ISSN 2307-8960 (online)

World Journal of *Clinical Cases*

World J Clin Cases 2023 April 16; 11(11): 2363-2581

Published by Baishideng Publishing Group Inc

World Journal of Clinical Cases

Contents

Thrice Monthly Volume 11 Number 11 April 16, 2023

REVIEW

MINIREVIEWS

ORIGINAL ARTICLE

Retrospective Study

Observational Study

CASE REPORT

World Journal of Clinical Cases

Thrice Monthly Volume 11 Number 11 April 16, 2023

Contents

World Journal of Clinical Cases

Thrice Monthly Volume 11 Number 11 April 16, 2023

Contents

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Farooq Shahzad, FACS, MBBS, MS, Assistant Professor, Plastic Surgery Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY 10065, United States. fooqs@hotmail.com

AIMS AND SCOPE

The primary aim of *World Journal of Clinical Cases* (*WJCC*, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING

The *WJCC* is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Journal Citation Reports/Science Edition, Current Contents®/Clinical Medicine, PubMed, PubMed Central, Scopus, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2022 Edition of Journal Citation Reports® cites the 2021 impact factor (IF) for *WJCC* as 1.534; IF without journal self cites: 1.491; 5-year IF: 1.599; Journal Citation Indicator: 0.28; Ranking: 135 among 172 journals in medicine, general and internal; and Quartile category: Q4. The *WJCC*'s CiteScore for 2021 is 1.2 and Scopus CiteScore rank 2021: General Medicine is 443/826.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Hua-Ge Yu*; **Production Department Director:** *Xiang Li*; **Editorial Office Director:** *Jin-Lei Wang*.

NAME OF JOURNAL
World Journal of Clinical Cases

ISSN
ISSN 2307-8960 (online)

LAUNCH DATE
April 16, 2013

FREQUENCY
Thrice Monthly

EDITORS-IN-CHIEF
Bao-Gan Peng, Jerzy Tadeusz Chudek, George Kontogeorgos, Maurizio Serati, Ja Hyeon Ku

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/2307-8960/editorialboard.htm

PUBLICATION DATE
April 16, 2023

COPYRIGHT
© 2023 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

© 2023 Baishideng Publishing Group Inc. All rights reserved. 7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
E-mail: bpgoffice@wjgnet.com https://www.wjgnet.com

World Journal of Clinical Cases

Submit a Manuscript: https://www.f6publishing.com

World J Clin Cases 2023 April 16; 11(11): 2452-2456

DOI: 10.12998/wjcc.v11.i11.2452

ISSN 2307-8960 (online)

CASE REPORT

Aicardi-Goutières syndrome type 7 in a Chinese child: A case report

Shuang-Zhu Lin, Jing-Jing Yang, Tian-Long Xie, Jia-Yi Li, Jia-Qi Ma, Si Wu, Na Wang, Yong-Ji Wang

Specialty type: Genetics and heredity

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Mirsalehi M, Iran

Received: August 13, 2022
Peer-review started: August 13, 2022
First decision: November 11, 2022
Revised: February 22, 2023
Accepted: March 17, 2023
Article in press: March 17, 2023
Published online: April 16, 2023

Shuang-Zhu Lin, Jing-Jing Yang, Tian-Long Xie, Yong-Ji Wang, Diagnosis and Treatment Center for Children, Affiliated Hospital of Changchun University of Chinese Medicine, Changchun 130021, Jilin Province, China

Jia-Yi Li, Jia-Qi Ma, Si Wu, Na Wang, College of Traditional Chinese Medicine, Changchun University of Chinese Medicine, Changchun 130017, Jilin Province, China

Corresponding author: Yong-Ji Wang, MD, Professor, Diagnosis and Treatment Center for Children, Affiliated Hospital of Changchun University of Chinese Medicine, No. 185 Shenzhen Street, Nanguan Economic and Technological Development Zone, Changchun 130021, Jilin Province, China. 18943188651@189.cn

Abstract

BACKGROUND

IFIH1 is a protein-coding gene. Disorders associated with *IFIH1* include Aicardi-Goutières syndrome (AGS) type 7 and Singleton-Merten syndrome type 1. Related pathways include RIG-I/MDA5-mediated induction of the interferon (IFN)-α/β pathway and the innate immune system. AGS type 7 is an autosomal dominant inflammatory disorder characterized by severe neurological impairment. In infancy, most patients present with psychomotor retardation, axial hypotonia, spasticity, and brain imaging changes Laboratory assessments showed increased IFN-α activity with upregulation of IFN signaling and IFN-stimulated gene expression. Some patients develop normally in the early stage, and then have episodic neurological deficits.

CASE SUMMARY

The 5-year-old girl presented with postpartum height and weight growth retardation, language retardation, brain atrophy, convulsions, and growth hormone deficiency. DNA samples were obtained from peripheral blood from the child and her parents for whole-exome sequencing and test of genome-wide copy number variation. Heterozygous mutations in the *IFIH1* gene were found. Physical examination at admission found that language development was delayed, the reaction to name calling was average, there was no communication with people, but there was eye contact, no social smile, and no autonomous language. However, the child had rich gesture language and body language, could understand instructions, had bad temper. When she wants to achieve something, she starts crying or shouting. Cardiopulmonary examination showed no obvious abnormality, and abdominal examination was normal. Bilateral muscle strength and muscle tone were symmetrical and slightly decreased. Physiological reflexes exist, but pathological reflexes were not elicited.

CONCLUSION
We reported the clinical characteristics of a Chinese child with a clinical diagnosis of AGS type 7, which expanded the mutational spectrum of the *IFIH1* gene.

Key Words: Aicardi-Goutières syndrome type 7; *IFIH1* gene; Children; Case report

©The Author(s) 2023. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: We report a 5-year-old girl with Aicardi-Goutières syndrome type 7. The clinical characteristics included postnatal height and weight retardation, delayed language development, brain atrophy, convulsions, and growth hormone deficiency. Whole exome test showed c.1093A>G (p.Lys365Glu) and heterozygous mutation in *IFIH1* gene, and the mutation source was her father. This report provides a molecular basis for etiological diagnosis and treatment of the child, as well as for genetic counseling for the pedigree.

Citation: Lin SZ, Yang JJ, Xie TL, Li JY, Ma JQ, Wu S, Wang N, Wang YJ. Aicardi-Goutières syndrome type 7 in a Chinese child: A case report. *World J Clin Cases* 2023; 11(11): 2452-2456
URL: https://www.wjgnet.com/2307-8960/full/v11/i11/2452.htm
DOI: https://dx.doi.org/10.12998/wjcc.v11.i11.2452

INTRODUCTION

Aicardi-Goutières syndrome (AGS) is a rare, genetically determined early-onset progressive encephalopathy[1-4]. Individuals affected with AGS typically suffer from progressive microcephaly associated with severe neurological symptoms, such as hypotonia, dystonia, seizures, spastic quadriplegia[5,6], and severe developmental delay. On brain imaging, AGS is characterized by basal ganglia calcification, white matter abnormalities, and cerebral atrophy cerebrospinal fluid analyses show chronic lymphocytosis and elevated levels of the interferon (IFN)-α[7] and neopterin. AGS-affected individuals are often misdiagnosed as having intrauterine infections, such as Pseudo-TORCH syndrome[8] (Pseudo-TORCH syndrome is a rare, chronic disorder that is characterised by dimorphic features such as microcephaly, intracranial calcification, seizures, mental retardation, hepatosplenomegaly and coagulation disorders), because of the similarities of these disorders, particularly the intracranial calcifications. AGS type 7 (AGS7) is an autosomal dominant inflammatory disorder characterized by severe neurological impairment. Episodic neurological deficits occur after the onset. Therefore, diseases related to mutations at the genetic locus must be diagnosed in the early phase so as to be treated in timely.

CASE PRESENTATION

Chief complaints

She was 3 years old at the time of her first visit and presented on 16 September 2020 due to language delay. She is 5 years old now.

History of present illness

Since age 6 mo, she had had obvious slow growth in height and weight. Language development was delayed. Her response to name calling was normal but there was no communication with people. Her eyes could not be met and there was no social smile. There was no autonomous language, However, the child had rich gesture language and body language, she could understand instructions, had a short temper, and when she wants to achieve something, she starts crying or shouting. She was thin, with a weight of 9 kg and height of 83 cm.

History of past illness

There was no obvious abnormality at birth, weight 3 kg, height 50 cm. She raised her head at 3 mo, crawled at 7 mo, and walked at 15 mo. She had a history of febrile convulsions twice, each lasting about 2 min, which resolved spontaneously, and a 1-year history of ulcerative colitis.

Personal and family history

Both parents were healthy.

Physical examination

Body temperature was 36.2 °C, heart rate 96 beats/min, breathing 24 beats/min, blood pressure 100/60 mmHg, height 83.0 cm and weight 9 kg. There was no special sick face, and cardiopulmonary and abdominal examinations showed no obvious abnormalities. Bilateral muscle strength and muscle tone were symmetrical and slightly decreased. Physiological reflexes were present but pathological reflexes were not elicited.

Laboratory examinations

Routine blood and urine examinations, myocardial enzymes, lactic acid, liver function, renal function, electrolytes, blood glucose, thyroid function, and hematuria showed no obvious abnormalities. The peak growth hormone challenge test was 5.77 ng/mL.

Imaging examinations

Video electroencephalography showed no abnormalities. Magnetic resonance imaging (MRI) of the brain showed mild atrophy.

FINAL DIAGNOSIS

AGS7 caused by a missense mutation in the *IFIH1* gene.

TREATMENT

Symptomatic nutritional support and rehabilitation were undertaken.

OUTCOME AND FOLLOW-UP

The child was followed up for 1 year and 9 mo. Her weight increased to 12 kg and height to 90 cm. Language ability improved, and simple conversations could be conducted.

DISCUSSION

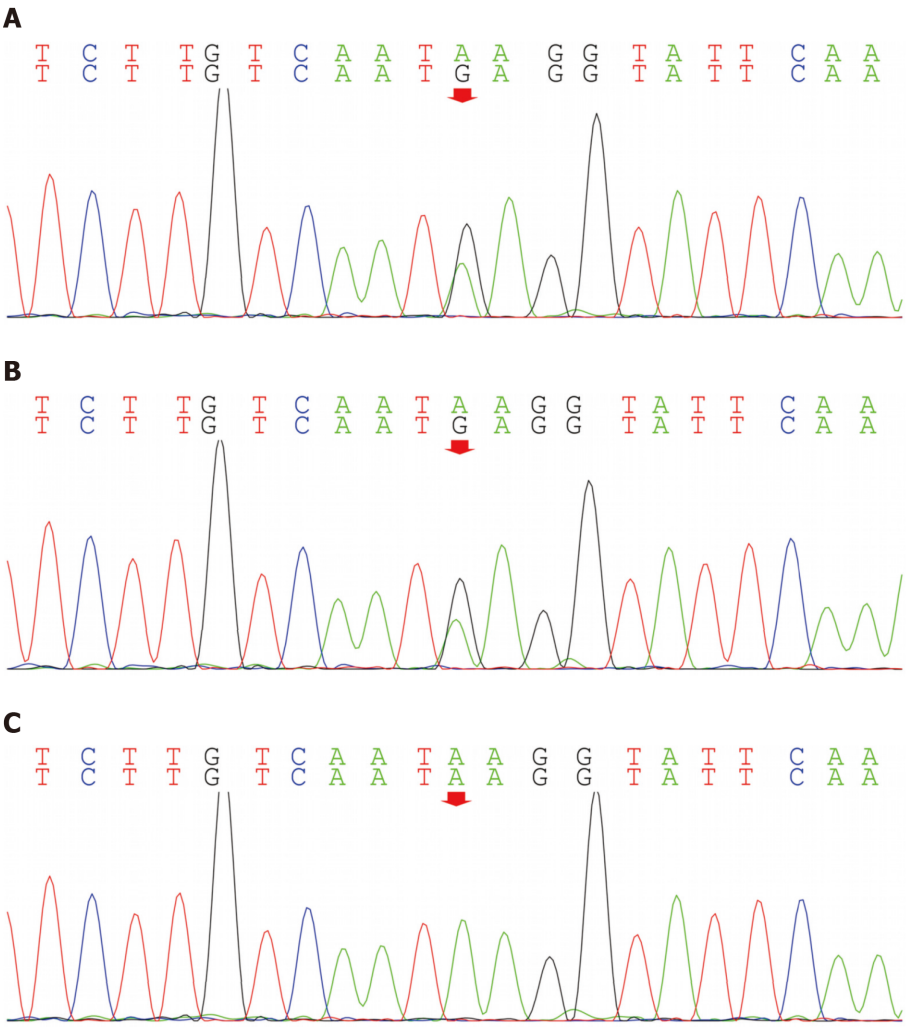
Our patient presented with growth retardation, language retardation, brain atrophy and convulsions as the main clinical manifestations. Among the various examination indicators of our patient, we particularly noticed that the peak value of growth hormone was decreased, and MRI of the brain showed brain atrophy, Combined with the patient's clinical symptoms and physical and chemical examination results, we considered the possibility of hereditary metabolic disease or genetic disease. Subsequent genetic metabolic screening for hematuria showed no obvious abnormality.

Whole exome analysis showed that the *IFIH1* gene had a c.1093A>G (p.Lys365Glu) heterozygous mutation, and the source of the mutation was her father (Figure 1A-C). *IFIH1* gene can cause two diseases, AGS7, and Singleton-Merten syndrome type 1. According to their clinical manifestations, children are more likely to have AGS7[1]. AGS (MIM 615846) is a rare genetic disorder characterized by aberrant type 1 IFN production and systemic, chronic inflammation. *IFIH1* gene[2-4] may lead to changes in MDA5[7] and type 1 IFN (Mutations in the *IFIH1* gene lead to overproduction of type 1 interferons, resulting in the AGS phenotype). AGS 7 may lead to an increase in type 1 IFN, and there are clinical manifestations caused by elevated type 1 IFN. Our patient had similar manifestations, but due to the patient's clinical conditions, we did not examine the IFN concentration.

It has been reported that the *IFIH1* gene is inherited in an autosomal dominant manner, with high heterogeneity and incomplete penetrance. Our patient had c.1093A>G (p.Lys365Glu) heterozygous mutation, and the pathogenicity of this variant has been reported previously. The clinical manifestations of the child were consistent with the clinical features of AGS7.

CONCLUSION

In summary, we reported the clinical characteristics of a Chinese child with a clinical diagnosis of AGS7, which expanded the mutational spectrum of the *IFIH1* gene.



DOI: 10.12998/wjcc.v11.i11.2452 **Copyright** ©The Author(s) 2023.

Figure 1 Whole-exome gene sequencing. A: *IFIH1* gene of the patient was found to have c.1093A>G (p.Lys365Glu), and heterozygous mutation. B: The source of mutation was her father. C: The sequencing of the patient's mother.

FOOTNOTES

Author contributions: Lin SZ wrote the manuscript; Yang JJ and Xie TL analyzed the data; Li JY, Ma JQ, Wu S, Wang N contributed to data collation; Wang YJ provided the medical records; all authors approved the final version of the manuscript to be published.

Informed consent statement: Informed consent has been obtained with the support of the child's family.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

Country/Territory of origin: China

ORCID number: Shuang-Zhu Lin 0000-0001-5333-2138; Jia-Yi Li 0000-0002-7729-4479; Yong-Ji Wang 0000-0001-7222-5645.

S-Editor: Gong ZM
L-Editor: A

P-Editor: Gong ZM

REFERENCES

1 **Oda H**, Nakagawa K, Abe J, Awaya T, Funabiki M, Hijikata A, Nishikomori R, Funatsuka M, Ohshima Y, Sugawara Y, Yasumi T, Kato H, Shirai T, Ohara O, Fujita T, Heike T. Aicardi-Goutières syndrome is caused by IFIH1 mutations. *Am J Hum Genet* 2014; **95**: 121-125 [PMID: 24995871 DOI: 10.1016/j.ajhg.2014.06.007]

2 **Adang LA**, Frank DB, Gilani A, Takanohashi A, Ulrick N, Collins A, Cross Z, Galambos C, Helman G, Kanaan U, Keller S, Simon D, Sherbini O, Hanna BD, Vanderver AL. Aicardi goutières syndrome is associated with pulmonary hypertension. *Mol Genet Metab* 2018; **125**: 351-358 [PMID: 30219631 DOI: 10.1016/j.ymgme.2018.09.004]

3 **Amari S**, Tsukamoto K, Ishiguro A, Yanagi K, Kaname T, Ito Y. An extremely severe case of Aicardi-Goutières syndrome 7 with a novel variant in IFIH1. *Eur J Med Genet* 2020; **63**: 103646 [PMID: 30965144 DOI: 10.1016/j.ejmg.2019.04.003]

4 **Rice GI**, Del Toro Duany Y, Jenkinson EM, Forte GM, Anderson BH, Ariaudo G, Bader-Meunier B, Baildam EM, Battini R, Beresford MW, Casarano M, Chouchane M, Cimaz R, Collins AE, Cordeiro NJ, Dale RC, Davidson JE, De Waele L, Desguerre I, Faivre L, Fazzi E, Isidor B, Lagae L, Latchman AR, Lebon P, Li C, Livingston JH, Lourenço CM, Mancardi MM, Masurel-Paulet A, McInnes IB, Menezes MP, Mignot C, O'Sullivan J, Orcesi S, Picco PP, Riva E, Robinson RA, Rodriguez D, Salvatici E, Scott C, Szybowska M, Tolmie JL, Vanderver A, Vanhulle C, Vieira JP, Webb K, Whitney RN, Williams SG, Wolfe LA, Zuberi SM, Hur S, Crow YJ. Gain-of-function mutations in IFIH1 cause a spectrum of human disease phenotypes associated with upregulated type I interferon signaling. *Nat Genet* 2014; **46**: 503-509 [PMID: 24686847 DOI: 10.1038/ng.2933]

5 **Liu N**, Chen J, Xu C, Shi T, Li J. Hereditary spastic paraplegia associated with a rare IFIH1 mutation: a case report and literature review. *Hereditas* 2019; **156**: 28 [PMID: 31427910 DOI: 10.1186/s41065-019-0104-x]

6 **Crow YJ**, Zaki MS, Abdel-Hamid MS, Abdel-Salam G, Boespflug-Tanguy O, Cordeiro NJ, Gleeson JG, Gowrinathan NR, Laugel V, Renaldo F, Rodriguez D, Livingston JH, Rice GI. Mutations in ADAR1, IFIH1, and RNASEH2B presenting as spastic paraplegia. *Neuropediatrics* 2014; **45**: 386-393 [PMID: 25243380 DOI: 10.1055/s-0034-1389161]

7 **Lamborn IT**, Jing H, Zhang Y, Drutman SB, Abbott JK, Munir S, Bade S, Murdock HM, Santos CP, Brock LG, Masutani E, Fordjour EY, McElwee JJ, Hughes JD, Nichols DP, Belkadi A, Oler AJ, Happel CS, Matthews HF, Abel L, Collins PL, Subbarao K, Gelfand EW, Ciancanelli MJ, Casanova JL, Su HC. Recurrent rhinovirus infections in a child with inherited MDA5 deficiency. *J Exp Med* 2017; **214**: 1949-1972 [PMID: 28606988 DOI: 10.1084/jem.20161759]

8 **Meuwissen ME**, Schot R, Buta S, Oudesluijs G, Tinschert S, Speer SD, Li Z, van Unen L, Heijsman D, Goldmann T, Lequin MH, Kros JM, Stam W, Hermann M, Willemsen R, Brouwer RW, Van IJcken WF, Martin-Fernandez M, de Coo I, Dudink J, de Vries FA, Bertoli Avella A, Prinz M, Crow YJ, Verheijen FW, Pellegrini S, Bogunovic D, Mancini GM. Human USP18 deficiency underlies type 1 interferonopathy leading to severe pseudo-TORCH syndrome. *J Exp Med* 2016; **213**: 1163-1174 [PMID: 27325888 DOI: 10.1084/jem.20151529]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com

© 2023 Baishideng Publishing Group Inc. All rights reserved.