neurogenetics (2022) 23:179–185
https://doi.org/10.1007/s10048-022-00691-8

ORIGINAL ARTICLE

Identification of a 5 bp duplicate in the *AP1S2* gene of an individual with X-linked intellectual disability

Dengna Zhu[1] · Mingmei Wang[1] · Yiran Xu[1,2] · Jiamei Zhang[1] · Fan Yang[3] · Zuozhen Yang[3]

Received: 26 December 2021 / Accepted: 25 March 2022 / Published online: 7 April 2022

Abstract

Adaptor-related protein complex 1 subunit sigma 2 (AP1S2) is a subunit of AP1 that is crucial for the reformation of the synaptic vesicle. Variants in *AP1S2* have been reported to cause a rare neurodevelopmental disorder, Pettigrew syndrome (PGS) (OMIM: 304,340), which is characterized by walking delay, abnormal speech, mild to profound X-linked intellectual disability (XLID), and abnormal brain, and behaviors. Here, we describe a 2-year- and 5-month-old male patient who presented with global developmental delay (GDD). Trio whole exome sequencing (WES) revealed a 5 bp duplicate in the *AP1S2* gene (NM_003916.5: exon 2: c.96_100dup, p. Leu34Glnfs*8) predicted to cause early termination of translation, which was inherited from the unaffected mother. The clinical features of our patient were consistent with previous reports. This is the second case in the Chinese family and the eleventh variant found in *AP1S2*-related XLID. Our findings expand the *AP1S2* variant spectrum in neurodevelopmental disorders and provide evidence for the application of WES in PGS diagnosis.

Keywords AP1S2 · Whole-exome sequencing · XLID

Introduction

Intellectual disability (ID) is a type of neurodevelopmental disorder [1] characterized as substantial impediments in both intellectual functioning and adaptive behavior. The worldwide prevalence of ID has been estimated at 2–3% [2], and it can be divided into "isolated" or "syndromic" according to its clinical symptoms. The fundamental reasons for ID are extremely heterogeneous and the genetic factors are significant. With the development of next-generation sequencing, 2588 ID-related genes have been identified [3]. However, a large number of patients with ID have unknown etiologies, and more than 1000 genes related to developmental disorders have not yet been identified [4].

X chromosome genes account for approximately 4% of the human genome, and 10 ~ 15% of ID is related to gene variants in the X chromosome [5]. Males have been deeply affected due to harboring only a single X-chromosome, and 5–10% among all cases of male mental retardation were X-linked ID (XLID) [6]. It is not surprising that 40% of protein-encoding genes on the X chromosome are expressed in the brain [7], which may be important for cognition. Pettigrew syndrome (PGS) is an XLID disorder caused by a mutation in the *AP1S2* gene on chromosome Xp22. Patients with PGS characterized with basal ganglia disease, seizures, and Dandy-Walker malformation were first described in 1972 by Fried, and later, the genetic variants of *AP1S2* in patients with PGS were clarified [8]. Nonetheless, cases for PGS are still rare, and only nine variants in nine families have been reported thus far.

The *AP1S2* gene encodes a subunit of AP1 that is located in the Golgi complex to recruit clathrin and recognize sorting signals [9]. AP1S2 deficiency in mice reduced synaptic vesicle recycling and increased endosomes [10], which may reveal the pathogenic mechanism by which AP1S2 affects neurodevelopment by influencing synaptic transmission.

✉ Dengna Zhu
zhudengna@126.com

1 Henan Key Laboratory of Child Brain Injury and Henan Pediatric Clinical Research Center, Third Affiliated Hospital and Institute of Neuroscience of Zhengzhou University, Zhengzhou 450052, China

2 Commission Key Laboratory of Birth Defects Prevention, Henan Key Laboratory of Population Defects Prevention, Zhengzhou 450052, China

3 Cipher Gene LLC, Beijing 100080, China

Due to the rarity of *AP1S2*-related XLID, the clear pathogenic mechanism needs to be further explored.

Here, we report a proband in a Chinese family with GDD. Whole-exome sequencing (WES) identified a 5 bp duplicate of the *AP1S2* gene (NM_003916.5: exon 2: c.96_100dup, p. Leu34Glnfs*8) in the patients, and it was inherited from their mother. The PGS cases that we report are the second in the Chinese family, and our findings expand the genotype spectrum of *AP1S2*.

Methods

Editorial policies and ethical considerations

Written informed consent was obtained from the legal guardians of the patients to participate in this study. This study was approved by the Human Ethics Committees of the Third Affiliated Hospital of Zhengzhou University.

Patient

The clinical manifestations, brain magnetic resonance imaging (MRI), malformations, investigations of other organs, and gene variations were analyzed. We also combined the cases of the *AP1S2* variant reported previously in our analysis. Additional phenotypes and genetic findings for individuals are summarized in Table 1.

WES

Genomic DNA was extracted from the peripheral blood of the patient and his parents. The genomic DNA library was captured using the IDT XGen Exome Research Panel. Then WES was performed on the NovaSeq 6000 Sequencing platform using Paired-end reads. After sequencing, Bcl2Fastq, Burrows-Wheeler aligner (BWA), Annovar [11], Genome Analysis Toolkit software (GATK), SIFT, Polyphen2, LRT, MutationTaster, and FATHMM were used for data processing and analysis. The detected variants were analyzed using the dbSNP, OMIM, HGMD, and ClinVar databases. All detected variants were filtered by clinical characteristics, inherent pattern, type, frequency, and databases included. Subsequently, Sanger sequencing was performed to validate the variants identified by WES.

Copy number variation sequencing

Copy number variation sequencing (CNV-seq) has been supplemented for genome-wide CNV detection. Genomic DNA was fragmented and sequencing libraries were prepared using the TruSeq Library Construction Kit. Libraries were sequenced using a high-throughput sequencing platform (Illumina, San Diego, USA). Sequences were aligned to the human reference genome hg38 using the Burrows-Wheeler algorithm. CNVs were detected through tools containing CNVkit and CNVnator and subsequently annotated. The reference databases for the detection of the pathogenicity of the CNVs include OMIM, DECIPHER, DGV, Orphanet, and other databases.

Modeling 3D protein structures

A 3D protein modeling analysis was performed to show gene variation in our patient. The structure of wild-type (WT) and mutated proteins were predicted by AlphaFold [12] and SWISS-MODEL [13]. UCSF Chimera [14] was used to visualize the WT and mutated structures.

Results

Clinical features

The 2-year- and 5-month-old male patient was delivered by cesarean section at 38 weeks due to hyperglycemia of the mother during pregnancy. He is the third child (G3P3) of non-consanguineous patients (Fig. 1a). He had a normal birth history with a birth weight of 4.2 kg and a head circumference of 34.5 cm. Subsequently, he was hospitalized at a local hospital for four days due to "poor response" and was diagnosed with "neonatal hypoxic-ischemic encephalopathy, neonatal pneumonia, high-risk infant, and macrosomia." His could raising his head at 3 months old, sitting without support at 7 months old, and his development was delayed with becoming aware of grasping objects at 8 months old.

A brain MRI revealed brain effusion when he was 1 year old, which was followed by rehabilitation treatment. A repeat MRI when he was 2 years old (Supplementary Fig. 1a–c) showed short corpus callosum, abnormal signals at the posterior horns of the bilateral ventricles, and bilateral maxillary sinus, ethmoid sinus, and bilateral middle ear mastoid effusion. During the recent follow-up, he was able to walk at 1 year and 5 months. However, he has no language, and mainly expresses himself through hand gestures at 2 years and 5 months. The MRI results were normal from March 2022 and showed no obvious abnormalities in the brain parenchyma or FLAIR signal and no ventricle enlargement or midline structure displacement (Supplementary Fig. 1d–f). The Gesell development scale was evaluated for the patient in March 2022. His adaptive ability assessment indicated moderate developmental delay with DA12.9 M, DQ43.9, his gross motor assessment indicated mild developmental delay with DA21.6 M, DQ73.5, his fine motor assessment indicated moderate developmental

Table 1 Clinical features of patients with AP1S2 variation

Study	Our study		Strain et al., 1997				Carpenter et al., 1999					Turner et al., 2003							Tzschach et al., 2015
Variant	c.96_100dup, p.Leu34Glnfs*8		c.266G > T, p.Gln66*				c.154C > T, p.Arg52*					c.106C > T, p.Gln36*							**c.367C > T, p.Gln123***
Patient	proband	brother	III26	III35	III41	III.30	II-1	III-1	III-2	IV-1	IV-2	II-4	III-12	IV-13	V-8	IV-18	IV-12	IV-23	family 1
Hypotonia	-	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N/A
Seizure	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	N/A
Age at walking	1y 5 m	2y	3y	2y	N/A	2.5y	3.5y	6y	3–4y	3–4y	3–4y	N/A	7y	8y	N/A	4y	3y	1.6y	N/A
Speech	Absent	Present	Present	N/A	Present	Absent	Present	Absent	Absent	Present	Absent	N/A	N/A	Absent	N/A	Present	N/A	Present	N/A
Aggressive	-	+	-	-	-	-	+	+	-	-	-	+	+	+	+	-	+	-	+
Degree of ID	Mild	Profound	Profound	Profound	N/A	N/A	Mild	Profound	Profound	Moderate	Mild	Profound	Profound	Profound	Profound	Moderate	Profound	Moderate	Profound
Facial abnormalities	-	-	+	+	-	-	+	+	+	-	-	+	+	-	+	+	+	+	-
Microcephaly	-	-	-	-	-	-	-	-	-	+	+	+	+	+	-	+	+	+	+
Other clinical features		suspected autism																	
Study	Tarpey et al., 2006				Saillour et al., 2007					Borck et al., 2008				Cacciagli et al., 2014				**Huo et al., 2019**	**Cappuccio et al., 2019**
Variant	c.180-5_180-2delTACA				c.288 + 5G > A					c.154C > T, p.Arg52*			c.289-1G > C	c.426 + 1G > T				**c.1–1 G > C**	**c.217C > T, p.Gln73***
Patient	III-1	III-2	III-4	II-7	VI	IV6	III4	II4	IV8	III1	III4	II4	II.2	III8	III14	IV8	V1	IV4	proband
Hypotonia	+	+	+	+	+	+	+	+	+	+	+	N/A	+	-	+	+	-	+	+
Seizure	+	-	-	-	-	-	+	-	-	-	-	N/A	-	+	-	-	-	-	-
Age at walking	6y	4y	6y	N/A	2.5y	6y	14 m	N/A	N/A	2y	2y	N/A	N/A	26 m	2y	7y	3y	3.5y	3y
Speech	Absent	Present	limited	Present	Present	Absent	Present	N/A	N/A	Present 7y	Present	N/A	Present	N/A	Present	Absent	Present	Present	Present
Aggressive	-	-	-	+	+	-	-	N/A	N/A	-	+	N/A	+	+	-	+	-	+	+
Degree of ID	Profound	Mild	Moderate	Moderate	Moderate	Profound	Mild	N/A	N/A	Profound	Profound	Profound	Profound	N/A	Mild	Profound	Mild	Profound	Profound

Table 1 (continued)

Facial abnormalities	-	-	-	-	-	-	-	-	N/A	-	+	+	-	-	-	+	-			
Microcephaly	-	-	-	-	-	-	-	+	N/A	+	-	-	-	-	-	-	+			
Other clinical features					Congenital hydrocephalus	Congenital hydrocephalus	Small penis, ASD	ASD					Dilation of the fourth ventricle	Periventricular nodular heterotopia	CSF protein,NSE evaluated		ASD			

MR, mental retardation; *CSF*, cerebrospinal fluid; *NSE*, neuron-specific enolase; *N/A*, not mention

delay with DA12.6 M, DQ42.9, his language assessment indicated moderate developmental delay with DA13.6 M, DQ46.3, and his social behavior assessment indicated mild developmental delay with DA17.7 M, DQ60.2.

The patient's brother has a similar phenotype: he could raise his head at 10 months old, sat alone at 1 year old, and walked at 2 years old. He developed autistic behavior (he liked "spinning things"), and self-harming behavior (hit his head on the floor when he was upset) at 3 years old. His parents described the diagnosis as "suspected autism" by the local doctor, but the details were unknown, and the relevant evaluation results were not provided.

The brother is now 5 years and 4 months old. Six months after a head injury, his development was significantly regressed. He could run and jump at 4 years and 10 months old. He has intelligence developmental delay and can speak 4–5 words and engage in only simple communication with others. His consciousness was impaired for 1 month after the head injury. Now he walks alone unsteadily, being prone to falls, and can only speaking few words. We supplemented the MRI examination for the brother recently, but due to his poor cooperation, we failed to complete the examination. We improved the Gesell developmental scale assessment of the brother, and the results revealed that his adaptability assessment indicated severe developmental delay with DA18.9 M and DQ29.3, the gross motor assessment indicated very severe developmental delay with DA15.3 M and DQ23.8, the fine motor assessment indicated severe developmental delay with DA17M and DQ26.4, the language assessment indicated severe developmental delay DA19.8 M and DQ30.7, and the social behavior assessment indicated severe developmental delay DA21.9 M and DQ34. The patient's older sister was healthy and did not have a similar phenotype.

Identification of AP1S2 variant related to XLID patients

A novel X-linked nonsense variant of *AP1S2* (NM_003916.5: exon2: c.96_100dup, p. Leu34Glnfs*8) was identified by further gene testing (Table 2). Furthermore, no CNV was found that could clearly explain the patient's phenotype. The *AP1S2* variant found in our patients was inherited from their mother, which was confirmed by Sanger sequencing (Fig. 1a and b). Fortunately, his sister and aunt did not have the variant in *AP1S2* (Fig. 1b). Five bases (GTTCT) were inserted, which was predicted to cause a frame change and early termination of protein coding. The *AP1S2* variant in our patient was not included in gnomAD, the Exome Aggregation Consortium (ExAC), or other databases (Table 2). Moreover, only 11 single-nucleotide variants (SNVs) and one base insertion were found in the *AP1S2* variations (https://www.ncbi.nlm.nih.gov/clinvar) in ClinVar. The variants reported in *AP1S2* are all splicing or nonsense variants that lead to

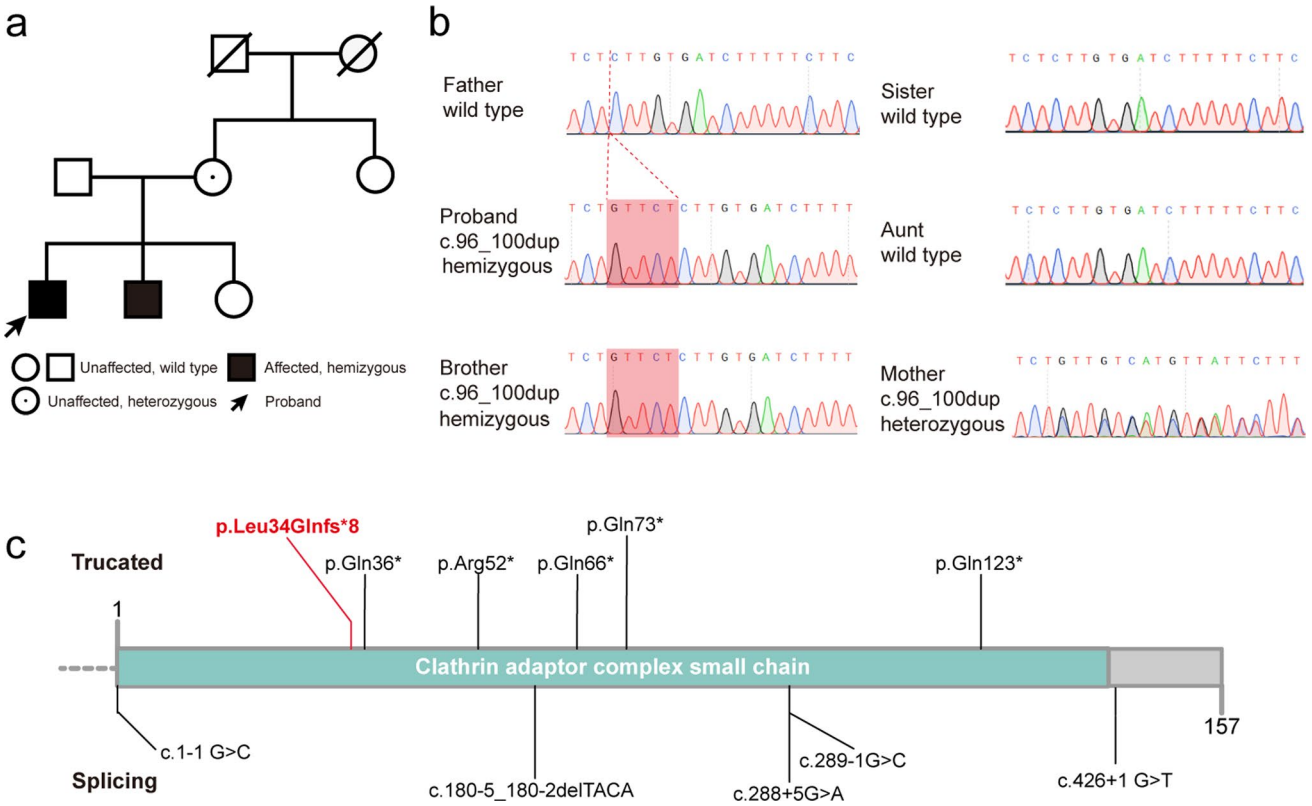

Fig. 1 Identification of a duplicated variant in *AP1S2*. **a** Pedigree of the family. The proband and his brother affected by GDD and likely ASD are indicated by filled symbols. **b** Sanger sequencing of the proband, his brother, his sister, his aunt, and his parents showed a variant c.96_100dup (red translucent box) in the proband. The *AP1S2* gene, which was inherited from the mother. **c** Domain structure and modeling of *AP1S2* variants in previous studies. The upper panel shows the truncated variants. The splicing variants are presented below. The AP1S2 protein contains a clathrin adaptor complex small chain domain (1–139 aa) is indicated in green. The variant detected in our patient is highlighted in red

Table 2 Variant information

Gene	Variant	Inheritance	MAF			Category
			ExAc	gnomAD	1000 genome	
AP1S2	c.96_100dup (p.Leu34Glnfs*8)	XLR	NE	NE	NE	LP (PVS1 + PM2_Supporting)

Transcript, NM_003916.5; *XLR*, X-linked recessive inheritance; *MAF*, minor allele frequency; *NE*, not exist; *LP*, likely pathogenic

frameshift or early termination. In particular, they are classified as pathogenic or likely pathogenic (our study) according to the American College of Medical Genetics and Genomics (ACMG) guidelines. It seems that SNVs are extremely rare, and their evidence of pathogenicity has been sufficient.

Protein analysis for the AP1S2 variant

The truncated protein was visualized to understand the molecular structures of the mutated AP1S2 (Fig. 2). The *AP1S2* gene contains five exons that encode 157 amino acids. The 5 bp duplication (GTTCT) in exon 2 leads to a frame change and early termination at 41 amino acids (Fig. 2a). The 34th amino acid changed from leucine to glutamine and is conserved in multiple species (Fig. 2b). The 3D protein structures showed that the variation c.96_100dup (p.Leu34Glnfs*8) loses most of the functional domain, which is likely to affect the function of the protein (Fig. 2c).

Discussion

The *AP1S2* gene is composed of five exons and encodes the σ1B subunit of the heterotetrameric AP1 complex, which mediates the recruitment of clathrin and the recognition of transmembrane receptors [15]. There are three σ1 subunits

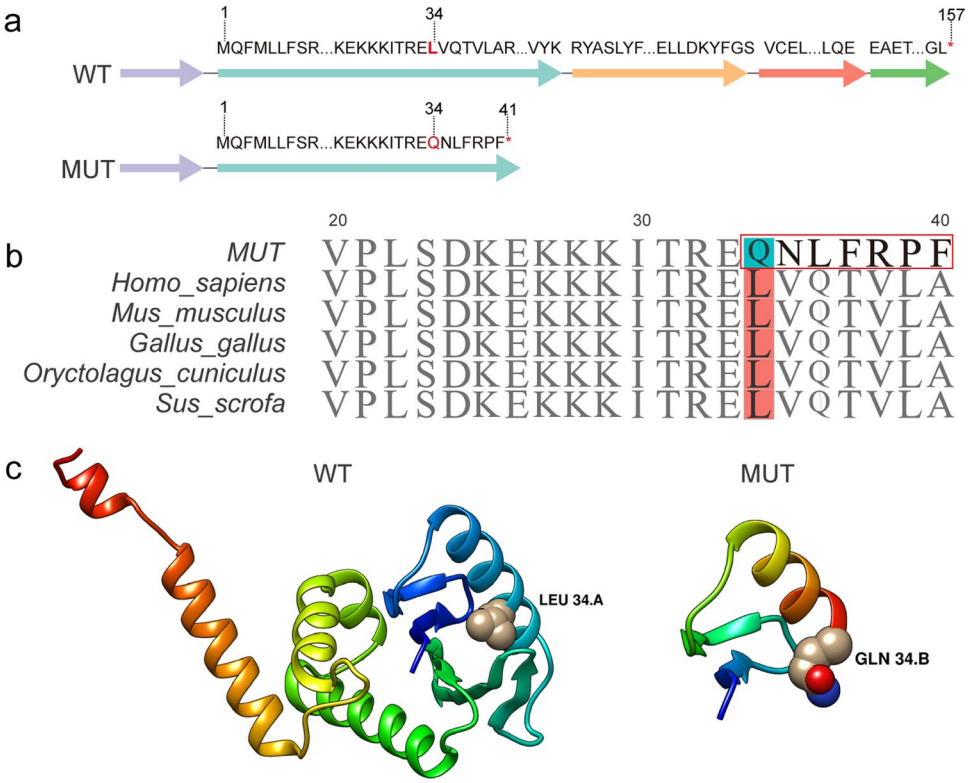

Fig. 2 Protein changes in WT and the *AP1S2* variant. **a** The WT protein, containing 157 aa is shown in the upper panel and the *AP1S2* variant leads to a frameshift and early termination (1–41 aa), as shown in the lower panel. The arrows in different colors represent each exon. **b** Species conservation analysis of AP1S2. The amino acids from 34 to 41 which changed by the variant were conserved in different species. **c** 3D protein structures in WT and variant proteins. The 3D models revealed early termination in the variant protein. The mutated 34th amino acid is highlighted by the sphere

expressed in vertebrates: σ1A, σ1B, and σ1C [16, 17]. Additionally, σ1A and σ1B have the highest expression levels in the brain [18, 19], meaning that they may play an important role in the brain. Mice with σ1B deficiency have reduced motor coordination and severely disabled long-term spatial memory [19]. An in vitro experiment indicated that the reformation of the synaptic vesicle (SV) in σ1B-deficient mice decreases upon stimulation. This will uncover the molecular mechanism for severe human X-chromosome-linked ID.

This disorder, which is related to *AP1S2* variations (MIM 300,629) was well known in 2006 in patients with mild to profound XLID, abnormal behavior, and neurodevelopmental problems [8]. The abnormal behaviors manifested itself in walking delay, abnormal speech, hypotonia, and aggressive behavior (Table 1). Some of the patients had abnormal brain development, such as hydrocephalus, microcephaly, cerebral calcification, and iron deposition in the basal ganglia. The patient in our study had a development delay with becoming aware of grasping objects at 8 months old. Moreover, he has no language and mainly expresses himself in hand gestures up to now. The Gesell development scale results showed moderate developmental disability. Similar phenotypes were also shown in the patient's brother. He had developmental delay and walked at 2 years old. The brother also has language disorder. He could speak only 4–5 words and was capable of only simple communication with others when he was 4 years old. Furthermore, he developed autistic behavior (he liked "spinning things"), and self-harming behavior (headbutting the floor when he was upset) at 3 years old. The Gesell development scale results indicated severe developmental disability. The brother's more severe developmental delay may be related to his head injury 6 months ago. No facial abnormalities, microcephaly, or epilepsy were found in our study. Furthermore, the MRI examination when the patient was 2 years old indicated an abnormal signal in the posterior horns of both the lateral ventricles and the short corpus callosum. The MRI results in March 2022 revealed no obvious abnormalities in the brain parenchyma or FLAIR signal. No ventricle enlargement or midline structure displacement (Supplementary Fig. 1d–f). The variable clinical characteristics are consistent with previous reports.

The severity of the phenotype does not appear to be related to the variants. Interestingly, variant types in the *AP1S2* gene have been reported to be only spliced or truncated. Epilepsy was reported to be correlated with splicing variants since all patients with epilepsy had splicing variations in *AP1S2* except one patient reported in 2019 [20]. Our patient, who has a truncated variant (p. Leu34Glnfs*8) in *AP1S2*, does not have epilepsy. This may also be a consequence of the fewer variants (Fig. 1c) currently identified in *AP1S2*. The duplicated variant in our patient leads to a frameshift and early termination in AP1S2 (Fig. 2a), which results in the loss of the functional domain and likely affects the function of AP1S2. The mechanisms of AP1S2 deficiency with neurodevelopment were reported to affect the SV recycling in synapses. AP-1/σ1A and AP-1/σ1B compete

in the regulation of early endosome maturation and degradation of SV proteins, thus controlling the transport of synaptic vesicle proteins into a degradative pathway [9]. The change in the AP1S2 protein (Fig. 2c) will affect competition binding and break the balance of SV regulation, further leading to the phenotype observed in our patients.

In conclusion, our study reports a novel variant in the *AP1S2* gene that resulted in GDD in a Chinese family. Truncated and spliced were the main types of variation. Next-generation sequencing helped obtain a clear diagnosis of PGS for our patient. Furthermore, the application of WES in patients with GDD, variable ID, walking delay and abnormal speech, behavior, and brain is needed for the confirmation of PGS.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10048-022-00691-8.

Acknowledgements We wish to gratefully thank the patient's parents for allowing us to publish this clinical report. And also thank Cipher Gene for their sequencing knowledge support. This work was supported by Joint Open Research Fund of Henan Key Laboratory of Child Brain Injury and Henan Pediatric Clinical Research Center (KFKT2021102), the Henan Medical Science and Technique Foundation (212102310221, LHGJ20190337), and the national Health Commission Key Laboratory of Birth Defects Prevention and Henan Key Laboratory of Population Defects Prevention (2021-03).

Author contribution DZ and MW conceived and designed the experiments. YX and JZ did the patient recruitment and clinical analysis. FY and ZY did the WES and molecular analysis. DZ wrote the first draft of the manuscript. All authors reviewed and approved the final manuscript.

Data availability The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors declare that they have no competing interests.

References

1. Fell CW, Nagy V (2021) Cellular models and high-throughput screening for genetic causality of intellectual disability. Trends Mol Med 27(3):220–230
2. van Bokhoven H (2011) Genetic and epigenetic networks in intellectual disabilities. Annu Rev Genet 45:81–104
3. Kochinke K, Zweier C, Nijhof B, Fenckova M, Cizek P, Honti F, Keerthikumar S, Oortveld MA, Kleefstra T, Kramer JM et al (2016) Systematic phenomics analysis deconvolutes genes mutated in intellectual disability into biologically coherent modules. Am J Hum Genet 98(1):149–164
4. Kaplanis J, Samocha KE, Wiel L, Zhang Z, Arvai KJ, Eberhardt RY, Gallone G, Lelieveld SH, Martin HC, McRae JF et al (2020) Evidence for 28 genetic disorders discovered by combining healthcare and research data. Nature 586(7831):757–762
5. Ropers HH (2008) Genetics of intellectual disability. Curr Opin Genet Dev 18(3):241–250
6. Lubs HA, Stevenson RE, Schwartz CE (2012) Fragile X and X-linked intellectual disability: four decades of discovery. Am J Hum Genet 90(4):579–590
7. Ropers HH, Hamel BC (2005) X-linked mental retardation. Nat Rev Genet 6(1):46–57
8. Tarpey PS, Stevens C, Teague J, Edkins S, O'Meara S, Avis T, Barthorpe S, Buck G, Butler A, Cole J et al (2006) Mutations in the gene encoding the Sigma 2 subunit of the adaptor protein 1 complex, AP1S2, cause X-linked mental retardation. Am J Hum Genet 79(6):1119–1124
9. Candiello E, Kratzke M, Wenzel D, Cassel D, Schu P (2016) AP-1/σ1A and AP-1/σ1B adaptor-proteins differentially regulate neuronal early endosome maturation via the Rab5/Vps34-pathway. Sci Rep 6:29950
10. Kratzke M, Candiello E, Schmidt B, Jahn O, Schu P (2015) AP-1/σ1B-dependent SV protein recycling is regulated in early endosomes and is coupled to AP-2 endocytosis. Mol Neurobiol 52(1):142–161
11. McKenna A, Hanna M, Banks E, Sivachenko A, Cibulskis K, Kernytsky A, Garimella K, Altshuler D, Gabriel S, Daly M et al (2010) The genome analysis toolkit: a MapReduce framework for analyzing next-generation DNA sequencing data. Genome Res 20(9):1297–1303
12. Jumper J, Evans R, Pritzel A, Green T, Figurnov M, Ronneberger O, Tunyasuvunakool K, Bates R, Žídek A, Potapenko A et al (2021) Highly accurate protein structure prediction with AlphaFold. Nature 596(7873):583–589
13. Waterhouse A, Bertoni M, Bienert S, Studer G, Tauriello G, Gumienny R, Heer FT, de Beer TAP, Rempfer C, Bordoli L et al (2018) SWISS-MODEL: homology modelling of protein structures and complexes. Nucleic Acids Res 46(W1):W296-w303
14. Pettersen EF, Goddard TD, Huang CC, Couch GS, Greenblatt DM, Meng EC, Ferrin TE (2004) UCSF Chimera–a visualization system for exploratory research and analysis. J Comput Chem 25(13):1605–1612
15. Kongsvik TL, Höning S, Bakke O, Rodionov DG (2002) Mechanism of interaction between leucine-based sorting signals from the invariant chain and clathrin-associated adaptor protein complexes AP1 and AP2. J Biol Chem 277(19):16484–16488
16. Baust T, Czupalla C, Krause E, Bourel-Bonnet L, Hoflack B (2006) Proteomic analysis of adaptor protein 1A coats selectively assembled on liposomes. Proc Natl Acad Sci U S A 103(9):3159–3164
17. Borner GH, Harbour M, Hester S, Lilley KS, Robinson MS (2006) Comparative proteomics of clathrin-coated vesicles. J Cell Biol 175(4):571–578
18. Takatsu H, Sakurai M, Shin HW, Murakami K, Nakayama K (1998) Identification and characterization of novel clathrin adaptor-related proteins. J Biol Chem 273(38):24693–24700
19. Glyvuk N, Tsytsyura Y, Geumann C, D'Hooge R, Hüve J, Kratzke M, Baltes J, Boening D, Klingauf J, Schu P (2010) AP-1/sigma1B-adaptin mediates endosomal synaptic vesicle recycling, learning and memory. Embo j 29(8):1318–1330
20. Huo L, Teng Z, Wang H, Liu X: A novel splice site mutation in AP1S2 gene for X-linked mental retardation in a Chinese pedigree and literature review. *Brain Behav* 2019, **9**(3):e01221.