Received: 18 September 2019 | Revised: 15 February 2020 | Accepted: 24 February 2020

DOI: 10.1002/mgg3.1220

ORIGINAL ARTICLE

Molecular Genetics & Genomic Medicine Open Access WILEY

Congenital dyserythropoiesis anemia type Ia with a novel *CDAN1* mutation diagnosed by whole exome sequencing

Pei-Chin Lin[1,2,3] | **Chao-Neng Cheng**[4] | **Hsi-Yuan Huang**[5,6] | **Yu-Hsin Tseng**[3] | **Ya-Sian Chang**[5,6,7,8] | **Chien-Yu Lin**[9] | **Jan-Gowth Chang**[5,6,7,8,10]

[1]Division of Hematology and Oncology, Department of Pediatrics, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan

[2]Department of Pediatrics, School of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

[3]Department of Pediatrics, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

[4]Division of Hematology and Oncology, Department of Pediatrics, National Cheng Kung University Hospital, Tainan, Taiwan

[5]Center for Precision Medicine, China Medical University Hospital, Taichung, Taiwan

[6]Department of Laboratory Medicine, China Medical University Hospital, China Medical University, Taichung, Taiwan

[7]Epigenome Research Center, China Medical University Hospital, Taichung, Taiwan

[8]School of Medicine, China Medical University, Taichung, Taiwan

[9]Graduate Institute of Clinical Medical Science, School of Medicine, China Medical University, Taichung, Taiwan

[10]Department of Bioinformatics and Medical Engineering, Asia University, Taichung, Taiwan

Correspondence
Jan-Gowth Chang, Department of Laboratory Medicine, China Medical University Hospital, No. 2, Yuh-Der Road, Taichaung, Taiwan.
Email: d6781@mail.cmuh.org.tw

Funding information
Ministry of Science and Technology, Grant/Award Number: MOST 106-2314-B-037-079-MY2; Kaohsiung Medical University, Grant/Award Number: KMUH107-7R41

Abstract

Background: Congenital dyserythropoiesis anemia type Ia (OMIM:224120), is a rare hereditary anemia. The diagnosis is difficult to make and usually delayed in part due to its rarity and nonspecific clinical manifestations.

Methods: Whole exome sequencing was applied for the genetic diagnosis of a 12-year-old boy who has suffered from hemolytic anemia since birth and who requires regular transfusions. Sanger sequencing of the variants detected in whole exome sequencing was performed in the patient and his parents.

Results: Compound heterozygous mutations of *CDAN1* gene, including one previously reported and one novel mutation, which is a splicing change, were detected in the whole exome sequencing and confirmed by Sanger sequencing. The autosomal recessive inheritance was confirmed by pedigree analysis.

Conclusion: To our knowledge, this is the first case report of congenital dyserythropoiesis anemia type Ia with genetic diagnosis to be located in Taiwan. Because of the rarity of CDA Ia and the overlapping of the clinical manifestations with other hereditary anemias, the next-generation sequencing approach is effective for conclusive diagnosis of CDA Ia.

KEYWORDS

congenital dyserythropoiesis anemia, hemolytic anemia, hyperbilirubinemia, whole exome sequencing

Pei-Chin Lin and Chao-Neng Cheng contributed equally to this study.

1 | INTRODUCTION

Congenital dyserythropoiesis anemia (CDA) is a group of rare hereditary hemolytic anemias characterized by ineffective erythropoiesis and morphological abnormalities of erythroid precursors in the bone marrow (Iolascon, Esposito, & Russo, 2012; Iolascon, Russo, & Delaunay, 2011). CDAs are classified into type I (CDA I), type II and type III, based on the dysplastic changes observed in bone marrow erythroblasts by means of light and electron microscopy, the pattern of inheritance, and the associated dysmorphisms (Fujino et al., 2013). Although CDAs have traditionally been defined in morphological terms, they have come to be genetically defined in recent years. CDA Ia is an autosomal recessive disease characterized by erythroid hyperplasia, binuclear erythroblasts, and chromatin bridges between the nuclei of erythroblasts in bone marrow light microscopic (LM) examinations and a spongy appearance of heterochromatin of erythroblasts in electron microscopic examinations (Iolascon, Heimpel, Wahlin, & Tamary, 2013). Patients with CDA Ia would present moderate to severe macrocytic anemia, jaundice, splenomegaly, and iron overload. Skeletal abnormalities of distal limbs have been described (Tamary et al., 2005). The anemia and jaundice were usually recognized in neonatal or early childhood situations (Heimpel et al., 2006; Shalev et al., 2004; Shalev, Tamary, Shaft, Reznitsky, & Zaizov, 1997). However, such diagnosis is difficult to make, and it is often delayed because of its rarity and obscure erythroblast abnormalities, in which case it would take an experienced expert to think of such a possibility or an occurrence. Here, we present the case of a 12-year-old boy with transfusion-dependent hemolytic anemia since infancy and genetically diagnosed as CDA Ia with compound heterozygous *CDAN1(CDAN1; 607465)* mutations, one of which was previously reported and the other novel variant determined using whole exome sequencing.

2 | MATERIALS AND METHODS

2.1 | Ethical compliance

This study was approved by the Institutional Review Board-II Kaohsiung Medical University Chung-Ho Memorial Hospital (KMUHIRB-G(II)-20160043).

The 12-year-old male patient with clinically diagnosed with congenital hemolytic anemia was enrolled for whole exome sequencing (WES) analysis. Sanger sequencing for possible disease-causing variants were performed for the patient and his parents. The detailed methods of WES and Sanger sequencing were as previously described (Lin et al., 2018). The primer sequences for Sanger sequencing of the two *CDAN1* variants were: exon14 forward: 5′-CGGTCCTGGA TGTGCGGACT-3′; exon14 reverse: 5′-GCCAGCCCAGGACAGCAAGT-3′; exon18 forward: 5′-GACAATGCGCCT GTGGTGGA-3′; exon18 reverse: 5′-GCAGCCCCTGGCTGGTCT-3′. The GenBank reference sequence and version number for CDAN1 was NM_138477.4.

3 | RESULTS

This 12-year-old male patient was diagnosed with hemolytic anemia since birth. He was a prematurity with low birth weight (gestational age: 36 + 2 weeks, birth body weight: 1,950 mg). Delayed crying, pale appearance, poor physical activity, and grunting were noted at birth. Severe anemia (Hemoglobin (Hb): 4 g/dl), hyperbilirubinemia (total bilirubin: 5.5 g/dl), and highly elevated lactate dehydrogenase (LDH: 5,908 U/L) were noted. Dyspnea with desaturation developed soon after birth and intubation with mechanical ventilation support were given. Echocardiogram showed a large patent ductus arteriosus with right heart failure. Abdominal ultrasound showed hepatomegaly. Blood exchange transfusion was performed for severe anemia and hyperbilirubinemia. Small left fourth toe and malposition of right fourth toe were also noted. Chromosome study of the peripheral blood revealed normal karyotype (46 XY). After intensive care, PDA reduced, right heart failure subsided, and anemia improved (Hb: 10.9 g/dl). He was discharged at the age of 1 month. At the age of 2 months, severe anemia (Hb: 3.9 g/dl) developed again and a blood transfusion was performed. Subsequent to the initial transfusion, regular visits to the hematology department were made. Blood transfusions were administered intermittently for 1 year; however, low Hb levels (around 5–6 g/dl) and poor body weight gain were noted. Bone marrow aspiration was performed and erythroid hyperplasia was impressed. Regular transfusion with targeted trough Hb levels above 10 g/dl started post 1-year-old. A splenectomy was performed at the age of 6 years in an attempt to reduce transfusion requirement under the impression of transfusion-dependent anemia, but the eventual requirement for transfusion was not reduced significantly.

Red blood cell (RBC) indices taken 2 weeks after latest blood transfusion showed normocytic anemia (RBC count: 2.66×10^6/ul; Hb: 8.0 g/dl; MCV: 88.7 fl; MCH:30.1 Pg; MCHC: 33.9 g/dl). The reticulocyte count was 2.2% (reference range: 0.87–2.26%) and the reticulocyte production index was 0.64. The peripheral blood smear showed macrocytic RBC, shistocytes, bite cells, and target cells (see Figure 1). Direct and indirect anti-globulin test were both negative. Plain film of his left foot showed the absence of left third middle and distal phalages.

WES using DNA extracted from the mononuclear cells of the peripheral blood was performed. The workflow of analysis

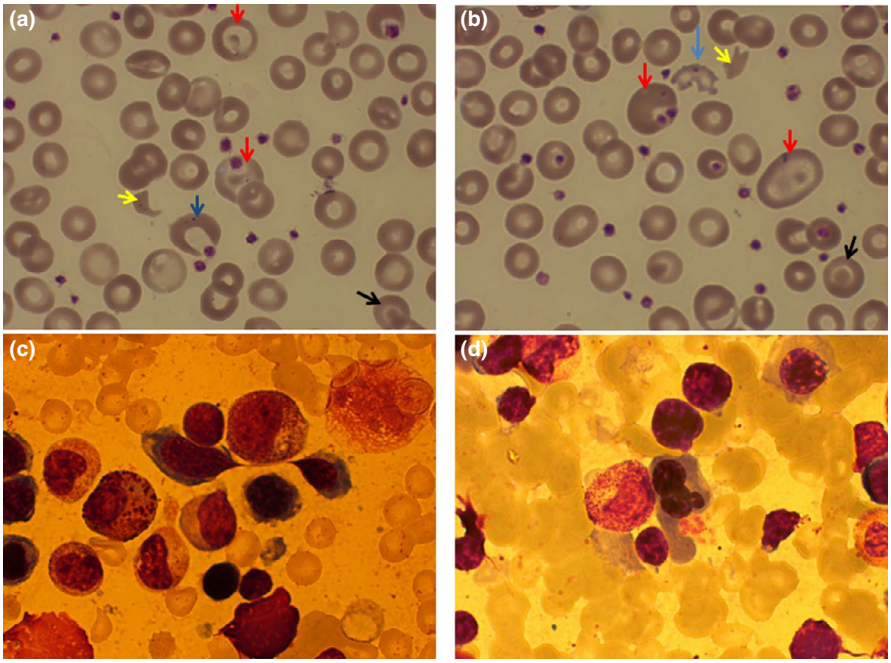


FIGURE 1 The peripheral blood smear (a, b, Liu stain, 1000×) showed macrocytic RBC (red arrow), shistocytes (yellow arrow), bite cells (blue arrow), and target cells (black arrow). Bone marrow smear (Liu stain, 1000×) showed nuclear bridging (c), megaloblastic changes, nuclear lobulations, and multinuclearity (d)

of WES data and the variants of the coding regions in genes of RBC membrane disorders, hyperbilirubinemia, and other congenital hemolytic anemia discovered were annotated in Figure 2. For heterozygous variants in genetic diseases, the variant allele frequency in genomic DNA from tissue approaches 50% in general. To screen more variants, and to avoid the sequencing bios and alignment bios, we selected variants with a ratio no less than 30%. The 525 variants with a ratio no less than 30% and global minor allele frequency less than 1% were listed in supplement (Data S1).The panels of the target genes for searching the possible causative variants were published previously (Lin et al., 2018). A heterozygous *CDAN1* variant (c.2140C>T, p.R714W) in exon14 was detected (sequence depth/ratio of variant: 29/59 (49.15%)). Sanger sequencing of the patient and the parents showed a paternal origin of this variant. Previous literature showed that *CDAN1* mutations was associated with CDA I. All proven cases of CDA I reported were autosomal recessive, including homozygous or compound heterozygous mutations involving coding and/or splicing regions. Tamary et al. reported 12 polymorphic sites of the *CDAN1* gene in their study and none of them were found in the WES result of our patient (Tamary et al., 2005). Therefore, we re-analyzed the WES data for searching for variants of *CDAN1* splicing regions. A *CDAN1* variant (NM_138477:exon18:c.2408-2A>G), which was predicted as interfering with splicing, and which has not been previously reported or listed in the Human Gene Mutation Database (HGMD), was detected (sequence depth/ratio of variant: 12/32 (37.50%)). The exon18:c.2408-2A>G likely affects the acceptor splice site of exon 18, which may result in exon18 skipping or the usage of the cryptic exonic or intronic splice sites that leads to the inclusion of an intron fragment or exon fragment skipping (see Figure 3; Anna & Monika, 2018). Sanger sequencing of the patient and the parents showed a maternal origin of this variant. Finally, the patient was diagnosed genetically as CDA Ia with compound heterozygous *CDAN1* mutations (c.2140C>T, p.R714W and exon18:c.2408-2A>G; see Figure 4).

4 | DISCUSSION

CDA Ia was more prevalently reported in the population of Israeli Bedouin and of Europeans (Heimpel et al., 2006; Tamary et al., 1996). Single cases have been similarly reported in the United States, Japan, India, and China (Fujino et al., 2013; Kawabata et al., 2012; Kumar, Kushwaha, & Singh, 2014; Ru et al., 2014, 2008; Wang et al., 2018; Wickramasinghe & Wood, 2005). The estimated cumulative incidence of CDA Ia in Europe is approximately 0.24/million (Iolascon et al., 2012). To date, 63 *CDAN1* mutations were recorded in The Human Gene Mutation Database, including 42 missense mutations, 4 splicing mutations, 16 small deletions/insertions, and 1 gross deletion. Although no particular frequent mutations were reported, the majority of patients showed mutations of at least one allele from exons 6 to 28 (Iolascon et al., 2012). No phenotype–genotype correlation was established. The disease diversities noted in the homozygous Bedouin patients and the existence of patients with phenotypic CDA Ia in which no mutations of *CDAN1* gene have been found to suggest the presence of a promoter defect or modifier genes (Dgany et al., 2002; Iolascon et al., 2012). Our patient showed a compound heterozygous *CDAN1* mutations (c.2140C>T, p.R714W and exon18:c.2408-2A>G). The missense mutation (c.2140C>T, p.R714W) has been reported in European descents and Chinese (Dgany et al., 2002;

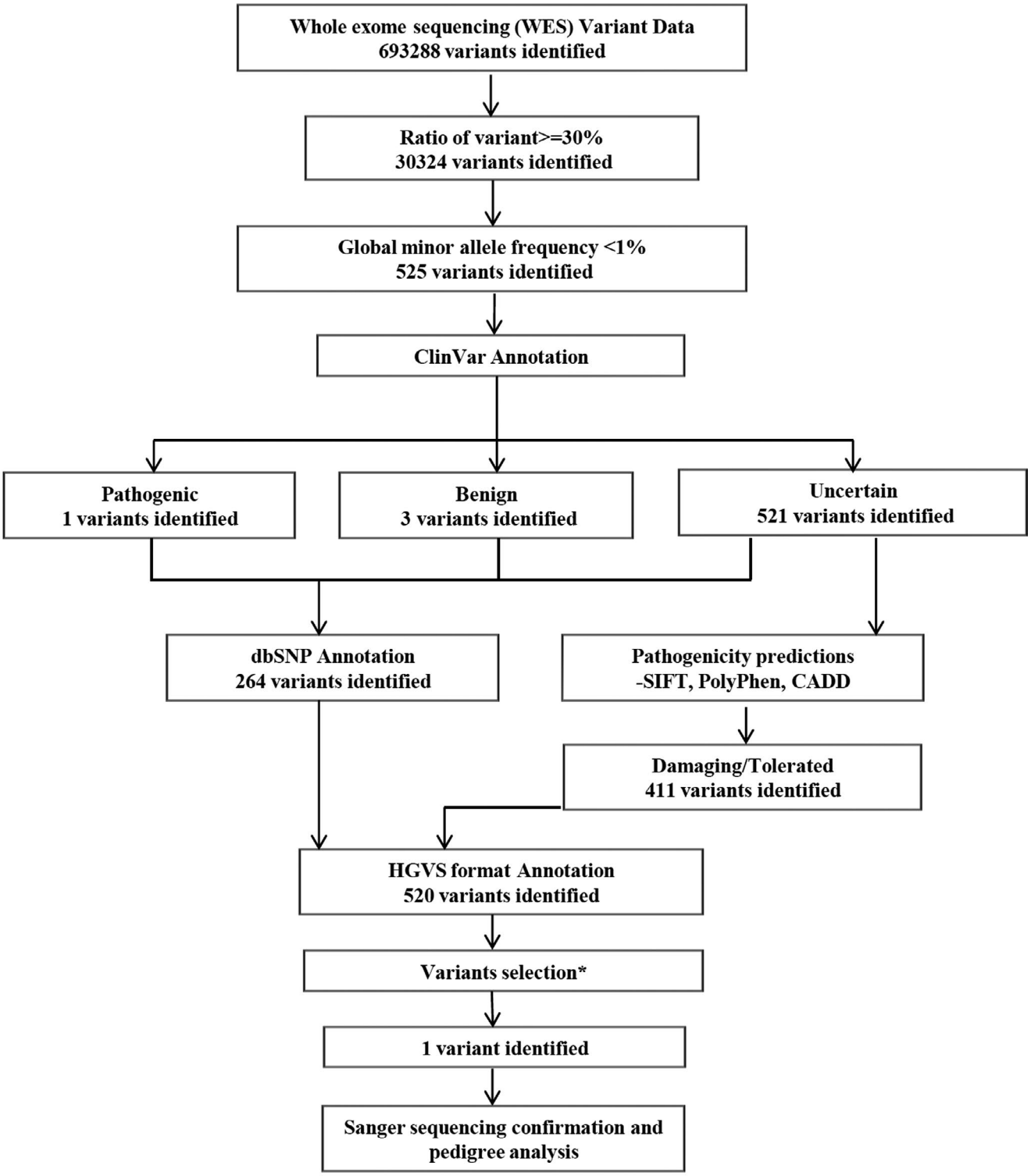
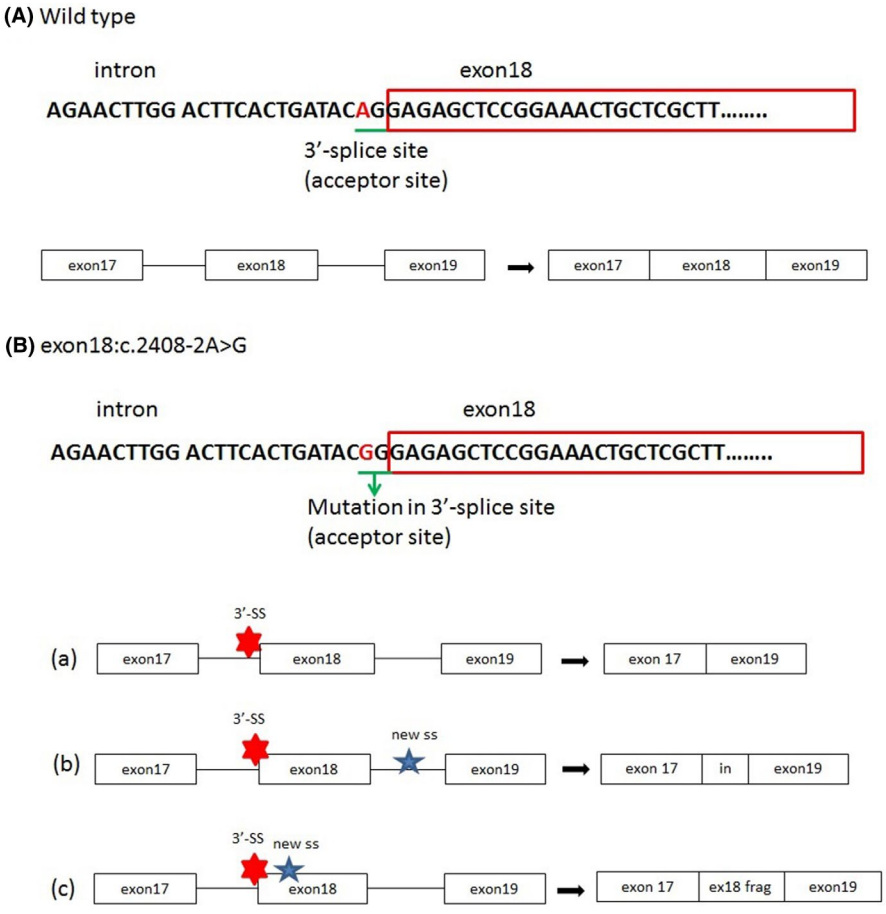


FIGURE 2 The workflow of analysis of whole exome sequencing data and the variants in the coding regions identified in every step were annotated



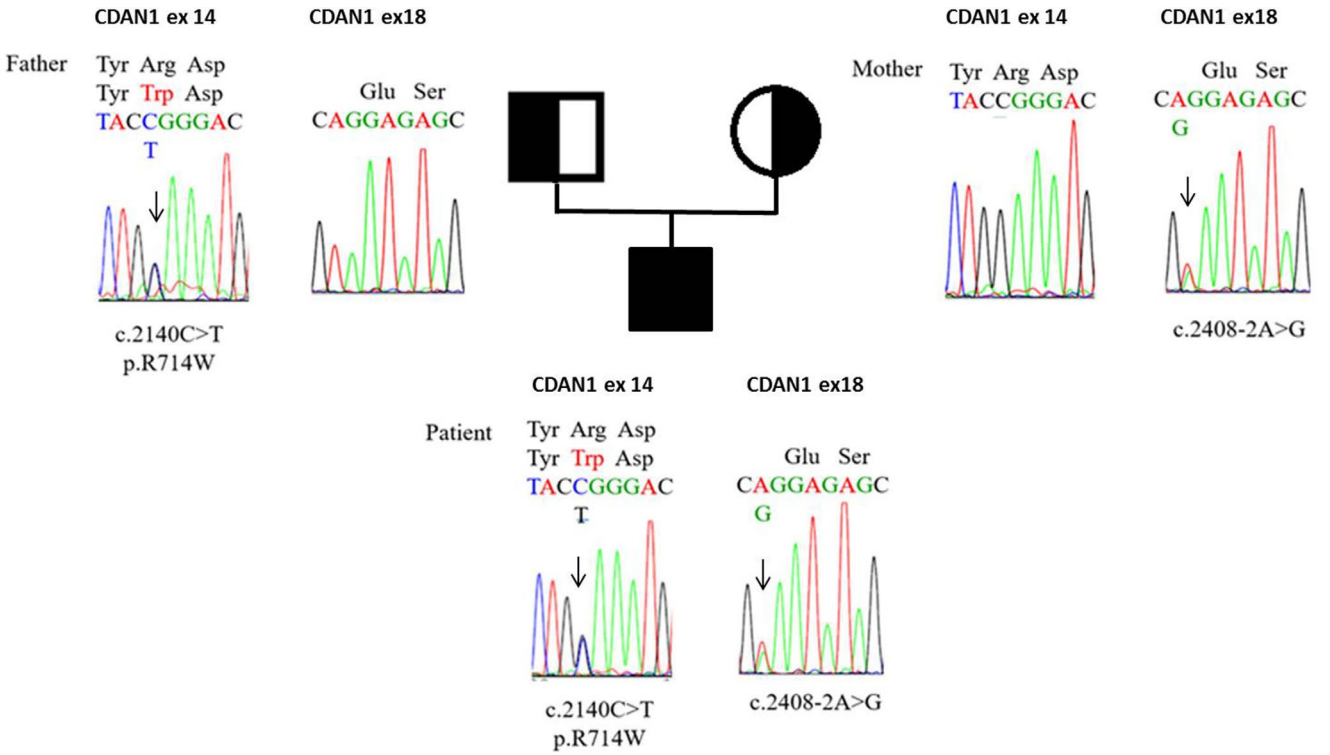


FIGURE 3 The exon 18 intron/exon boundary sequences of wild type (A) and the exon18:c.2408-2A>G (B) were shown. The exon18:c.2408-2A>G likely affects the acceptor splice site of exon 18, which may result in exon18 skipping (a) or the usage of the cryptic intronic (b) or exonic (c) splice sites that leads to the inclusion of an intron fragment or exon fragment skipping. (3′-ss, 3′-splicing site; ex18 frag, exon 18 fragment; in, intron fragement; new ss, new splicing site). Adapted from figure 3, Anna and Monika (2018)

FIGURE 4 The electropherograms indicate compound heterozygous *CDNA1* mutations (c.2140C>T, p.R714W and exon18:c.2408-2A>G) of the patient and the origins of the mutations. The GenBank reference sequence and version number for CDAN1 was NM_138477.4

Tamary et al., 2005; Wang et al., 2018). Splicing mutants were found in 13% of patients with CDA Ia; and, as such, we found a novel splicing mutant present in our patient.

In the German CDA Registry, the age of diagnosis ranged from 0.1 to 45 years (median, 17.3 years). Prior incorrect diagnosis was noted in 30% of their 74 patients with CDA Ia, including pernicious anemia, iron-deficient anemia, thalassemia, or unclassified congenital hemolytic anemia (Heimpel et al., 2006). On the contrary, in an Italian study using NGS based multigene panel testing for patients with hereditary anemias, most of the patients with a nonmatched, clinical diagnosis, and genetic mutations were previously suspected to have suffered from CDA, and nearly half of them exhibited a conclusive diagnosis of enzymatic defects, such as pyruvate kinase deficiencies (Russo et al., 2018). Molecular studies searching the *CDAN1* gene mutations are helpful for making a conclusive diagnosis (Heimpel et al., 2006; Iolascon et al., 2013).

Our patient showed a congenital hemolytic anemia with inadequate reticulocyte count, persistent indirect hyperbilirubinemia, elevated LDH, and feet deformities. The bone marrow smear showed an erythroid hyperplasia; however, the characteristic nuclear bridging, nuclear lobulations, and multinuclearity of erythroblasts were subtle enough to make the diagnosis difficult (see Figure 1). Although most of the patients with CDA Ia showed moderate hemoglobin levels, some transfusion-dependent patients have been reported (Ayas et al., 2002; Parez et al., 2000; Wickramasinghe et al., 1998). A splenectomy is considered to be in vain in order to increase the patient's hemoglobin levels. Long-term complications include iron overload, liver cirrhosis, heart failure, endocrine dysfunction, extramedullary bulk, and leg ulcers (Heimpel et al., 2006). Complicated pregnancies have been reported (Bank, Ermens, Van Der Linden, & Brand, 2012; Shalev et al., 2008). Hematopoietic stem cell transplantation (HSCT) or interferon-α have been successfully applied in transfusion-dependent CDA Ia cases (Ayas et al., 2002; Heimpel et al., 2006; Iolascon et al., 2013). Our patient did not receive HSCT or interferon-α treatment due to the lack of precise diagnosis of a disease before this WES approach study. Correct diagnosis for patients with CDA Ia is important for optimal management purposes. Our group has applied the WES approach with targeted gene panel analysis in the genetic diagnosis of red cell membrane disorders (Lin et al., 2018). In this particular patient, we applied a similar approach and successfully discovered the causative gene mutations as a result. Due to the rarity of CDA Ia, and the overlapping of the clinical manifestations with other hereditary anemias, a next-generation sequencing approach is effective to afford a conclusive diagnosis of CDA Ia.

In conclusion, we present the first case report of CDA Ia in Taiwan. Molecular study of patients with hereditary hemolytic anemia significantly assists in definite diagnosis, disease management and genetic counseling.

ACKNOWLEDGMENTS

This study was supported by grants from the Ministry of Science and Technology (MOST 106-2314-B-037-079-MY2) and the Kaohsiung Medical University Hospital (KMUH107-7R41). The authors thank Paul C. Talley, Ph.D. and Ms. Grace Pei-Chen Lin for language editing.

CONFLICT OF INTEREST

The other authors have no conflicts of interest to disclose.

AUTHOR CONTRIBUTIONS

JGC and PCL conceived of the study and participated in its design and coordination. Clinical data acquisition and analysis were carried out by CNC. YHT, YSC, and CYL carried out the laboratory experiments. HYH conducted the bioinformatics analysis. PCL and CNC wrote this manuscript. All authors have read and approved the final version of the manuscript.

DATA AVAILABILITY STATEMENT

Authors elect to not share data due to privacy/ethical restrictions. The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Pei-Chin Lin https://orcid.org/0000-0002-3371-3010
Chao-Neng Cheng https://orcid.org/0000-0003-3487-9511
Hsi-Yuan Huang https://orcid.org/0000-0001-8453-4939
Yu-Hsin Tseng https://orcid.org/0000-0002-2558-2209
Ya-Sian Chang https://orcid.org/0000-0003-0444-2941
Chien-Yu Lin https://orcid.org/0000-0003-2705-9742
Jan-Gowth Chang https://orcid.org/0000-0003-0375-1427

REFERENCES

Anna, A., & Monika, G. (2018). Splicing mutations in human genetic disorders: Examples, detection, and confirmation. *Journal of Applied Genetics*, *59*(3), 253–268. https://doi.org/10.1007/s13353-018-0444-7

Ayas, M., Al-Jefri, A., Baothman, A., Al-Mahr, M., Mustafa, M. M., Khalil, S., … Solh, H. (2002). Transfusion-dependent congenital dyserythropoietic anemia type I successfully treated with allogeneic stem cell transplantation. *Bone Marrow Transplantation*, *29*(8), 681–682. https://doi.org/10.1038/sj.bmt.1703526

Bank, I., Ermens, A. A., Van Der Linden, J. M., & Brand, A. (2012). A life-threatening episode of treatment-resistant haemolysis in a pregnant patient with dyserythropoietic anaemia (CDA) type I. *Transfusion Medicine*, *22*(2), 145–147. https://doi.org/10.1111/j.1365-3148.2011.01096.x

Dgany, O., Avidan, N., Delaunay, J., Krasnov, T., Shalmon, L., Shalev, H., … Tamary, H. (2002). Congenital dyserythropoietic anemia type I is caused by mutations in codanin-1. *American Journal of Human Genetics*, *71*(6), 1467–1474. https://doi.org/10.1086/344781

Fujino, H., Doisaki, S., Park, Y. D., Hama, A., Muramatsu, H., Kojima, S., & Sumimoto, S. (2013). Congenital dyserythropoietic anemia type 1 with a novel mutation in the CDAN1 gene previously diagnosed as congenital hemolytic anemia. *International Journal of Hematology*, *97*(5), 650–653. https://doi.org/10.1007/s12185-013-1338-4

Heimpel, H., Schwarz, K., Ebnöther, M., Goede, J. S., Heydrich, D., Kamp, T., … Kohne, E. (2006). Congenital dyserythropoietic anemia type I (CDA I): Molecular genetics, clinical appearance, and prognosis based on long-term observation. *Blood*, *107*(1), 334–340. https://doi.org/10.1182/blood-2005-01-0421

Iolascon, A., Esposito, M. R., & Russo, R. (2012). Clinical aspects and pathogenesis of congenital dyserythropoietic anemias: From morphology to molecular approach. *Haematologica*, *97*(12), 1786–1794. https://doi.org/10.3324/haematol.2012.072207

Iolascon, A., Heimpel, H., Wahlin, A., & Tamary, H. (2013). Congenital dyserythropoietic anemias: Molecular insights and diagnostic approach. *Blood*, *122*(13), 2162–2166. https://doi.org/10.1182/blood-2013-05-468223

Iolascon, A., Russo, R., & Delaunay, J. (2011). Congenital dyserythropoietic anemias. *Current Opinion in Hematology*, *18*(3), 146–151. https://doi.org/10.1097/MOH.0b013e32834521b0

Kawabata, H., Doisaki, S., Okamoto, A., Uchiyama, T., Sakamoto, S., Hama, A., … Takaori-Kondo, A. (2012). A case of congenital dyserythropoietic anemia type 1 in a Japanese adult with a CDAN1 gene mutation and an inappropriately low serum hepcidin-25 level. *Internal Medicine*, *51*(8), 917–920. https://doi.org/10.2169/internalmedicine.51.6978

Kumar, A., Kushwaha, R., & Singh, U. S. (2014). Congenital dyserythropoietic anemia type I: Report of a case. *Indian Journal of Hematology and Blood Transfusion*, *30*(1), 48–50. https://doi.org/10.1007/s12288-012-0187-2

Lin, P.-C., Chiou, S.-S., Lin, C.-Y., Wang, S.-C., Huang, H.-Y., Chang, Y.-S., … Chang, J.-G. (2018). Whole-exome sequencing for the genetic diagnosis of congenital red blood cell membrane disorders in Taiwan. *Clinica Chimica Acta*, *487*, 311–317. https://doi.org/10.1016/j.cca.2018.10.020

Parez, N., Dommergues, M., Zupan, V., Chambost, H., Fieschi, J. B., Delaunay, J., … Tchernia, G. (2000). Severe congenital dyserythropoietic anaemia type I: Prenatal management, transfusion support and alpha-interferon therapy. *British Journal of Haematology*, *110*(2), 420–423.

Ru, Y., Liu, G., Bai, J., Dong, S., Nie, N., Zhang, H., … Eyden, B. (2014). Congenital dyserythropoietic anemia in China: A case report from two families and a review. *Annals of Hematology*, *93*(5), 773–777. https://doi.org/10.1007/s00277-013-1933-8

Ru, Y. X., Zhu, X. F., Yan, W. W., Gao, J. T., Schwarz, K., & Heimpel, H. (2008). Congenital dyserythropoietic anemia in a Chinese family with a mutation of the CDAN1-gene. *Annals of Hematology*, *87*(9), 751–754. https://doi.org/10.1007/s00277-008-0519-3

Russo, R., Andolfo, I., Manna, F., Gambale, A., Marra, R., Rosato, B. E., … Iolascon, A. (2018). Multi-gene panel testing improves diagnosis and management of patients with hereditary anemias. *American Journal of Hematology*, *93*(5), 672–682. https://doi.org/10.1002/ajh.25058

Shalev, H., Avraham, G. P., Hershkovitz, R., Levy, A., Sheiner, E., Levi, I., & Tamary, H. (2008). Pregnancy outcome in congenital dyserythropoietic anemia type I. *European Journal of Haematology*, *81*(4), 317–321. https://doi.org/10.1111/j.1600-0609.2008.01109.x

Shalev, H., Kapelushnik, J., Moser, A., Dgany, O., Krasnov, T., & Tamary, H. (2004). A comprehensive study of the neonatal manifestations of congenital dyserythropoietic anemia type I. *Journal of Pediatric Hematology/oncology*, *26*(11), 746–748. https://doi.org/10.1097/00043426-200411000-00011

Shalev, H., Tamary, H., Shaft, D., Reznitsky, P., & Zaizov, R. (1997). Neonatal manifestations of congenital dyserythropoietic anemia type I. *Journal of Pediatrics*, *131*(1 Pt 1), 95–97. https://doi.org/10.1016/S0022-3476(97)70130-6

Tamary, H., Dgany, O., Proust, A., Krasnov, T., Avidan, N., Eidelitz-Markus, T., … Delaunay, J. (2005). Clinical and molecular variability in congenital dyserythropoietic anaemia type I. *British Journal of Haematology*, *130*(4), 628–634. https://doi.org/10.1111/j.1365-2141.2005.05642.x

Tamary, H., Shalev, H., Luria, D., Shaft, D., Zoldan, M., Shalmon, L., … Zaizov, R. (1996). Clinical features and studies of erythropoiesis in Israeli Bedouins with congenital dyserythropoietic anemia type I. *Blood*, *87*(5), 1763–1770. https://doi.org/10.1182/blood.V87.5.1763.1763

Wang, Y., Ru, Y., Liu, G., Dong, S., Li, Y., Zhu, X., … Nie, G. (2018). Identification of CDAN1, C15ORF41 and SEC23B mutations in Chinese patients affected by congenital dyserythropoietic anemia. *Gene*, *640*, 73–78. https://doi.org/10.1016/j.gene.2017.10.027

Wickramasinghe, S. N., Vora, A. J., Will, A., Winfield, D. A., Hughes, R. G., Sekhar, M., & Loftus, G. (1998). Transfusion-dependent congenital dyserythropoietic anaemia with non-specific dysplastic changes in erythroblasts. *European Journal of Haematology*, *60*(2), 140–142. https://doi.org/10.1111/j.1600-0609.1998.tb01013.x

Wickramasinghe, S. N., & Wood, W. G. (2005). Advances in the understanding of the congenital dyserythropoietic anaemias. *British Journal of Haematology*, *131*(4), 431–446. https://doi.org/10.1111/j.1365-2141.2005.05757.x

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Lin P-C, Cheng C-N, Huang H-Y, et al. Congenital dyserythropoiesis anemia type Ia with a novel *CDAN1* mutation diagnosed by whole exome sequencing. *Mol Genet Genomic Med*. 2020;8:e1220. https://doi.org/10.1002/mgg3.1220