Dear Editors and Reviewers:

Thank you for giving us an opportunity to revise our manuscript. We appreciate the editor and reviewers very much for their positive and constructive comments and suggestions on our manuscript entitled “Two Chinese infants with transient diabetes mellitus due to a novel de novo ABCC8 variant treated with sulfonylurea” (Manuscript NO: 94430). Those comments are all valuable for revising and improving our paper and providing necessary guidance and significance to our future research. We have studied the comments carefully and have made corrections, which we hope will meet with approval. Responses to the reviewer’s comments:

Corresponding Author’s Comments to Editor:

Reply: Thank you for your comments.

①In this study, author Shengnan Wu is the correct name.

②Children's Hospital Affiliated to Zhengzhou University, Henan Children's Hospital Zhengzhou Children's Hospital is a correct author and corresponding author affiliation.

③450018 is the correct postcode.

Item No.1

Reviewer #1:

There are several minor recommendations: Authors state: “Early genetic testing of neonatal diabetes mellitus aids in accurate diagnosis and treatment,
avoiding pain from daily insulin injections.

Although injections are painful and are linked to complications there is another side of neonatal diabetes. These patients rarely benefit from insulin injections and their glycated hemoglobin is high. I would recommend adding to the conclusions that patient do not benefit from the treatment with insulin.

Reply: Thank you for your comments. For neonatal diabetes mellitus patients, insulin therapy is usually required but can be difficult to manage in infants. This is due to the irregular feeding habits of infants; therefore, these patients usually require multiple subcutaneous insulin injections. Moreover, both infants in our manuscript presented with ketoacidosis at onset and required insulin therapy. Following the first heterozygous activating ABCC8 variations causing NDM described in humans, which was reported in 2006, sulfonylurea oral drugs are efficacious and well-tolerated in patients with KATP channel variations. However, not all patients with ABCC8 variations respond effectively to sulfonylurea drugs, and insulin treatment is still required. Therefore, the recommendation that patients do not benefit from insulin treatment should be carefully considered.

Please indicate the time of follow-up.

Reply: Thank you for your comments. The follow-up period extends until just before the submission.

Please compare the current cases with other types of MODY or neonatal diabetes.
Reply: Thank you for your comments. Neonatal diabetes is a rare disease, and neonatal diabetes mellitus (NDM) caused by ABCC8 variants is a rare type of neonatal diabetes mellitus. The current literature we searched primarily comprised case reports, which typically focus on clinical presentations that share experiential insights. We acknowledge that some of the pathogenic ABCC8 variants may cause monogenic diabetes with phenotypic variability between and within families and incomplete penetrance in some circumstances. For example, Silvestri F et al. reported that the Arg1379His heterozygous variant in ABCC8 causes monogenic diabetes with variable phenotype presentation and incomplete penetrance. Arg1379His variant caused NDM in an infant but was unlinked to a diabetic phenotype in his carrier father. Silvestri F et al. literature review confirmed that this variant is associated with variable clinical presentation, from NDM to MODY (at different ages of onset) among family members carrying the variant or patients misdiagnosed with type 2 diabetes. The patient carrying the ABCC8/Arg1379His presents with diabetic ketoacidosis and can also be successfully treated with sulfonylureas. However, the long-term follow-up status remains unclear.

Ozsu E et al. reported the successful transition to sulfonylureas in two Iraqi siblings with permanent NDM (PNDM) due to ABCC8 homozygous missense variant (p.R826W), one with iDEND. The two siblings also highlight the fact that patients can have phenotypic variability with an identical mutation.

Literature review shows that the current reported pathogenic variations in ABCC8 (Leu213Pro, Leu225Pro, Val360Ala, Ser459Arg, Thr540Ile+4415-13G>A, Phe577Leu, Asp811Val, Arg825Trp, Gly832Cys,
Thr1381Asn, Arg1182Gln, Arg1380Cys, Arg1380His, Glu1141Gly, Pro1199Ser, Pro1199Gln, Val1523Met, Val1540Met) can cause TNDM. The ABCC8 gene variants associated with TNDM were reviewed and summarized in Figure 4. A total of 12 cases with detailed clinical information and the outcomes of sulfonylurea therapy transfer have been summarized in Table 1 (including the 2 cases in our manuscript).

Our manuscript describes the ABCC8 c.3880C>T (Leu1294Phe) heterozygous variant causing TNDM in two infants from two unrelated families. This variant has not been previously reported. The two infants were successfully treated with sulfonylurea therapy.

Please take into account the recommendation in the spirit of improving the quality of the submission.

Reply: Thank you for your comments. We sincerely appreciate the valuable feedback you have provided. We will diligently follow your suggestions to comprehensively revise and enhance the article, aiming to meet the publication standards of academic journals. Thank you again for your guidance.

Yours sincerely,

Linghua Shen

Reviewer #2:
The manuscript discusses cases of transient neonatal diabetes mellitus (TNDM) attributed to a specific ABCC8 variant. While the described mutation (c.3880C>T) may be novel, it's essential to note that the link between ABCC8 mutations and neonatal diabetes treated with sulfonylurea therapy has been previously reported in the literature. For instance, articles dating back to 2006 have documented similar cases, albeit with different mutations in the
ABCC8 gene. Therefore, while the specific mutation identified in the manuscript may be new, the broader association between ABCC8 mutations and neonatal diabetes is not novel. Additionally, it's important to consider that the manuscript may still contribute valuable insights, particularly in characterizing the clinical manifestations and treatment outcomes associated with this specific ABCC8 variant. However, the novelty of the manuscript lies primarily in the detailed description of the c.3880C>T mutation and its implications for diagnosis and treatment in these specific cases. Moreover, the manuscript could benefit from a clearer discussion regarding the significance of identifying this particular mutation, especially in terms of its clinical implications and potential therapeutic approaches. Providing a more in-depth analysis of the specific mutation's impact on disease presentation, treatment response, and long-term prognosis would enhance the manuscript's overall contribution to the field of neonatal diabetes research. Overall, it's crucial to recognize that while the manuscript presents new cases, its contribution may be limited if it merely repeats existing findings without offering substantial insights into the clinical relevance or management of the identified mutation. It is highlighted the need for the manuscript to offer novel insights beyond the identification of the specific mutation. To ensure the work is novel and not repetitive, the authors could consider the following suggestions:

1. Connect the Mutation with New Management: The authors should explore potential novel diagnostic or therapeutic approaches associated with the identified mutation. This could involve investigating unique treatment responses, prognostic implications, or therapeutic targets specific to this mutation.
Reply: Thank you for your comments. Neonatal diabetes mellitus is a rare disease, and TNDM caused by ABCC8 variants is a rare type of neonatal diabetes mellitus. The current literature we reviewed primarily comprised case reports, which typically aim to share experiential insights. We acknowledge that some of the pathogenic ABCC8 variants may give rise to monogenic diabetes with phenotypic variability between and within families and incomplete penetrance in some circumstances. ABCC8 variations are associated with a variable clinical presentation and can cause Transient Neonatal Diabetes Mellitus (TNDM), Permanent Neonatal Diabetes Mellitus (PNDM), and Maturity-Onset Diabetes of the Young 12 (MODY12). Following the first heterozygous activating ABCC8 variations causing NDM, which was described in humans in 2006, it has been reported that sulfonylurea oral drugs are efficacious and well-tolerated in those patients with KATP channel variations. Sulfonylurea oral medications have benefitted numerous patients with neonatal diabetes, including those with neurological symptoms (iDEND), by alleviating the daily burden of insulin injections and facilitating clinical and home management. However, not all patients with ABCC8 variations respond effectively to sulfonylurea drugs. Our manuscript described the ABCC8 c.3880C>T (Leu1294Phe) heterozygous variant causing TNDM in two infants from two unrelated families and explored therapeutic approaches associated with the identified variant. This variant has not been previously reported. The two infants presented with ketoacidosis at onset, and our clinical evidence proved that the two infants were successfully treated with sulfonylurea therapy. This genetic diagnosis will inform clinicians on the probable course and best management of the patient's diabetes and the likely future development of additional clinical features. Therefore, the manuscript
may help guide future clinical management.

Comparative Analysis with Other Mutations: Conduct a comparative analysis between this newly identified mutation and other known mutations in the ABCC8 gene. Highlighting any differences or similarities in clinical presentation, treatment response, or disease progression could reveal unique features of the mutation.

Reply: Thank you for your comments. The literature we reviewed predominantly includes case reports that focus on clinical presentations and the efficacy of sulfonylurea drugs in NDM treatment, and in most cases, the clinical data was not completely intact. Therefore, we reviewed the current reported pathogenic variants in ABCC8 associated with TNDM, which was Leu213Pro, Leu225Pro, Val360Ala, Ser459Arg, Thr540Ile+4415-13G>A, Phe577Leu, Asp811Val, Arg825Trp, Gly832Cys, Thr1381Asn, Arg1182Gln, Arg1380Cys, Arg1380His, Glu1141Gly, Pro1199Ser, Pro1199Gln, Val1523Met, and Val1540Met. The ABCC8 gene variants associated with TNDM were reviewed and summarized in Figure 4.

However, the newly identified variant Leu1294Phe in ABCC8 can still be compared with other known variants in the ABCC8 gene. For example, Silvestri F et al. reported that the Arg1379His heterozygous variant in ABCC8 causes monogenic diabetes with variable phenotype presentation and incomplete penetrance. Arg1379His variant caused TNDM in an infant but was unlinked to a diabetic phenotype in his carrier father. Silvestri F et al. literature review confirmed that this variant is associated with variable clinical presentation, from TNDM to MODY (at different ages of onset) among family members carrying the variant or patients misdiagnosed with type 2 diabetes. The patient carrying the ABCC8/Arg1379His presented with
diabetic ketoacidosis and can also be successfully treated with sulfonylureas. However, the long-term follow-up status remains unclear.

Ozsu E et al. reported the successful transition to sulfonylureas in two Iraqi siblings with permanent NDM (PNDM) due to ABCC8 homozygous missense variant (p.R826W), one with iDEND. The two siblings also highlight the fact that patients can have phenotypic variability with an identical mutation. The two patients in this report presented with diabetic ketoacidosis, did not manifest iDEND. They were successfully treated with sulfonylureas, which was discontinued after 1 month and 1 year of oral administration, respectively. No significant side effects of glyburide were observed. Notably, all these differences or similarities in clinical presentation, treatment response, or disease prognosis reveal the unique features of the mutation. A total of 12 cases with detailed clinical information and the outcomes of sulfonylurea therapy transfer have been summarized in Table 1 (including the 2 cases in our manuscript).

③Functional Studies: Conduct functional studies to elucidate the biological significance of the mutation. This could involve in vitro or in vivo experiments to assess its impact on cellular function, insulin secretion, or other relevant physiological processes.
Reply: Thank you for your comments. Functional in vitro or in vivo experiments to clarify the biological significance of the de novo variant are valuable suggestions. We apologize, but we are unable to address this comment as this study was performed retrospectively based on clinical observations, and we cannot perform any further experiments. Due to ABCC8 variations, patients with TNDM have a high possibility of recurrence in the future; therefore, we will continue to follow up with the children for an extended period.

④Clinical Correlation: Investigate the clinical correlation of the mutation with disease severity, treatment outcomes, or comorbidities. This could involve retrospective or prospective cohort studies to determine if the mutation confers any specific clinical characteristics or risks.

Reply: Thank you for your comments. Neonatal diabetes is a rare disease; however, TNDM caused by ABCC8 variants is a type of neonatal diabetes mellitus. The literature we reviewed predominantly includes case reports that focus on clinical presentations and the efficacy of sulfonylurea drugs in NDM treatment. In most cases, the clinical data is not completely intact and cannot be acquired. The clinical correlation of the variant with disease severity, treatment outcomes, or comorbidities has already been described in detail in the manuscript. And a total of 12 cases with detailed clinical information and the outcomes of sulfonylurea therapy transfer have been summarized in Table 1(including the 2 cases in our manuscript).

⑤Exploration of Understudied Aspects: Explore understudied aspects related to the mutation, such as its association with other conditions, epigenetic modifications, or interactions with environmental factors.
Reply: Thank you for your comments. Exploring understudied aspects associated with the mutation, such as its association with other conditions, epigenetic modifications, or interactions with environmental factors, is a valuable suggestion. ABCC8 variations are associated with a variable clinical presentation and can cause Transient Neonatal Diabetes Mellitus (TNDM), Permanent Neonatal Diabetes Mellitus (PNDM), and Maturity-Onset Diabetes of the Young 12 (MODY12). Patients with pathogenic ABCC8 variants have variable phenotypes, between and within families, and even with identical mutation. Given the complexity of the pathogenic mechanism, additional understudied aspects should be explored in future research.

By incorporating one or more of these strategies, the authors can ensure their work provides novel insights and advances our understanding of the clinical significance of the identified mutation in neonatal diabetes mellitus.
Reply: Thank you for your comments. Our manuscript described the ABCC8 c.3880C>T (Leu1294Phe) heterozygous variant causing TNDM in two infants from two unrelated families and explored therapeutic approaches associated with the identified variant. This variant has not been previously reported. The two infants presented with ketoacidosis at onset, and our clinical evidence proved that the two infants were successfully treated with sulfonylurea therapy. This genetic diagnosis will inform clinicians on the probable course and best management of the patient's diabetes and the likely future development of additional clinical features. Therefore, the manuscript could advance our understanding of the clinical significance of the identified variant in neonatal diabetes mellitus and help guide future clinical management.

Thank you again for your guidance.

Yours sincerely,

Linghua Shen

Item No.2

1 Scientific quality: The authors submitted a case report of two Chinese infants with transient diabetes mellitus treated with sulfonylureas due to a novel ABCC8 gene variant.

(1) Classification: Grade B and Grade B.

(2) Summary of the Peer-Review Report: Reviewer notes: In the current presentation, the study does not offer new findings beyond the identification of a specific mutation. However, without introducing novel diagnostic or therapeutic approaches associated with this mutation, its significance remains unclear. It is suggested that the authors explore potential connections between this new mutation and innovative management strategies to elucidate its clinical implications effectively. Alternatively, they could compare this mutation with others, highlighting any differences or similarities. If the mutation’s effects are found to be comparable to known mutations on the same ABCC8 gene, it would suggest a lack of distinction among them. Therefore, emphasizing any unique features or implications of this
mutation is essential to enhance the manuscript's impact and significance in the field;

**Reviewer 2 notes:** The authors note that “early genetic testing for neonatal diabetes can help to accurately diagnose and treat the condition and avoid the pain associated with daily insulin injections.” While insulin injections are painful and associated with complications, there is another side to neonatal diabetes. These patients rarely benefit from insulin injections and they have high glycosylated hemoglobin. It is recommended that the following be added to the conclusion that “patients do not benefit from insulin therapy.” Please indicate the duration of follow-up. Please compare the current case with other types of MODY or neonatal diabetes. The questions raised by the reviewers should be answered.

(3) **References recommendations:** The reviewer didn’t request the authors to cite improper references published by him/herself.

(4) **Manuscript Type:** After verification, the manuscript type is "Case Report".

**2 Specific comments**

(1) The language classification is Grade B and Grade A. Please visit the following website for the professional English language editing companies that we recommend: https://www.wjgnet.com/bpg/gerinfo/240.

(2) **Manuscript Title:** The title will concisely summarize the main topic of the study, being not overly long (no more than 18 words). If a title contains a colon, please capitalize the first letter of the first word after the colon. For example: Unexplained fetal tachycardia: A case report.

(3) **The “Key Words” does not meet the requirements:** Please do not use abbreviations for the keywords (e.g., Ulcerative colitis, not UC). An example of correct formatting is: Non-alcoholic fatty liver disease; Alcoholic liver disease; Non-alcoholic steatohepatitis; Insulin resistance; Oxidative stress.

(4) **Please revise the reference formatting.** The reference does not require superscripts, please modify it. The correct format is "the spleen hilum[3]."

To ensure the accuracy of the references, please use "Edit References by Auto-Analyser" (https://www.f6publishing.com/Forms/main/ArticleReferenceTool.aspx) to edit the references of the manuscript.

(5) **Figures.** In the meantime, authors should provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor, and upload it to the file destination of “Image File” in the F6Publishing system.

(6) The main text of case report contains “INTRODUCTION”; “CASE PRESENTATION”: [(1) Chief complaints; (2) History of present illness; (3) History of past illness; (4) Personal and family history; (5) Physical examination upon admission; (6) Laboratory examinations; and (7) Imaging examinations]; “FINAL DIAGNOSIS”; “TREATMENT”; and “OUTCOME AND FOLLOW-UP”; “DISCUSSION” and “CONCLUSION”.
Item No.3

When revising the manuscript, it is recommended that the author supplement and improve its highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply PubMed, or a similar literature database tool, such as the new Reference Citation Analysis (RCA) which is sourced upon PubMed. RCA is a unique artificial intelligence system for citation index evaluation of medical science and life science literature. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve the content and timely context of an article under preparation/peer-review/revision. Please visit our RCA database for more information at: https://www.referencecitationanalysis.com/, or visit PubMed at: https://pubmed.ncbi.nlm.nih.gov/.

Reply: Thank you for your comments. By referring to the RCA database (https://www.referencecitationanalysis.com/) and PubMed (https://pubmed.ncbi.nlm.nih.gov/), we have enriched the manuscript with up-to-date research findings, thereby improving its content.

Item No.4

Manuscript title. The title will concisely summarize the main topic of the study, being not overly long (no more than 18 words). The words “case report or case report and review of the literature” should be in the title along with the area of focus. Key elements of the case should be mentioned in the title and might include the presenting symptoms, diagnosis, intervention, or outcome. If a title contains a colon, please capitalize the first letter of the first word after the colon. For example: Unexplained fetal tachycardia: A case report
Reply: Thank you for your comments. The manuscript title concisely summarizes the main topic of the study, adhering to the recommended length of no more than 18 words, according to the specified suggestions above.

Item No.5

Running title: A short running title of no more than 6 words should be provided. Abbreviations are permitted. For example: Losurdo G et al. Two-year follow-up of HCC

Reply: The running title "Linghua S et al. ABCC8 variant-related TNDM" has been provided.

Item No.6

Author list. Author names (unabbreviated) should be given as first name, middle name initial (with no period) and family (sur)name, and typed in bold with the first letter of each capitalized. A hyphen should be included between the syllables of Chinese names. For example: Yi-Fan Chang, Jia-Jing Li, Tao Liu, Chong-Qing Wei, Li-Wei Ma, Vladimir N Nikolenko, Wei-Long Chang

Reply: The author list has been revised to Linghua Shen, Yan Cui, Dong-Xia Fu, Wei Yang, Sheng-Nan Wu, Hui-Zhen Wang, Hai-Hua Yang, Yong-Xing Chen, Hai-Yan Wei

Item No.7

Authors and institution(s): Author names should be written out first (as first name, middle name initial (with no period) and family (sur)name; with a hyphen included between the syllables of Chinese names) and typed in bold, followed by a comma and the complete name of the affiliated institution, city, province/state, postcode and country typed in non-bold. Examples for authors name and institutions are:
Example 1:

Yi-Fan Chang, Tao Liu, Chong-Qing Wei, Wei-Long Chang, Department of Gastrointestinal Surgery, The First Affiliated Hospital of Zhengzhou University, Zhengzhou 450052, Henan Province, China

Jia-Jing Li, Department of Pathology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou 450052, Henan Province, China

Li-Wei Ma, Department of Clinical Laboratory, The First Affiliated Hospital of Zhengzhou University, Zhengzhou 450052, Henan Province, China

Vladimir N Nikolenko, Department of Human Anatomy and Histology, I.M. Sechenov First Moscow State Medical University (Sechenov University), Moscow 119991, Russia

Example 2: In the case that one author represents two institutions, the institutions will be listed separately, as shown here:

Jin-Yu Pei, Bin Tan, Peng Liu, Guang-Hua Cao, Zu-Sen Wang, Lin-Lin Qu, Department of Hepatopancreatobiliary Surgery, The Affiliated Hospital of Qingdao University, Qingdao 266555, Shandong Province, China

Jin-Yu Pei, Peng Liu, Guang-Hua Cao, Medical College, Qingdao University, Qingdao 266071, Shandong Province, China

Reply: Authors and institution(s) are

Ling-Hua Shen, Yan Cui, Dong-Xia Fu, Wei Yang, Sheng-Nan Wu, Hui-Zhen Wang, Hai-Hua Yang, Yong-Xing Chen, Hai-Yan Wei, Department of Endocrinology and Metabolism, Henan Key Laboratory of Children's Genetics and Metabolic Diseases, Children's Hospital Affiliated to Zhengzhou University, Henan Children's Hospital Zhengzhou Children's Hospital, Zhengzhou 450018, Henan Province, China

Item No.8
Co-first authors and co-corresponding authors. Designation of co-first authors and co-corresponding authors is permitted. The example for bibliographic formatting of co-first or co-corresponding authors is:

Co-first authors: Jia-Ru Fan and Li Ma.

Co-corresponding authors: Jin-Lei Wang and Lian-Sheng Ma.

Co-first authors will not be allowed to be co-corresponding authors and vice versa. For co-first authors, there should be a statement of support that justifies the equal contribution. For co-corresponding authors, there should be a statement of support that justifies the equal contribution.

Although co-corresponding authorship may be allowed designation in the Author contributions section, the listing of contact information will be provided for only one of the co-corresponding authors. The two co-corresponding authors should choose which one of them will be responsible for all contact and correspondence with the journal.

Reply: There are no designated co-first authors or co-corresponding authors.

[Y]

Item No.9

Author contributions: The ‘Author contributions’ passage describes the specific contribution(s) made by each author. The author’s names will be listed in the following format: full family (sur)name, followed by abbreviated first and middle names. For example, Bryan L Copple should be revised as Copple BL. A full multi-author example is: Wang CL, Liang L, Fu JF, Zou CC, Hong F and Wu XM designed the research study; Wang CL, Zou CC, Hong F and Wu XM performed the research; Xue JZ and Lu JR contributed new reagents and analytic tools; Wang CL, Liang L and Fu JF analyzed the data and wrote the manuscript; All authors have read and approved the final manuscript.
Reply: Author contributions: Shen LH designed and performed the research study and wrote the manuscript; Cui Y and Fu DX designed the research and supervised the report; Wang HZ and Yang HH designed the research and contributed to the analysis; Chen YX provided clinical advice; Wei HH made many suggestions for the revised manuscript. All authors have read and approved the final manuscript.

Item No.10

Supportive foundations. If the manuscript has supportive foundations, authors must provide and specify the complete name(s) of the supportive foundation(s) and identification number(s) of grants or other financial support. Insert a semicolon (;) between funds, and end with a period (.). An example is:

Supported by National Natural Science Foundation of China, No. 31501861 and No. 31672286; and Natural Science Foundation of Shandong Province, China, No. ZR2015CM013.

Reply: Supportive foundations: Supported by the Department of Science and Technology of Henan Province, China, No. 222102310461.

Item No.11

Corresponding author. The corresponding author’s contact information will be provided in the following format: written out first name (with a hyphen included between the syllables of Chinese names), middle name initial (with no period) and family (sur)name, and typed in bold and ending with a comma, followed by the corresponding author’s relevant honorifics (such as PhD, MD, Chief of Surgery, Assistant Professor, etc.) in bold. This is followed immediately by the affiliation (non-bold text), written out as complete name of the institution, street address, city and postcode, province/state, and country, and ending with a period. Immediately following the terminal period and a single space will be the corresponding
author’s E-mail address; this E-mail address must be issued by his/her institution. All the letters in the E-mail address should be typed in lowercase. Examples for corresponding author are:

Example 1:

Andrzej S Tarnawski, MD, PhD, DSc (Med), Professor, Chief, Department of Gastroenterology, VA Long Beach Health Care System, University of California, Irvine, 5901 E Seventh St, Long Beach, CA 90822, United States. astarnaw@uci.edu

Example 2:

Zong-Ming Zhang, MD, PhD, Chief Doctor, Professor, Department of General Surgery, Beijing Electric Power Hospital, State Grid Corporation of China, Capital Medical University, No. 1 Taipingqiaoxili, Fengtai District, Beijing 100073, China.
zhangzongming@mail.tsinghua.edu.cn

Reply: Corresponding author: Haiyan Wei, MD, Chief Doctor, Department of Endocrinology and Metabolism, Henan Key Laboratory of Children's Genetics and Metabolic Diseases, Children's Hospital Affiliated to Zhengzhou University, Henan Children's Hospital Zhengzhou Children's Hospital, No.33 Longhu Outer Ring East Road, Zhengdong New District, Zhengzhou city, Henan Province, Zhengzhou, 450018, China.

haiyanwei2009@163.com.

Item No.12

Received:

Revised:

Accepted:

Published online:
Reply: [N].

Item No. 13

Abstract. An informative, structured abstract of no more than 250 words should accompany each manuscript. Abbreviations should be avoided, but if used should be spelled out at first mention. The 3 sections of the structured abstract are:

(1) BACKGROUND (no more than 80 words). This section should clearly describe what this case report adds to the medical literature, and why you wrote it up.

(2) CASE SUMMARY (no more than 150 words). This section should clearly describe the chief complaints, diagnoses, interventions, and outcomes of the patient.

(3) CONCLUSION (no more than 20 words). This section should clearly describe the main “take-away” lesson from this case.

Reply: The abstract has been revised according to these specified requirements.

Item No. 14

Key words. The ‘Key words’ list will provide 5-10 keywords that reflect the main content of the study. Please do not use abbreviations for the keywords (e.g., Ulcerative colitis, not UC). The first letter of each keyword will be capitalized, and each keyword will be separated by a semicolon, with no terminal period. An example of correct formatting is:

Key words: Non-alcoholic fatty liver disease; Alcoholic liver disease; Non-alcoholic steatohepatitis; Insulin resistance; Oxidative stress; Case report

Reply: The list of ‘key words’ has been revised in the correct format following the specified requirements mentioned above.

Item No. 15
**Citations.** All authors’ short names should be listed in the following format: full family (sur)name, followed by abbreviated first and middles names. Each author's short name is separated by a comma and ends with a period. Afterwards, list the title of the manuscript, and ends with a period, then *name of journal* year; In press.

*For example:*


*World J Gastroenterol* 2024; 0(0): 0000-0000

**URL:** https://www.wjgnet.com/1007-9327/full/v0/i0/0000.htm

**DOI:** https://dx.doi.org/10.3748/wjg.v0.i0.0000

**Reply:** The Citations have’t been revised in the correct format in accordance with the specified requirements mentioned above.[N]

**Item No.16**

**Core Tip.** The Core Tip is a short paragraph that is independent of the content of the Abstract. The ‘Core Tip’ will provide a succinct summary of the study that outlines its most innovative and important arguments. This section should be less than 100 words. Abbreviations must be defined upon first appearance in the Core Tip. Do not use non-standard abbreviations, unless they appear at least two times in the text preceding the first usage/definition. An example of correct formatting is:

**Core Tip:** The magnetic compression technique can be used to treat patients with rectal stenosis that have also undergone an enterostomy. However, the existing magnetic ring cannot be used in patients without enterostomy. We designed a Y–Z deformable magnetic ring (Y–Z DMR), which can realize the single channel of the magnet placed through the anus. This paper reports the first successful clinical case of using the Y–Z DMR for the treatment of rectal stenosis.
Reply: The Core Tip has been summarized in the correct format following the specified requirements mentioned above.

Item No.17

Audio core tip. In order to attract readers to read the full-text article, we request that the first author make an audio file describing the final core tip. This audio file will be published online, along with the article. Please submit audio files according to the following specifications:

Acceptable file formats: .mp3, .wav, or .aiff

Maximum file size: 10 MB

To achieve the best quality, when saving audio files as an .mp3, use a setting of 256 Kbps or higher for stereo or 128 Kbps or higher for mono. Sampling rate should be either 44.1 kHz or 48 kHz. Bit rate should be either 16 bit or 24 bit. To avoid audible clipping noise, please make sure that audio levels do not exceed 0 dBFS.

Reply: The first author has made an audio file describing the final core tip of the full-text article and has submitted the audio files following the specified requirements above.

Item No.18

Main text. The main text contains (1) INTRODUCTION; (2) CASE PRESENTATION; (3) MULTIDISCIPLINARY EXPERT CONSULTATION (if relevant); (4) FINAL DIAGNOSIS; (5) TREATMENT; (6) OUTCOME AND FOLLOW-UP; (7) DISCUSSION; and (8) CONCLUSION. These eight first level subtitles should be all capitalized, bolded and underlined. For example: “INTRODUCTION”

Under each first-level subtitle, there can be several second-level subtitles. For formatting,
Item No.19

Case Presentation. Under the heading of Case Presentation, the following seven aspects must be presented in this order: (1) Chief complaints; (2) History of present illness; (3) History of past illness; (4) Personal and family history; (5) Physical examination upon admission; (6) Laboratory examinations e.g., routine blood tests, routine urine tests and urinary sediment examination, routine fecal tests and occult blood test, blood biochemistry, immune indexes, and infection indexes; and (7) Imaging examinations e.g., ultrasound, plain abdominal and pelvic CT scan, high-resolution chest CT scan, and head MRI. The patient case presentation should be descriptive, organized chronologically, accurate, salient, and presented in a narrative form.

Reply: The case presentation in our manuscript has been revised in accordance with the seven suggested aspects above and is now presented in a narrative form. [Y]

Item No.20

Units. Use SI units.

For example: body mass, m (B) = 78 kg; blood pressure, p (B) = 16.2/12.3 kPa; incubation time, t (incubation) = 96 h, blood glucose concentration, c (glucose) 6.4 ± 2.1 mmol/L; blood CEA mass concentration, p (CEA) = 8.6 ± 24.5 g/L; CO₂ volume fraction, 50 mL/L CO₂, not 5% CO₂;
likewise, for 40 g/L formaldehyde, not 10% formalin; and mass fraction, 8 ng/g, etc. Arabic numerals such as 23,243,641 (i.e. 23 million, 243 thousand, and 641) should be written as 23243641, with no commas and no spaces.

**For example:** week, hour, minute, seconds, millimeter, kilometer, gram, and kilogram should be abbreviated as wk, h, min, s, mm, km, g, and kg, respectively.

The format for how to accurately write common units and quantums can be found at: [https://www.wjgnet.com/bpg/gerinfo/189](https://www.wjgnet.com/bpg/gerinfo/189).

**Reply:** The Units and quantums in our manuscript have been accurately revised, as specified at the following link:

[https://www.wjgnet.com/bpg/gerinfo/189](https://www.wjgnet.com/bpg/gerinfo/189) provided above.[Y]

**Item No.21**

**Abbreviations.** Standard abbreviations should be defined in the abstract and in the main body of the manuscript upon first mention in the text. In general, terms should not be abbreviated unless they are used two times or more and the abbreviation is helpful to the reader. Permissible abbreviations are listed in Units, Symbols and Abbreviations: A Guide for Biological and Medical Editors and Authors (Ed. Baron DN, 1988) published by The Royal Society of Medicine, London. Certain commonly used abbreviations, such as DNA, RNA, HIV, LD50, PCR, HBV, ECG, WBC, RBC, CT, ESR, CSF, IgG, ELISA, PBS, ATP, EDTA and mAb, do not need to be defined and can be used directly.

**Reply:** The abbreviations in our manuscript have been revised following the suggestions provided above. [Y]

**Item No.22**

**Italics.** Quantities: t time or temperature, c concentration, A area, l length, m mass, V volume. Genotypes: gyrA, arg1, c myc, c fos, etc. Restriction enzymes: EcoRI, HindI, BamHI, KboI, KpnI, etc. Biological nomenclature: H. pylori, E. coli, etc. Latin terms: i.e., e.g., via, etc.
Reply: The paper has been revised following the suggestions provided above.

Item No.23

Acknowledgements. Brief acknowledgements of persons who have made genuine contributions to the manuscript and who endorse the data and conclusions should be included. The Acknowledgments section should not include funding source, language editing companies, and other biomedical institutions providing paid services.

Reply: Acknowledgements: We express our gratitude to the children, parents, and caregivers who willingly participated in this study.

Item No.24

Reference numbers in the main text. The author should number the references in Arabic numerals according to the citation order in the text.

The format of in-text citation of references should be [References Number], which should be with no space between “[ ]” and the preceding word. Example: The pathophysiology is thought to be due to an increased arterial flow that leads to secondary hepatocellular hyperplasia[1,2].

If the name of the author(s) of a reference is listed in the sentence, the reference number should be placed immediately after the author(s) of the reference.

Example: Mandal et al[8] proposed that retractor aponeurosis disinsertion is the most likely cause of congenital low lid entropion.

In addition, please verify the order and total number of references cited to ensure that all references in the list are cited and in a correct numeric order.
Reply: The reference numbers and in-text citation format in the main text have been revised following the suggestions mentioned above.

We have ensured the accuracy of the order and total number of cited references to verify that they are listed in the correct numerical order. [Y]

Item No. 25

**Edit References by Auto-Analyser.** Authors should edit the references in their paper using the Auto-Analyser at https://www.f6publishing.com/Forms/main/ArticleReferenceTool.aspx to ensure the correctness of all reference information. The specific steps for editing references by Auto-Analyser are:

**Step 1: Copy all references to the Auto-Analyser.** Each reference should include its corresponding PMID and DOI numbers, unless those numbers are not present in the literature. The reference list should begin with Arabic number “1”, and please do not use brackets for the references numbers.

**Reminder:** If the PMID and DOI numbers are currently not included for the references, please click on the “Crossref (DOI and PMID)” button to obtain the PMIDs/DOIs for the reference list. Please select the two options "Include PubMed IDs in results" and "List all possible DOIs per reference" before submitting.

**Step 2: Edit references by the Auto-Analyser.** Upon clicking on the “Edit References by Auto-Analyser” button, the Auto-Analyser will edit and proofread the references based on information retrieved from PubMed/Crossref through the PMID/DOI numbers of the references.

**Reminder:** If there is a numbering error or duplicate reference in the reference list, the system will display an error message. The author will then need to modify the reference list, copy the
newly modified references to the Auto-Analyser, and click on the “Edit References by Auto-Analyser” button again.

**Step 3: Proofreading of the References.** Verify the list of references that have undergone automatic editing and standardization in the “Proofreading of the References” and “Auto-Edited References Preview” pages under the “Result of Analyze”.

**Step 4: Save and Continue.** After verifying that the auto-edited references are correct, authors need to click on the "Save and Continue" button to go to next step. The system will automatically export the edited references to a Word document.

*For references that PMID and DOI numbers are not present the literature, please revise the references according to the Format for References Guidelines (PDF).*

**Reply:** The references in our paper were revised using the Auto-Analyser available at [https://www.f6publishing.com/Forms/main/ArticleReferenceTool.aspx](https://www.f6publishing.com/Forms/main/ArticleReferenceTool.aspx).

This was done to verify the accuracy of all reference details following the specified steps mentioned above.[Y]

**Footnotes**

**Item No.26**

**Informed consent statement.** Any research article describing a study involving humans should contain a statement clearly in the footnotes section stating that all involved persons (subjects or legally authorized representative) gave their informed consent (written or verbal, as appropriate) prior to study inclusion.

**Sample wording:** All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

**Reply:** All study participants, or their legal guardians, provided informed
written consent before study enrollment.[Y]

**Item No.27**

**Conflict-of-interest statement:** A conflict-of-interest statement is required for all article and study types. In the interests of transparency and helping reviewers to assess any potential bias in a study’s design, interpretation of its results or presentation of its scientific/medical content, we require all authors of each paper to declare any conflicting interests (including but not limited to commercial, personal, political, intellectual or religious interests) that are related to the work submitted for consideration of publication in the Footnotes section.

**Sample wording:** [Name of individual] has received fees for serving as a speaker, a [position; such as consultant and/or an advisory board member] for [name(s) of organization(s)]. [Name of individual] has received research funding from [name(s) of organization(s)]. [Name of individual] is an employee of [name(s) of organization(s)]. [Name of individual] owns stocks and/or shares in [name(s) of organization(s)]. [Name of individual] owns patent [patent identifier information (including patent number, two-letter country code, and kind code) and a brief description].

**Reply:** The authors declare that they have no conflict of interest (including but not limited to commercial, personal, political, intellectual, or religious interests) to disclose.[Y]

**Item No.28**

**CARE Checklist (2016) statement:** In order to improve the quality of Case Report manuscripts, authors should download and complete the ‘CARE Checklist – 2016: Information for writing a case report’ to ensure that the manuscript meets the requirements of the “CARE Checklist – 2016: Information for writing a case report”. Authors must state on the
title page of the manuscript that the guidelines of the CARE Checklist (2016) have been adopted.

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

**Reply:** The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016). [Y]

**Item No.29**

**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/

**Reply:** Thank you, I have carefully read the license and agreement along with its contents. [Y]

**Item No.30**

**Corresponding Author's Membership in Professional Societies:**

**Reply:** Corresponding Author's Membership in Professional Societies: No. [N]

**Specialty type:**

**Reply:** Specialization in pediatric Endocrinology and Metabolic.

**Item No.32**

**Country/Territory of origin:**
Figures and Tables

Item No. 33

Figures. Figures must be presented in the order that they appear in the main text of the manuscript (numbered as 1, 2, 3, etc.). All figures must have a detailed figure legend that provides a clear and comprehensive description of the information presented in the figure, so that the reader can understand without having to refer back to any other portion of the manuscript. Uniform presentation should be used for figures showing the same or similar contents; for example, “Figure 1 Pathological changes of atrophic gastritis after treatment. A: ..., B: ..., C: ..., D: ..., E: ..., F: ..., G: ...”.

Abbreviations must be defined upon first appearance in the Figure Legends. Do not use non-standard abbreviations, unless they appear at least two times in the text preceding the first usage/definition.

Original figure documents. Authors should provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs and/or design components (such as arrows) and/or text portions can be reprocessed by the journal’s editorial staff, and finally upload it to the file destination of “Image File”. [Sample]

Reminder: Please click and download the Guidelines for preparation of bitmaps, vector graphics, and tables in revised manuscripts (PDF), and prepare the figures and tables of the manuscript accordingly.

Reply: Figures 1, 2, and 3 in our study have been revised based on the requests above and have been uploaded to the specified "Image File" location.[Y]

Item No. 34
Tables. Tables must be presented in the order that they appear in the main text of the manuscript (numbered as 1, 2, 3, etc.). A brief, one-line title must be provided for each table. Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Authors should provide decomposable Tables (in which all components are movable and editable), organize them with Table Titles and Table Notes into a single Word file, and finally upload the table document to the file destination of “Table File”.

Reply: Table 1 in our study have been revised based on your suggestions and now meet the standard criteria for the three-line table. [Y]

Item No.35

Notes in figures and tables. Data with statistical significance in a figure or table should be denoted using superscripted alphabetical lettering (don’t include symbols, such as *, #, †, §, ‡, ¥, @….), such that a\textsuperscript{P} < 0.05 and b\textsuperscript{P} < 0.01. If there are other series of \textit{P} values, the alphabetical subscripted denotation format is continued, such that c\textsuperscript{P} < 0.05 vs control, d\textsuperscript{P} < 0.01 vs control, e\textsuperscript{P} < 0.05 vs group A, and f\textsuperscript{P} < 0.01 vs group B. Data that are not statistically significant should not be denoted, i.e. \textit{P} > 0.05 is not an allowed denotation.

Reply: The data that demonstrates statistical significance in a figure or table in our study has been annotated following this commendable suggestion. [Y]

Non-native speakers of English authors, Supportive foundations, Ethics approval documents, Copyright license agreement

Item No.36

Non-Native Speakers of English Authors. It is necessary to perform further language
polishing that will ensure all grammatical, syntactical, formatting and other related errors be resolved, so that the revised manuscript will meet the publication requirement (Grade A). Authors are requested to send their revised manuscript to a professional English language editing company or a native English-speaking expert to polish the manuscript further. **Authors must provide a new language certificate along with the manuscript.** Please visit the following website for the professional English language editing companies that we recommend:  [https://www.wjgnet.com/bpg/gerinfo/240](https://www.wjgnet.com/bpg/gerinfo/240)

**Reply:** We have submitted a new language certificate with the manuscript. [Y]

**Item No. 37**

**Approved Grant Application Form(s) or Funding Agency Copy of any Approval Document(s).** If the manuscript has supportive foundations, authors are required to upload the primary version (PDF) of the Supportive foundation’s official approval, prepared in the official language of the authors’ country to the system; for example, authors from China should upload the Chinese version of the document, authors from Italy should upload the Italian version of the document, *etc.* If not, delete those without supporting documents.

**Reply:** The Department of Science and Technology of Henan Province, China funded the study, under grant No. 222102310461. The initial version (PDF) of the Chinese document has been uploaded (Approved Funding Document). [Y]

**Item No. 38**

**Signed Consent for Treatment Form(s) or Document(s).** Authors are required to upload the primary version (PDF) of the Consent for Treatment Form(s) or Document(s) or that has been signed by the patients in the study, prepared in the official language of the authors’ country to the system; for example, authors from China should upload the Chinese version of the document, authors from Italy should upload the Italian version of the document, *etc.* [Sample]
Note: To obey the publication ethics and improve the protection of all patients' rights to privacy, the authors should provide the informed consent form on which the patient's name, address, birthday, address, ward, bed number, hospital number and other private information are obfuscated.

Reply: The parents of the two patients signed the informed consent document, and the ethics committee of Henan Children's Hospital Zhengzhou Children's Hospital approved the study (Approval No. 2023-K-123).

To obey the publication ethics and safeguard the privacy rights of the two patients, we have obscured sensitive information such as the patient's name, address, date of birth, ward, bed number, hospital number, and other private details on the informed consent form. [Y]

Item No.39

Conflict-of-Interest Disclosure Form: Authors should click and download the fillable ICMJE Form for Disclosure of Potential Conflicts of Interest (PDF), and fill it in. The Corresponding Author is responsible for filling out and uploading this form.

Reply: All authors have accessed and completed the fillable ICMJE Form for Disclosure of Potential Conflicts of Interest (PDF). The Corresponding Author has filled out and uploaded the form accordingly. [Y]

Item No.40

CARE Checklist–2016. Authors should click and download the fillable ‘CARE Checklist – 2016: Information for writing a case report’ (PDF), fill it in, and upload the filled-in form to F6Publishing.
**Reply:** We have downloaded the fillable 'CARE Checklist-2016: Information for writing a case report' (PDF), completed it, and have already uploaded the completed form to F6Publishing. [Y]

**Item No.41**

**Video and supplementary materials.** If the manuscript has “Video” or “Supplementary Material”, authors need to submit those two types of documents online to F6Publishing.

**Reply:** Our manuscript does not include a “Video” or “Supplementary Material”. [N]

**Item No.42**

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**Reply:** I am willing to pay the Article Processing Charge.[Y]

**Item No.43**

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