Supplementary

Table S1 Main results of the proband's serum biochemical examination

Items	Value	Reference range
Enzymes		
ALT (U/L)	20	9.0–50.0
AST (U/L)	68	15.0–45.0
AST/ALT ratio	3.4	0.23–2.47
ALP (U/L)	135.6	45.0–125.0
GGT (U/L)	11.3	10.0–60.0
LDH (U/L)	365.7	100.0–240.0
CK (U/L)	85	24.0–194.0
CK-MB (IU/L)	36.3	0.0–25.0
Metabolism		
Bilirubin, total (μmol/L)	4.4	2.0–22.0
Bilirubin, direct (μmol/L)	0.8	0.0–6.0
Bilirubin, indirect (μmol/L)	3.6	0.0–16.0
Serum proteins		
Protein, total (g/L)	77.1	65.0–85.0
Hemoglobin (g/L)	118	110–160
Albumin (g/L)	48.8	40.0–55.0
Globulin (g/L)	28.3	20.0–40.0
A/G ratio	1.72	1.2–2.4
Serum electrolytes		
Cl^- (mmol/L)	102	96–108
Ca^{2+} (mmol/L)	1.28	1.05–1.29
Na^+ (mmol/L)	143	135–145
K^+ (mmol/L)	4.26	3.5–5.5
HCO_3^- (mmol/L)	22.8	22.0–27.0
Kidney function		
BUN (mmol/L)	4.31	2.86–8.20
Creatinine (μmol/L)	19.7	49.0–97.0
Uric acid (μmol/L)	135.1	149.0–416.0
Thyroid function		
TSH (μIU/mL)	1.93	0.35–5.5
Triiodothyronine (nmol/L)	3.25	0.89–2.44
Thyroxine (nmol/L)	135.5	62.68–150.84

ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, gamma-glutamyl transferase; LDH, lactate dehydrogenase; CK, creatine kinase; CK-MB, creatine kinase-myoglobin binding; A/G, albumin/globulin; BUN, blood urea nitrogen; TSH, thyroid-stimulating hormone.

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Table S2 ROH regions detected by CMA

ROH regions	Size (kb)	Genes	Inherited pattern
4q31.21-q32.1	14417	*SLC10A7*	AR
		FGA	AR
		FGB	AR
		FGG	AR
		TRIM2	AR
		LRBA	AR
		LRAT	AR
		GAB1	AR
		MMAA	AR
		MAB21L2	AD/AR
		TDO2	AR
		GUCY1A3	AR
1p21.3-p12	19092	*AGL*	AR
		AMPD1	AR
		IGSF3	AR
		PTPN22	AD/AR
		AMPD2	AR
		SLC35A3	AR
		TSHB	AR
		CDC14A	AR
		NGF	AR
		GPR88	AR
		SARS	AR
		COL11A1	AR
		CASQ2	AR
		LRIG2	AR
		RNPC3	AR
		SLC16A1	AD/AR
		GPSM2	AR
		ALX3	AR
		AP4B1	AR
		DBT	AR
		TAF13	AR
		SASS6	AR
		DRAM2	AR
22q12.2-q13.31	16052	*LARGE1*	AR
		XPNPEP3	AR
		NCF4	AR
		CYP2D6	AR
		TRIOBP	AR
		TXN2	AR
		NDUFA6	AR
		SLC5A1	AR
		CSF2RB	AR
		TRMU	AR
		DNAL4	AR
		ACO2	AR
		MCM5	AR
		FBXO7	AR
		PLA2G6	AR
		NAGA	AR
		TMPRSS6	AR
		CYB5R3	AR
		IFT27	AR
		TNFRSF13C	AR
		ADSL	AR

ROH, runs of homozygosity; CMA, chromosome microarray analysis; AR, autosomal recessive; AD, autosomal dominant.

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Appendix 1

DNA extraction

Peripheral blood was collected from the members of the enrolled family. Total genomic DNA was isolated by using QIAamp® DNA Blood Mini Kit (Qiagen GmbH, Germany) according to the manufacturer's protocol. DNA purity and concentration were further measured by a NanoDrop spectrophotometer.

Chromosome microarray analysis (SNP-array)

Detection of genomic CNVs was performed with AffymetrixCytoScan HD (Affymetrix, Santa Clara, USA) following the manufacturer's instructions. Array results were visualized and analyzed by Chromosome Analysis Suite software (Affymetrix GeneChip Convert Console, Santa Clara, USA) and Chromosome Analysis Suite Version 2.0.0. Log2 ratio and B allele frequency (BAF) values were plotted along chromosomal coordinates, allowing the detection of both copy number changes and copy neutral ROH. The size threshold for CNVs analysis was set at >50 kb for gains, >25 kb for losses, and >10 Mb for loss of heterozygosity. Data interpretation followed the ACMG guideline.

Whole exome sequencing

For whole-exome sequencing of the proband, 1~3 μg genomic DNA was used for fragmentation, and DNA library construction was prepared according to the manufacturer's protocols (Agilent Technologies, Inc., Santa Clara, CA, USA). Genomic DNA was randomly fragmented to an average size of 150–220 bp by Covaris® S220 sonicator (Thermofisher, MA, USA). DNA fragments were end-repaired and phosphorylated, followed by A-tailing and ligation at the 3' ends with paired-end multiple indexing adaptors. The quality of the DNA library was assessed using Life Qubit Fluorometer 3.0 and Agilent 2200 TapeStation Instrument (Agilent Technologies, Inc.). Sequencing was performed on the Illumina HiSeq X-ten (Illumina, CA, USA) in high-output mode with 150 bp paired-end reads. The original sequencing data were analyzed by FastQC software. Reads were aligned to the human reference sequence (GRCh37/hg19) using the Burrows-Wheeler Aligner tool (v0.7.15-r1140). The Genome Analysis Toolkit tool (v3.7-0) was used for base quality-score recalibration, calling, and filtering variants. Data were annotated with the Annovar and VEP software. Data interpretation followed the ACMG guideline.

Sanger sequencing

The *PLA2G6* c.1778C>T variant was confirmed by Sanger sequencing. Primers that were designed by Primer3 software according to information on the mutation site. Forward primer, ccacctatcccgaacagagg. Reverse primer, ctggtggaaggcaggtacag. Amplification of primers was performed using polymerase chain reaction (PCR), then screened by Mutation Surveyor. The genomic DNA samples of the enrolled family were analyzed by Sanger sequencing to determine variant status.

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