowing at the C1 and lumbar levels, increased lumbar lordosis, and angulation at the sacrococcygeal region, diffuse annular bulging at the L4–L5 and L5–S1 levels	-Intrauterine short stature -Breathing problem at age 12 -Sleep apnoea -Axial hypotonia -Delayed motor and language development -Delayed dentition	No	N/A
P4	18 y	M	**Birth week**: Term -**Height**: N/A -**Weight**: N/A -**Head circumference**: N/A	At 17 y 7 m; -**Height**: 137 cm (-6.17 SD) -**Weight**: 41 kg (-4.31 SD) -**Head circumference**: N/A	-Disproportionate short-trunk short stature - Increased arm span -Short 4-5th metatarsal -Scoliosis -Pectus carinatum -Short neck -Midface hypoplasia -Broad nose base -Thick lips	-**Thoracolumbar X-ray** (16 y 5 m): Increased lumbar lordosis, loss of height at the anterior–superior corners of the vertebral bodies, cortical irregularities of the vertebral endplates, deformed appearance of the bilateral femoral heads, and pseudoarthrosis between the bilateral femoral necks and the iliac bones -**Scoliosis radiograph** (17 y 9 m): Thoracic spine with minimal scoliosis concave to the left **Cranial CT** (16 y 8 m): Normal. **Long bone radiograph** (17 y 7 m): Deformed appearance of the femoral heads in both hip joints with pseudoarthrosis	-Macrocephaly noted in intrauterine period -Short stature in the newborn period -Developmental hip dysplasia	No	Father has similar findings
P5	4 y 9 m	F	-**Birth week**: 37 -**Height**: 45 cm (10p) -**Weight**: 2.7 kg (10-50p) -**Head circumference**: N/A	At 2 y 6 m; -**Height**: 82 cm (-2.73 SD) -**Weight**: 12.4 kg (25p) -**Head circumference**: 50 cm (85p)	-Relative macrocephaly -Disproportional short stature -Short extremities -Pes planus -Increased lordosis -Wide and prominent forehead -Webbed neck -Short neck	-**Hearing test** (4 y): Normal -**Skeletal survey** (4 y 7 m): Fragmented appearance of the femoral heads in both hip joints, with metaphyseal irregularity and widening at the femoral neck region - **Skeletal survey** (4 y 8 m): Medial displacement of the left femoral head, with superior displacement of the femoral neck and greater trochanter, the right femoral head appears small and fragmented	-Short extremities and stature noted in the intrauterine period	3rd degree	N/A
P6	16 y	M	**Birth week**: Term -**Height**: N/A -**Weight**: N/A -**Head circumference**: N/A	At 13 y 10 m; -**Height**: 131 cm (-4.18 SD) -**Weight**: 28.2 kg (-3.36 SD) -**Head circumference**: 52.5 cm (-2.17 SD)	-Short stature -Delayed bone age -Pronounced scoliosis -Thick eyebrows -Synophrys -Bilateral broad toes -Bilateral sandal gap	**Vertebral radiograph** (14 y 4 m): Scoliosis of the thoracolumbar region with the convexity to the right. - **Skeletal survey** (17 y): Loss of height in the anterior aspects of the C5–C7 vertebral bodies with abnormal cervical alignment; narrowed intervertebral disc spaces at the thoracic level with scoliosis convex to the right; loss of height in both femoral heads with short femoral necks; and a millimetric non-ossifying fibroma (NOF) at the medial aspect of the distal right femoral metaphysis		4th degree	N/A
P7	4 y	F	**Birth week**: 39 -**Height**: 41 cm (<3p) -**Weight**: 2.2 kg (<3p) -**Head circumference**: N/A	At 4 y; -**Height**: 84 cm (-4.43 SD) -**Weight**: 11.8 kg (-2.6 SD) -**Head circumference**: 51 cm (70p)	-Relative macrocephaly -Short stature -Increased lordosis -Pectus excavatum -Mild pes planus -Triangle face -Sparse hair -High anterior hairline -Wide and prominent forehead -Horizontal eyebrows -Short neck -Webbed neck -Mild laxity in hand fingers	-**Thyroid ultrasound** (4 y): Normal -**Echocardiography** (4 y): Normal - **Skeletal survey** (4 y): Normal -**Spinal MRI** (4 y): Normal -**Cranial MRI** (4 y): 5-mm nodular pathological signal change in the white matter of the left cerebellar hemisphere -**Abdomeinal ultrasound** (4 y): Normal	-Hypothyroidy -**Denver test** (4 t 11 m): Normal development for age with speech articulation difficulties	No	N/A
P8	14 y	F	**Birth week**: N/A **Height**: N/A -**Weight**: N/A -**Head circumference**:N/A	At 13 y 10 m -**Height**: 139,1 cm (-3.53 SD) -**Weight**: 43,3 kg (6p) -**Head circumference**: 56,5 cm (84p)	-Relative macrocephaly -Disproportionate short stature -Short trunk with increased arm span -Scoliosis -Clinodactyly of the 5th toe -Narrow forehead -Hypertelorism -Upslanted palpebral fissures -Prominent crus helix -Thin upper lip -Short neck -Hypertrichosis	**-Pelvic X-ray (14 y):** Irregular appearance of both acetabula; decreased height, irregularity, and fragmentation of both femoral heads; short femoral necks bilaterally; bilateral coxa vara appearance **Scoliosis X-ray (14 y):** Scoliosis convex to the right in the lower thoracic–lumbar region **Bone age (14 y):** Consistent with 15 years **Bilateral hip MRI (14 y):** Marked thinning of both epiphyses; flattening and heterogeneous signal intensity of both femoral heads compatible with bilateral sequelae of Perthes disease; mild bone marrow edema in both femoral heads; both acetabula broader and shallower than normal **Bilateral hip CT (14 y):** Shallow acetabula bilaterally; flattened femoral heads; subchondral cystic changes in both femoral heads; bilateral subluxations in femoroacetabular joints	-Normal motor and language development -Small for gestational age (SGA) at birth -Joint pain -Poor response to growth hormone therapy -Advanced bone age	No	N/A
P9	4 y 11 m	F	**Birth week**: 35 -**Height**: 40 cm (<3p) -**Weight**: 2.2 kg (25-50p) -**Head circumference**: N/A	At 4 y 4 m; -**Height**: 90.5 cm (-3.27 SD) -**Weight**: 13.6 kg (4.85p) -**Head circumference**: 47.5 cm (-1.93 SD)	-Short stature -Pectus carinatum -Short neck -Short 5th metacarps in right hand -Synophrys -Upslanted palpebral fissures - Columella below ala nasi - mild hypoplasic ala nasii -Thin lips -Skin laxity	-**Bone age** (4 y 9 m): Increased bone age (6 years) -**Skeletal survey** (4 y): Irregularities of the vertebral body surfaces at the thoracic and lumbar levels; shortening of the 2nd–5th metacarpals, more pronounced in the 5th metacarp of right hand; and sclerotic appearance of the epiphyses of the 2nd–4th distal phalanges in both hands	-	4th degree	N/A
P10	33 y	M	**Birth week**: Term -**Height**: N/A -**Weight**: N/A -**Head circumference**: N/A	At 31 y; -**Height**: 140 cm (-5.87 SD) -**Weight**: 45 kg (-3.72 SD) -**Head circumference**: 51 cm (-4.47 SD)	-Brachycephaly -Disproportionate short stature -Short extremities - Shortening of all metacarpals -Pectus excavatum -Kyphoscoliosis -Increased lordosis in neck -Narrow thorax -Facial asymmetry -Asymmetry of the mandible and maxilla on the left side due to bilateral developmental deficiency (based on dentistry evaluation). - Highly arched eyebrows -Ptosis - Broad nose base -High palate -Narrow mouth -Retrognathia - Posterior rotated ears -Restricted neck movements -Restricted foot dorsiflexion -Broad hallux -Sandal gap	-**Scrotal ultrasound** (30 y): Normal -**Bone densitometry** (31 y): Compatible with osteoporosis -**Hip MRI** (33 y): Non-displaced intertrochanteric fracture of the left femur with associated edema.	-Short stature noted in neonatal period -Amelogenesis imperfecta -Osteoporosis -Azoospermia -Excessive sweating -Xerostomia -Restrictive lung disease -Hypermetropia	3rd degree	N/A
P11	13 y	F	Birth week: Term -**Height**: N/A -**Weight**: N/A -**Head circumference**: N/A	At 12 y 3 m; -**Height**: 136 cm (-2.87 SD) -**Weight**: 26 kg (-3.37 SD) -**Head circumference**: 50 cm (-2.99 SD)	-Short stature -Micromyelia in upper limbs -Restricted jaw opening -Pseudocamptodactlia -Pes planus -Narrow forehead - Low anterior hairline -Blepharophimosis -Thick and broad eyebrows -Sad face appearance -Flat face -Posteriorly rotated ears -Low set ears - Overfolded helix -Pursed lips -Prognathism -Teeth anomalies -Webbed neck -Neck contractions	-**Scoliosis graphy** (12 y 3 m): Normal -**Bone age** (12 y 4 m): Normal		3rd degree	N/A
P12	10 y	F	**Birth week**: Term -**Height**: 45 cm (<3p) -**Weight**: 3.8 kg (85-90p) -**Head circumference**: N/A	At 7 y 9 m; -Height: 119 cm (11p) -Weight: NA -Head circumference: 49 cm (3.14 SD)	-Strabismus -Long eyelash - Broad eyebrows -Epicanthus in left eye -Sandal gap	-**Abdominal ultrasound** (8 y 4 m): Normal - **Skeletal survey** (8 y 4 m): Lumbar narrowing of the interpedicular distance toward the sacrum (suggestive of hypochondroplasia). -**Long bone graphy** (4 y): Enlarged distal femoral epiphyses -**Bone age** (9 y 3 m): 8.5 years	-Hearing loss -Delay in language development -Strabismus, retinal detachment -Borderline mental capacity -Frequent infection - Intoeing gait -Adenoid hypertrophy	3rd degree	N/A
P13	8 y	F	**Birth week**: Term -**Height**: N/A -**Weight**: N/A -**Head circumference**: N/A	At 7 y 7 m; -**Height**: 11 cm (-2.83 SD) -**Weight**: 25.9 kg (60p) -**Head circumference**: 52.5 cm (70p)	-Disproportionate short stature -Short extremities -Cubitus valgus - Tibial bowing -Medial deviation in feet -Broad forehead -Anteverted nostril -Midface hypoplasia	-**Skeletal survey** (7 y 6 m): Posterior arch fusion defect at S1, coxa vara in both femoral necks, metaphyseal widening and irregularity at the proximal and distal femoral ends, bowing of the femur and tibia, consistent with Schmid-type metaphyseal dysplasia. -**Bone age** (8 y): 8 years	- Waddling gait	No	N/A
P14	6 y 11 m	M	**Birth week**: 39w -**Height**: 51 cm (75p) -**Weight**: 3.2 kg (25p) -**Head circumference**: N/A	At 3 y 4 m; -**Height**: 88 cm (-2.77 SD) -**Weight**: 9.5 kg (-4.29 SD) -**Head circumference**: 46.2 cm (-2.83 SD)	-Short stature -Scoliosis -Round face -Sparse and broad eyebrows - Deep set eyes -Long eyelash - Bulbous nose tip -Thick lips -Sandal gap	-**Hearing test** (6 y): Normal -**Pelvis graphy** (2 y 1 m): The bony structures appear osteopenic with contour irregularities in the proximal femoral metaphyses (suggestive of metaphyseal dysplasia) -**Cranial CT** (3 y 4 m): Normal - **Skeletal survey** (5 y 10 m): Patchy digital impressions in the calvarium, multiple Schmorl nodes in the vertebral endplates, thoracic scoliosis with left convexity, shortened and thickened ribs with anterior cupping in the lower segments, absent coccyx; short and thick femoral necks with flattened femoral heads, irregularities in the proximal humeral and tibial metaphyses, distal femoral metaphyses, and acetabula with areas of sclerosis, and an increased cardiothoracic ratio -**Abdominal Ultrasound** (6 y 7 m): Normal -**Bone densitometry** (6y 7 m): Z score -1.7 -**Cranial MRI** (6 y 7 m): Millimetric nonspecific signal change in the supraventricular white matter of the left frontal lob	-Delay in motor and language development - **Denver test** (2 Y 15 d): delayed compared to peers. -Frequent infection -Chronic diarrhoea -Anaemia -Thrombocytopenia -Strabismus, astigmatism, hypermetropia, retinitis pigmentosa -Attention deficit hyperactivity disorder. -Hypotonia -Hyperactive deep tendon reflexes	3rd degree	Cousin of P14
P15	2y 6 m	M	-**Birth week**: 36w -**Height**: 47 cm (50p) -**Weight**: 3 kg (50-90p) -**Head circumference**: N/A	At 2 y 5 m; -**Height**: 88 cm (14p) -**Weight**: 12 kg (14p) -**Head circumference**: 47 cm (3.75p)	-3rd finger: 4 cm (3p) -Hypertelorism -Deep-set eyes - Columella below ala nasii -Prominent ears -Thin upper lip -Long philtrum - Carious teeth -Transverse crease in the chin - Ectopic left testis (located in inguinal canal)	-**Echocardiography** (10 m): Normal -**Cranial MRI** (2 y 5 m): Gliotic signal changes in the left corona radiata consistent with a previous ischemic event, mild prominence of both lateral ventricles, simple cyst in the pineal region - **Skeletal survey** (2 y 5 m): Schmorl nodes in vertebral bodies, irregularities in the femoral head metaphysis	-Delay in motor and language development -Hypotonia -Hearing loss in right ear -Frequent infection -Chronic diarrhoea -Neutropenia -Hypermetropia, retinopathy of prematurity (ROP), and strabismus in the left eye	5th degree	Cousin of P13
P16	6y 3 m	F	**Birth week**: Term -**Height**: N/A -**Weight**: 2.7 kg (10p) -**Head circumference**: N/A	At 5 y 4 m; -**Height**: 98 cm (-2,35SD) -**Weight**: 13 kg (-2,82SD) -**Head circumference**: 48 cm (-1,93SD)	-Disproportionate short stature -Short limbs (predominantly mesomelic) -Brachydactyly and syndactyly of hands and feet -Broad 2nd finger on the left hand -Hypoplastic nail on the left 2nd phalanx -Contractures of the left 3rd–4th phalanx -Broad thumbs and halluces -Pectus excavatum -Short neck -Coarse face -Flat facial profile -Frontal bossing -Hypertelorism -Wide palpebral fissures -Depressed and broad nasal bridge -Short nose -Gingival hyperplasia -Tented upper lip -Posteriorly rptated and inferiorly placed ears	**Skeletal survey (10 d):** Multiple thoracic vertebral anomalies and right-sided rib anomalies (butterfly vertebrae, hemivertebrae, fusion anomalies); mesomelic shortening of forearms; hypoplastic ulnae and radii; extra digit adjacent to left 2nd finger; hypoplastic right 2nd metatarsal; ectra metatarsal between 4th–5th metatarsals; hypoplastic left 3rd metatarsal and 2nd–3rd toes **Foot X-ray (2 y 3 m):** Syndactyly between 2nd–3rd toes bilaterally; accessory metatarsal between right 2nd–3rd metatarsals; dysmorphic proximal 4th metacarpal on the left; short left 3rd metacarpal **Skeletal survey (5 y 4 m):** Multiple segmentation anomalies in thoracic vertebrae (T12–11–9–8–7–5); fusion of right 8–9th rib posterior arches; thickened left 7th rib posterior arch; bilateral coxa valga; deformity and fusion of left 3–4th metatarsals; accessory bone at proximal right 2nd metatarsal; absent distal left 2nd phalanx **Abdominal ultrasound (5.5 y):** Normal.	-Disproportionate shortening of lower limbs during the antenatal period -Short stature in the neonatal period -Resuscitation and neonatal intensive care stay -Surgical correction of syndactyly between the 2nd–3rd fingers of the left hand -Motor and language developmental delay -Broad anterior fontanel	5th degree	N/A
P17	9y 8m	F	**Birth week**: Term -**Height**: 48cm (50p) -**Weight**: 2.8 kg (15-50p) -**Head circumference**: N/A	At 9 y 4 m; -**Height**: 119,5 cm (-2,44SD) -**Weight**: 29,5 kg (44p) -**Head circumference**: 51,6 cm (26p)	-Disproportionate short stature -Short limbs (micromelic) -Bracydactily -Short 5th metacarpal -Bilateral clinodactyly of the 5th fingers -Broad forehead -Thick and sparse eyebrows -Bilateral epicanthus -Anteverted nostrils -Thin upper lip	-**Cranial CT (7 y 7 m):** Suspected irregularity in the left temporo-occipital suture -**Bone age (9 y 4 m):** Consistent with 7.5 years -**Echocardiography (age 9 y)**: Normal	Normal motor and language developmental	No	Elder brother has similar findings

Supplementary Table 1. Continued

Patient	Age	Sex	Growth parameters at birth	Growth parameters	Skeletal findings	Laboratory and radiological findings	Other findings	Parental consanguinity	Family history
P18	9y 3m	F	**Birth week**: Term -**Height**: N/A -**Weight**: 2.7 kg (10p) -**Head circumference**: N/A	At 9 y 1 m; -**Height**: 118,8 cm (-2,45D) -**Weight**: 29,5 kg (44p) -**Head circumference**: 53 cm (65p)	-Disproportionate short stature -Short limbs (predominantly acromelic) -Short and broad fingers -Shortening of the 3rd, 4th, and 5th metacarpals -Shortening of the 4th and 5th toes -Pes planus and broad feet -Short neck -Increased lumbar lordosis -Bitemporal narrowing -Round face -Synophrys -Thin lips -Small mouth -Truncal obesity	-**Bone age (7 y 4 m):** Consistent with 8 years **Hand–wrist X-ray (7 y 4 m)**: Closed distal epiphyses; shortening of the 3rd, 4th, and 5th metacarpals in the left hand; shortening of middle phalanges relative to age; diaphyseal widening **Skeletal survey (9 y 1 m):** Shortening of the 3rd–5th metacarpals bilaterally, distal phalanges, and metatarsals (right: 3rd–4th; left: 4th); digital impressions in the cranium **Bone densitometry (9 y):** Z-score −0.2	-Short stature starting in the neonatal period -Slow growth velocity -Orthotic use due to pes planus -Normal motor and language development	No	N/A
P19	14	F	**Birth week**: Term -**Height**: 42 (<3p) -**Weight**: 1.7 kg (<3p) -**Head circumference**: N/A	At 14y -**Height**: 135 cm (-4,25SD) -**Weight**: 39,5 kg (-2,37SD) -**Head circumference**: 53,5 cm (10p)	-Short stature -Bilateral shortening of the 5th metacarpals (on inspection) -Shortening of the 4th–5th toes bilaterally -Broad feet -Broad forehead -Bilateral epicanthus -Mild midface hypoplasia	-**Bone age (14 y):** Consistent with 15 years **Cranial CT (14 y):** Nasal septum deviated to the right	-Primary amenorrhea -Strabismus surgery -Intelligence within normal limits -Normal motor and language development	Yes (Unknown degree)	N/A
P20	41 y	F	**Birth week**: N/A -**Height**: N/A -**Weight**: N/A -**Head circumference**: N/A	At 41y -**Height**: 160 cm (30p) -**Weight**: 68 kg -**Head circumference**: N/A	-Ptosis in the left eye -Bilateral cartilaginous ossification of the pinnae -Large ears -Hypoplasia of the left ala nasi -Erythematous lesions on the dorsum of the hands, lumbar region, and anterior trunk	-**Renal Doppler ultrasound (33 y):** Normal **Cranial CT (age 37 y):** Normal **Thoracic CT (age 38 y):** Multiple small sclerotic foci in the bones (compact bone islands?); type I hernia at the diaphragmatic hiatus; paraseptal and centriacinar emphysema in both lungs; bullae in the right lung; parenchymal bands with associated subsegmental atelectasis and peribronchial thickening in both lungs; fibrotic changes in the left lung; multiple calcified and non-calcified pulmonary nodules bilaterally **Neck CT (38 y):** Calcifications in the epiglottic and arytenoid cartilages with minimal narrowing of the airway at this level **Pelvic MRI (39 y):** Myoma uteri? bilateral follicular cysts in adnexa **Echocardiography (41 y):** Normal **Hearing test (41 y):** Bilateral mild sensorineural hearing loss **Paranasal sinus CT (41 y):** Calcifications in bilateral nasal alar and auricular cartilages; right middle turbinate of lamellar type, left middle turbinate of concha bullosa type, and bilateral pneumatization of pterygoid processes	-Cartilaginous ossification of the pinnae since childhood -Progressive widespread erythematous lesions in the body starting in the 30s -Thyroid papillary carcinoma (surgically treated) -Uterine myomas (surgically treated) -Hypertension (onset age: 30) -Infertility -Osteoarthritis in finger joints -Asthma -Recurrent otitis media -Laryngeal stenosis -Normal intelligence	3rd degree	Three sisters have similar findings
P21	1 y 6 m	F	**Birth week**: 30w 2d -**Height**: 34 cm (3p) -**Weight**: 1.2 kg (10-50p) -**Head circumference**: 27cm (50-90p)	at 19 days; (calculated according to corrected age: 32 weeks); -**Height**: 37 cm (3-10p) -**Weight**: 1.5 kg (50-90p) -**Head circumference**: 28.5 cm (50p)	-Right-sided pes equinovarus -Hypotonia -Skin laxity -Hypertrichosis on the back -Hypertelorism -Retrognathia	**Transfontanelle ultrasound (10 d):** Normal **Abdominal ultrasound (10 d):** Spleen length increased to 72 mm; bilateral pleural effusion; left-sided atelectasis **Electroencephalogram (1 m 1 w):** Mild active focal epileptic activity originating from central regions and right occipital area **Skeletal survey (1m 2 w):** Dense bone structures consistent with osteopetrosis; small hypodense lytic area in mid-diaphyseal region of right tibia (procedure-related); butterfly vertebra in the vertebral column **Orbital–cranial CT (1 m 20 d):** Skull and facial bones appear denser than normal; optic canal diameters below normal range for age **Visual evoked potential (VEP) test (1 m 20 d):** Bilaterally abnormal VEP responses **Echocardiography (3 m 10 d):** Pulmonary arterial hypertension, tricuspid insufficiency.	-Exitus at 3 months 12 days of age -Thrombocytopenia -Neutropenia -Reticulocytosis -Oligohydramnios -Bradycardia and apnea episodes -Prematurity -Osteopetrosis -Splenomegaly	5th degree	N/A
P22	69 y	F	**Birth week**: N/A -**Height**: N/A -**Weight**: N/A -**Head circumference**: N/A	At 69y -**Height**: 150 cm (<3p) -**Weight**: N/A -**Head circumference**: N/A	-Blue-gray sclerae -Beaked nose -Yellow and brittle teeth	**Pelvic CT (66 y):** Diffuse chronic sclerotic degenerative changes in the pelvic bones; anterior displacement and spondylolisthesis at S1–S2; transverse oblique insufficiency fractures, partially noncommunicating and mildly avulsed, more prominent on the left, involving both lateral plates at S1–S2; vacuum phenomenon in the inferior left sacroiliac joint due to degeneration; proximal diaphyseal region of the left femur with surgical screw fixation and associated density changes and clip artifacts. **Bone densitometry (69 y):** - anteroposterior spinal BMD values: T-score consistent with osteopenia, Z-score within normal range for age -Right proximal femoral neck BMD values: T-score and Z-score consistent with osteoporosis **Thoracic CT (69 y):** Osteophytic degenerative spurs at vertebral body corners; sequelae with contour irregularities in posterior ribs (right: 6–12; left: 6–7); increased heart size; atherosclerotic wall calcifications in the aorta, supra-aortic branch origins, and coronary arteries; bronchial wall thickening and mild peribronchial reticular density increase in both lungs; subsegmental atelectasis and parenchymal band formations in both lungs; well-circumscribed parenchymal nodule in the left lung; multiple subpleural and parenchymal nodules <5 mm in both lungs; hepatic lesions in segments 4, 5, and 2 consistent with hemangiomas.	-Recurrent femoral fractures with minor trauma and spontaneously (onset age: 62)	No	Grandchild has osteogenesis imperfecta. Cousins has pathologic fracture history
P23	11 y 9 m	M	**Birth week**: N/A -**Height**: N/A -**Weight**: N/A -**Head circumference**: N/A	N/A	-Joint hyperlaxity	**Echocardiography** (11 y 3 m): Normal **Bone densitometry** (11 y 7 m): Z-score −1.4 **Lumbar CT (11 y 9 m):** Normal **Lumbar MRI (11 y 9 m):** Normal **Skeletal survey (13 y):** Osteopenic bone structures; decreased vertebral body heights; coxa vara in the left femoral neck; increased sclerosis in the distal metaphysis of the left femur; fractures in both humeri, right scapula, and both femora **-Laboratory findings:** Alkaline phosphatase (ALP): Normal Procollagen-1-C-peptide (age 11 y 9 m): Normal	-Recurrent long bone fractures (onset age: 1 year)	3rd degree	N/A
P24	3 y 11 m	M	**Birth week**: 38w -**Height**: 48 cm (18p) -**Weight**: 2,4 kg (-213SD) -**Head circumference**: N/A	At 2,5y -**Height**: 83 cm (-2,13p) -**Weight**: 13,6 kg (45p) -**Head circumference**: 48,4 cm (18p)	-Short stature -Hypertelorism -Gray-blue sclerae -Downslanted palpebral fissures -Broad nasal bridge -Upturned ear lobules -Tented upper lip -Umbilical hernia	-**Abdominal ultrasound (1 y 11 m):** Normal -**Skeletal survey (2 y):** Bowing of both femurs -**Cranial MRI (2 y 2 m):** Mild prominence of the third and lateral ventricles, asymmetrically more on the left; diffuse and scattered millimetric hyperintense signal changes in periventricular white matter and centrum semiovale on T2W and FLAIR sequences (suggestive of periventricular leukomalacia? possible metabolic disorder?) -**Lower extremity X-ray (3 y 2 m):** Bowing of both femurs with proximal metaphyseal widening; displaced fracture line in the distal one-third of the left femoral diaphysis with a large plaster cast over the left lower extremity -**Bilateral femoral CT (3 y 2 m):** Displaced fracture line in the mid-diaphysis of the left femur; cortical thickening and irregularity medially proximal to the fracture; surrounding hematoma and edema; transverse radiolucent band in the distal metaphysis of the left femur **Echocardiography (3 y)**: Normal **Hearing test (3 y):** Bilateral moderate sensorineural hearing loss **Polysomnography (3 y, 10 m):** Central apnea; sleep-related movement disorders	-Femoral bowing detected antenatally -Femoral fracture with minor trauma and recurrent fractures (onset age: 3 years) -Gait disturbance **-Denver test (2 y 3 m):** developmental delay compared to peers -Hypothyroidism -Recurrent perianal abscesses -Factor VII deficiency -Apnea -Hearing loss	3rd degree	N/A
P25	11 m	F	**Birth week**: 38w -**Height**: 52 cm (90p) -**Weight**: 3,6 kg (50-90p) -**Head circumference**: N/A	At 1m 9d -**Height**: 57,5 cm (92p) -**Weight**: 5,1 kg (88p) -**Head circumference**: 40 cm (97p)	-Cranial shape anomaly (cloverleaf skull?) -Short neck -Frontal bossing -Shallow orbits -Proptosis -Hypertelorism -Downslanted palpebral fissures -Anteverted nostrils -Thin upper lip -Open mouth appearance -Tented upper lip -High-arched palate -Hypoplastic bilateral earlobes -Broad thumbs and halluces -Hemangioma at the back of the neck -Inverted nipples	**Fetal cranial MRI:** Increased occipitofrontal diameter (possible primary coronal suture pathology? craniosynostosis?) **Fetal echocardiography:** Normal **Transfontanelle ultrasound (1 day):** Corpus callosum appears thin **Abdominal ultrasound (1 d):** Normal **Thoracic CT (3 months):** Peripheral ground-glass opacities in posterior segments of upper and lower lobes bilaterally; findings suggestive of pulmonary edema or pneumonic infiltrations **Cranial MRI (10 m):** Calvarium irregular and asymmetric; increased anterior-posterior cranial diameter; hypoplastic falx; corpus callosum appears thin; bilateral parieto-occipital regions at the vertex with fluid-fluid level collections (~15 mm) containing hemorrhagic signals (subdural collections); hemosiderin deposition in right occipital lobe; small focal cystic lesion in subcortical white matter at right frontal prescentral gyrus; suprasellar cistern with significant indentation into the sella; mild perineural fluid increase around both optic nerves **Cranial CT (11 m, postoperation):** intracranial extra-axial air densities in anterior bilateral frontal lobes; postoperative changes in bilateral frontotemporal junctions; asymmetric enlargement of extra-axial cerebrospinal fluid spaces at the vertex level; chronic subdural effusion appearance at left lateral vertex	-Craniosynostosis detected antenatally -Failed at newborn hearing screening -Craniosynostosis surgery performed	No	N/A
P26	24 y	F	**Birth week**: N/A -**Height**: N/A -**Weight**: 3,3 kg -**Head circumference**: N/A	At 22 y -**Height**: 134 cm (-4,96SD) -**Weight**: 27 kg (-7,65SD) -**Head circumference**: 48,2 cm (-6,32SD)	-Short stature -Cachectic appearance -Brachydactyly -Scoliosis -Pes cavus -Short and broad halluces -Limited knee extension -Limited ankle dorsiflexion -Midface hypoplasia -Sparse frontal hair -Flat forehead -Prominent supraorbital ridge -Hypertelorism -Proptosis -Prominent nasal bridge -Columella below ala nasi -Beaked nose -Low-set posterior rotated ears -Short philtrum -High-arched palate -Yellowish and irregular teeth	**Lower abdominal MRI (22 y):** Uterine aplasia **Skeletal survey (24 y):** patient with a history of craniosynostosis surgery, temporoparietal craniectomy defect and postoperative opening at the coronal suture; brachycephaly; relative lucent areas in the calvarium associated with digital impressions and deepened sella on skull X-rays; straightened cervical lordosis; mild rotoscoliosis in the thoracolumbar region; bilateral genu valgum deformity; relatively distal positioning of medial and lateral malleoli in both ankles **Thoracic CT (24 y):** Normal	-Developmental delay -Craniosynostosis surgery at age 3 -Neurotrophic keratitis, entropion, vision loss in the left eye -Primary amenorrhea	3rd degree	Mother and siblings have similar findings
P27	8 y	M	**Birth week**: 40 w -**Height**: N/A -**Weight**: 3 kg (10p) -**Head circumference**: N/A	At 7 y 4 m -**Height**: 126 cm (69p) -**Weight**: 24,3 kg (59p) -**Head circumference**: 51 cm (20p)	-Brachycephaly -Narrow fontanelle -Mild facial asymmetry -Downslanted palpebral fissures -Wide palpebral fissures -Ptosis in the left eye -Long eyelashes -Columella below ala nasi -Bilateral syndactyly of the 2nd–3rd toes -Bilateral sandal gap	-**Cranial CT (1 m 13 d):** Partial closure of the coronal sutures bilaterally; brachycephaly; Wormian bone between the lambdoid sutures -**Cranial MRI (3 y 7 m):** Calvarium with brachycephalic appearance (possible bicoronal synostosis?); bilateral frontal lobes relatively small -**Bone age (7 y 4 m):** Consistent with 7–7.5 years -**Electroencephalogram (1.5 y):** Sharp and sharp-slow wave paroxysms originating synchronously in the bilateral centrotemporal regions, more prominent on the left centrotemporal side	-Craniosynostosis surgery -Epilepsy -Mild developmental delay	No	Mother has similar findings
P28	1.5 y	M	**Birth week**: 35 w 2 d -**Height**: N/A -**Weight**: 2,4 kg (10-50p) -**Head circumference**: N/A	At 11 m -**Height**: 59 cm (-5SD) -**Weight**: 5 cm (-5SD) -**Head circumference**: 34 cm (-8.6 SD)	-Short stature Microcephaly -Acrobrachycephaly -Prominent metopic ridge -Brachydactyly -Partial cutaneous syndactyly of the right 2nd–3rd fingers -Long and flat forehead -Periorbital edema -Hypertelorism -Proptosis -Left ear simple and cup-shaped -Edema in hands and feet -Single transverse palmar crease bilaterally -Overlapping toes -Hypotonia -Hypospadias -Sacral dimple	-**Skeletal survey (3 m):** Superior extension of the anterior cranial vault; increased acetabular index angle on the left side **Cranial CT (10 m):** Synostosis of the sagittal, metopic, and coronal sutures; lambdoid sutures remain open; cranial appearance oxycephalic with decreased anterior–posterior diameter; poorly defined hypodense areas in the mesencephalon, pons, bilateral medial thalami, and cerebral peduncles (suggestive of myelinolysis?); cavum septum pellucidum et vergae variation; mild decreased density in the subependymal white matter **Cranial and diffusion MRI (11 m):** Osmotic demyelination syndrome (central pontine–extrapontine myelinolysis); triventricular hydrocephalus; oxycephalic appearance consistent with craniosynostosis **Whole abdominal and renal color Doppler ultrasound (11 m):** Echogenic foci measuring 3–4 mm in both kidneys, suggestive of renal calculi **Echocardiography (1 y):** Hypertrophic cardiomyopathy; mild pulmonary stenosis; pulmonary artery dilatation; mild mitral regurgitation	-Exitus at 1.5 years of age -**Antenatal findings:** microcephaly, intrauterine growth restriction (IUGR), and increased nuchal translucency (NT) -Developmental delay -Hyponatremia	No	Father and dizygotic twin have similar findings
P29	1 y 8 m	F	**Birth week**: 37 w **Height**: N/A -**Weight**: 3,2 kg (50-90p) -**Head circumference**: N/A	At 1 y 4 m -**Height**: 77,5 cm (25p) -**Weight**: 11,8 kg (87p) -**Head circumference**: 50,3 cm (99p)	-Macrocephaly -Cranial shape abnormality (craniosynostosis?) -Duplicated thumb on the left hand -Preaxial polydactyly -Bilateral preaxial polydactyly of the feet -Broad left hallux -Bilateral pes equinovarus -Alopecic patch in the occipital region -Facial asymmetry -Frontal bossing -Broad forehead -Hypertrichosis from the forehead to the nose -Ectopic hair growth near both eyes -Microphthalmia in the left eye -Hypertelorism -Broad and depressed nasal bridge -Bilateral low-set ears -Cutaneous syndactyly in the left hand -Umbilical hernia -Abnormal hair growth on the shoulders and ankles -Hirsutism -Reticular hypo- and hyperpigmented areas	**Brain CT (1.5 m):** Agenesis of the corpus callosum? Leukomalacic changes? **Hearing test (6 m):** Severe sensorineural hearing loss in the right ear, profound sensorineural hearing loss in the left ear **3D Brain CT (7 m):** Mild narrowing of the anterior–posterior cranial diameter; frontal bone prominence anteriorly; other cranial sutures open; maxillary bone hypoplasia; prominent subarachnoid spaces in both frontal regions; subdural collection in the left frontal subarachnoid space; prominent frontal horns of both lateral ventricles; posterior horns of both lateral ventricles parallel in orientation (colpocephalic appearance); cavum septum pellucidum variation; corpus callosum not clearly visualized **Electroencephalogram (1 y 3 m):** Active focal epileptic disorder **Echocardiography (2 y):** Normal **Whole abdominal ultrasound (2 y):** Normal	-Agenesis of the corpus callosum detected antenatally -Congenital glaucoma -Bilateral severe sensorineural hearing loss -Phototherapy in the neonatal period -Developmental delay -Small and early-closed fontanelle -Chronic constipation	No	N/A
P30	11 m	F	**Birth week**: 39 w 3 d **Height**: 44 cm (-2,69 SD) -**Weight**: 3,1 kg (10-50p) -**Head circumference**: 35 cm (50-90p)	N/A	-Bilateral short and curved tibiae -Dimples over both tibiae -Fibular aplasia -Oligosyndactyly in the left hand -Oligodactyly in both feet -Minimal sacral dimple	-**Skeletal survey (2 m):** Bilateral tibiae shorter than normal; bilateral fibular aplasia; 4 metatarsals and phalanges in the right foot; 3 metatarsals and phalanges in the left foot; 4 metacarpals in the left hand -**Abdominal ultrasound (2 m):** Normal -**Pelvic ultrasound (2 m):** Normal -**Spinal ultrasound (2 m):** Normal -**Thyroid ultrasound (3 m):** Normal -**Echocardiography (11 m):** Normal	-Limb anomalies detected at birth	3rd degree	N/A

Supplementary Table 1. Continued

Patient	Age	Sex	Growth parameters at birth	Growth parameters	Skeletal findings	Laboratory and radiological findings	Other findings	Parental consanguinity	Family history
P31	15 y	M	**Birth week**: 37 w **Height**: N/A -**Weight**: 71 kg (<<3p) -**Head circumference**:N/A	At 14 y 6 m -**Height**: 151 cm (-2,16p) -**Weight**: 35,9 kg (-2,7 SD) -**Head circumference**: 53 cm (-2,13 SD)	-Short stature -Brachycephaly -Brachydactyly -Bilateral clinodactyly of the 5th fingers -Camptodactyly -Bilateral broad halluces -Medial deviation of the 3rd toe on the left foot -Scoliosis -Broad forehead -Flat face -Facial asymmetry? -Deep-set eyes -Broad nasal tip -Short philtrum -Thin lips -Hypoplasia of the 4th toenail on the left foot	**-Hearing test (15 y):** Mild sensorineural hearing loss in the left ear; severe mixed hearing loss in the right ear **-Bone age (14 y 3 m):** Consistent with 18 years **Portal system Doppler ultrasound (14 y 3 m):** Normal **Scrotal color Doppler ultrasound (14 y 3 m):** Cyst in the left epididymis measuring 21 × 11 mm **Scoliosis X-ray (14.5 y):** Cervicothoracic scoliosis convex to the right; mild curvature convex to the left at the thoracolumbar level	-Intrauterine growth restriction (IUGR) -Growth retardation -Bilateral undescended testes, orchiopexy performed -Motor and mental developmental delay -Autism -Delayed dentition (18 months) -Delayed fontanelle closure	No	N/A
P32	15 y 6 m	M	**Birth week**: N/A **Height**: N/A -**Weight**: 2,6 kg -**Head circumference**: N/A	At 14 y -**Height**: 144 cm (-2,67 SD)-**Weight**: 36 kg (-2,28 SD) -**Head circumference**: 54 cm (10p)	-Short stature -Borderline rhizomelic shortening in the upper limbs -Joint contractures Increased thoracic kyphosis and lumbar lordosis -Lateral deviation of bilateral halluces -Mild malar hypoplasia -Bilateral ptosis -Bilateral prominent and low-set ears -Thick lips -Dry skin with widespread lesions -Nail hypoplasia of the 2nd and 5th toes on the left foot	**-Bilateral temporomandibular joint MRI (13 y):** Irregular cortical surface at the superior aspect of both mandibular condyles; hypoplastic and irregular appearance of condylar fossae; limited movement in the open-mouth position; osteophytic spurs at the lateral aspects of both mandibular condyles **-Upper abdominal ultrasound (13 y):** Normal **Bone densitometry (13.5 y):** Z-score −1.4 **Bone age (14 y):** Consistent with 12.5 years **Skeletal survey (ages 13 & 16 y):** Erlenmeyer flask deformity at proximal tibiae bilaterally; ribs thicker than normal; posterior narrowing at C5–C6; short and thick clavicles; shortened femoral necks bilaterally; enlarged femoral heads with epiphyseal height loss; widened hip joint spaces; coxa magna deformity; mild cortical irregularity at proximal diaphysis of left femur; mild widening of diaphyseal regions of short tubular bones in the hands; Schmorl's nodes and mild height loss between L3–S1 vertebral endplates **Right knee MRI (15 y):** Subchondral millimetric cyst in the medial condyle; subchondral bone signal changes and chondral irregularity in the lateral condyle, consistent with stage II osteochondritis dissecans (OCD) **Lumbar MRI (15 y):** Discopathy	-Limitation of joint mobility -Muscle atrophy in the legs -Atopic dermatitis -Mild motor developmental delay	3rd degree	Elder brother has similar findings
P33	15 y	F	**Birth week**: 39 w **Height**: 50 cm (50p) -**Weight**: 3,3, kg (50p) -**Head circumference**: N/A	At 14 y 8 m -**Height**: 149 cm (-2,08 SD) -**Weight**: N/A -**Head circumference**: 56,2 cm (73p)	-Disproportionate short stature -Limb shortening (rhizomelic and mesomelic) -Relative macrocephaly-Synophrys-Micrognathia	**-Skeletal survey (14 y 8 m):** Normal **-Bone age (14 y 5 m):** Consistent with 15 years	-Normal motor and language development -Growth hormone therapy between ages 11–13 -Vitiligo	No	Sister of P34. Mother has short stature
P34	9 y	F	**Birth week**: 42 w **Height**: 51 cm (75p) -**Weight**: 3,5 kg (50-75p) -**Head circumference**: N/A	At 14 y 8 m -**Height**: 95 cm (-2,79 SD) -**Weight**: 15 kg (10p) -**Head circumference**: 49 cm (16p)	-Disproportionate short stature -Limb shortening (rhizomelic and mesomelic) --Synophrys --Transverse crease in the chin -Pes planus, -Broad halluxes	**Upper abdominal ultrasound (4 y 4 m):** Normal **Echocardiography (6 y 8 m):** Normal **Pelvic ultrasound (7 y 10 m):** Normal **Skeletal survey (9 y):** Decreased posterior vertebral body height at the lumbar level (more prominent inferiorly); anterior wedging of vertebral bodies at the cervical level **Bone age (9 y 7 m):** Consistent with 8 years	-Normal motor and language development	No	Sister of P33. Mother has short stature
P35	9 y	F	**Birth week**: term -**Height**: N/A -**Weight**: 2,8 kg (10-50p) -**Head circumference**: N/A	At 5 y -**Height**: 105 cm (12p) -**Weight**: 28 kg (98p) -**Head circumference**: 50,5 cm (38p)	-Obesity (BMI: 99th percentile) -Disproportionate short stature -Brachydactyly -Limb shortening (predominantly acromelic) -Shortening of the 4th and 5th metacarpals -Shortening of the 4th and 5th metatarsals on the right foot -Increased lumbar lordosis -Round face -Full cheeks -Epicanthus -Small mouth -Uplifted earlobes	**-Skeletal survey (5 y):** Blunted appearance of hand bones and widening of diaphyses of tubular hand bones; blunted appearance of the first metatarsals; possible hypochondroplasia? **Array CGH analysis (5 y):** Xp22.31 duplication **Bone age (5 y 10 m):** Consistent with 6 years 10 months **EEG (6 y 7 m):** Active focal epileptic disorder **Brain MRI (6 ym):** Cerebellar tonsils extending 5 mm below the foramen magnum **Thyroid ultrasound (9 y):** Normal **Abdominal ultrasound (9 y):** Normal **Bone age (10 y):** Consistent with 13.5 years	-Mild motor and language developmental delay	No	Sister of P36. Mother has short stature
P36	13 y	M	**Birth week**: term -**Height**: N/A -**Weight**: 2,8 kg (10-50p) -**Head circumference**: N/A	At 5 y -**Height**: 129,4 cm (9p) -**Weight**: 32 kg (50p) -**Head circumference**: 51 cm (4p)	-Disproportionate short stature -Limb shortening (predominantly acromelic) -Brachydactyly -Shortening of the 4th and 5th metacarpals -Shortening of the 4th and 5th metatarsals on the left foot -Round face -Synophrys -Epicanthus -Anteverted nostrils -Diastema -Upturned earlobes -Cup-shaped ears	**-Bone age (10 y):** Consistent with 13.5–14 years **Hand–wrist X-ray (10 y):** Hands appear short and stubby; diaphyseal widening of tubular bones; shortening of the 4th and 5th metacarpals **Brain MRI (11.5 y):** Millimetric, nonspecific pathological signal changes in the left supraventricular white matter **EEG (11.5 y):** Normal	-Mild motor and language developmental delay -Attention deficit hyperactivity disorder	No	Sister of P35. Mother has short stature

ALT: Alanine aminotransferase; aPTT: Activated partial thromboplastin time; AST: Aspartate aminotransferase; BMD: Bone mineral density; CT: Computed tomography; d: Day; M: Month; MRI: Magnetic resonance imaging; N/A: Not applicable; P: Percentile; PFO: Patent foramen ovale; ROP: Retinopathy of prematurity; SD: Standard deviation; w: Week; y: Year, SD: Standard deviation

Supplementary Table 2. ACMG and *in silico* predictions for the novel variants in P6, P9, P11-15, P17, P19, P24, and P28

Patient	Variant	Zygosity	Variant classification	ACMG criteria	Revel	AlphaMissense	SIFT	DANN	SpliceAI
P6	*COL2A1*:NM_001844.5:c.2095G>A (p.Gly699Ser)	Het	LP	PS2,PM2,PP2,PP3, PM5_P	Deleterious	Deleterious	Deleterious	Deleterious	-
P9	*PAPSS2*:NM_001015880.1:c.520+2T>A	Hom	LP	PVS1_M,PM2, PP5_M, PM3_P	-	-	-	-	Splice-Altering / strong
P11	*HSPG2*:NM_005529.7:c.4948T>G (p.Cys1650Gly)	Hom	LP	PM2,PP3, PM3_P, PP4_M	Deleterious	Deleterious	Deleterious	Deleterious	Splice-Altering / strong
P12	*COL9A1*:NM_001851.4:c.1852C>T (p.Arg618Ter)	Hom	Pathogenic	PVS1,PM2,PM3_P	-	-	-	Deleterious	-
P13	*COL10A1:* NM_000493.4:c.1766T>C (p.Phe589Ser)	Het	LP	PM1,PM2,PP3,PP4	Deleterious	Deleterious	Uncertain	Deleterious	-
P14	*EFL1*:NM_024580:c.277T>C (p.Ser93Pro)	Hom	LP	PM2,PP3,PM3_P, PP4,PP1	Deleterious	Deleterious	Uncertain	Deleterious	-
P15	*EFL1*:NM_024580:c.277T>C (p.Ser93Pro)	Hom	LP	PM2,PP3,PM3_P, PP4,PP1	Deleterious	Deleterious	Uncertain	Deleterious	-
P17	*FBN1*:NM_000138.4:c.5285G>A p.(Gly1762Asp)	Het	LP	PM2,PP2,PM5_P,PP1	Uncertain	Deleterious	Uncertain	Deleterious	-
P19	*CCDC8*:NM_032040.5:c.84_85delTA (p.Lys29AlafsTer118)	Hom	LP	PVS1,PM2,PM3_P	-	-	-	-	-
P24	*TMEM38B*:NM_018112.3:c.240_247dup (p.Ile83ThrfsTer21)	Hom	Pathogenic	PVS1,PM2,PM3_P,PP4	-	-	-	-	-
P28	*TWIST1*:NM_000474.4:c.464A>C (p.Tyr155Ser)	Het	LP	PM2,PM1_P,PP1,PP2,PP3	Deleterious	Deleterious	Deleterious	Deleterious	-

Supplementary Table 3. Clinical findings of patients with biallelic variants in the *PAPSS2* gene reported in the literature

Parameters	P9 (present study)	P1 (Iida et al., 2013)	P2 (Iida et al., 2013)	P7 (Iida et al., 2013)	P8 (Iida et al., 2013)	13 patients (Iida et al. 2013)	6 patients (Miyake et al., 2012)	P1 (Handa et al. (4), 2016)	18 patients (Bownass et al., 2019)
Variant (NM_001015880)	c.520+2T>A	c.227T>A/ c.520+2T>A	c.227T>A/ c.520+2T>A	c.520+2T>A	c.520+2T>A	Variable	Variable	c.1078del	Variable
Age (years old)/Sex	4.5/F	14/F	14/M	9/F	5/F	-	-	10/M	-
Height (cm)	90.5 (-3.27 SD)	130 (-5.12 SD)	137 (-3.6 SD)	107 (-4.32 SD)	92 (-3.73 SD)	-	-	124.2 (-2.26)	-
Neurodevelopmental delay	-	-	-	-	-	0/13	0/6	N/A	1/18*
Short trunk	-	+	+	+	+	12/13	6/6	+	18/18**
Short neck	+	+	+	+	+	6/13	6/6	N/A	N/A
Metacarpal shortening	+	+	-	+	+	10/13	6/6	N/A	5/13
Pectus anomalies	+	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1/18
Platyspondyly	-	+	+	+	+	13/13	N/A	+	14/17
Irregular vertebral end-plates	+	+	+	+	+	13/13	6/6	+	14/17
Other vertebral anomalies	-	+	+	+	+	13/13	6/6	+	14/17
Scoliosis	-	+	+	+	+	13/13	1/6	N/A	4/14
Kyphosis	-	-	-	-	+	2/13	3/6	N/A	7/17
Advanced bone age	+	-	-	+	-	5/13	4/4	N/A	4/12
Metaphyseal anomalies	-	+	+	+	+	9/13	4/6	N/A	10/16
Short femoral neck	+	+	+	+	+	13/13	6/6	N/A	8/16
Androgen excess	-	+	-	-	-	3/13	0/6	+	2/10
Epiphyseal sclerosis	+	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

*Pointing learning difficulties
**8 patients initially had short limbs and later had short trunks
F: Female, M: Male, N/A: Not applicable, SD: Standard deviation

Supplementary Table 4. Clinical findings of patients with biallelic variants in the *SLC10A7* gene reported in the literature

Parameters	P10 (present study)	P17 (Ashikov et al. (28), 2018)	P33 (Ashikov et al. (28), 2018)	P32 (Ashikov et al. (28), 2018)	P39 (Ashikov et al. (28), 2018)	6 patients (Dubail et al. (29), 2018)	H1 (Laugel-Haushalter et al., 2019)
Variant (NM_001029998)	c.335G>A	c.722-16A>G/ c.335G>A	c.722-16A>G/ c.335G>A	?*	?*	variable	c.908C>T
Age/Sex	31/M	31/M	33/F	24/M	8/M	-	7/F
Height (cm)	140 (-5.87 SD)	? (-7 SD)	? (-5.3 SD)	? (-3 SD)	? (-4 SD)	Short stature 6/6	106 (−3 SD)
Intellectual deficiency	-	+	+	+	+	N/A	-
Hearing loss	-	+	+	-	+	1/6	N/A
Short limbs	+	N/A	N/A	N/A	N/A	4/6	N/A
Metacarpal shortening	+	+	N/A	N/A	N/A	2/6	+
Pectus anomalies	+	-	-	+	-	-	N/A
Narrow thorax	+	-	-	-	-	1/6	N/A
Intrauterine growth retardation	+	N/A	N/A	N/A	N/A	6/6	+
Amelogenesis imperfecta	+?[a]	+	+	+	+	6/6	+
Kyphoscoliosis	+	+	+	+	-	6/6	+
Vertebra abnormalities	N/A	N/A	N/A	+	+	4/6	+
Osteoporosis	+	-	+	-	-	N/A	N/A
Multiple joint dislocations/joint hypermobility	-	-	-	+	-	6/6	-
Advanced bone age	N/A	N/A	N/A	N/A	N/A	6/6	+
Mandibular hypoplasia	+	-	+	-	-	N/A	N/A
Micrognathia/retrognathia	+	-	+	-	+	6/6	+
Genu valgum	-	+	+	-	-	2/6	+
Epiphyseal/metaphyseal anomalies	N/A	N/A	N/A	N/A	-	3/6	-

*No variant but loss of SLC10A7 mRNA.
F: Female, M: Male, N/A: Not applicable