

World Journal of *Clinical Cases*

World J Clin Cases 2024 October 26; 12(30): 6335-6424



EDITORIAL

- 6335 Unraveling autophagy-related pathogenesis in active ulcerative colitis: A bioinformatics approach
Hao WR, Cheng CY, Liu JC, Cheng TH
- 6339 Clinical approach for pulmonary alveolar proteinosis in children
Klubdaeng A, Tovichien P
- 6346 Rethinking Kawasaki disease diagnosis: Continuing the search for new biomarkers
Pan Y, Jiao FY
- 6349 Advances in the diagnosis and treatment of heterotopic pancreas
Lang L, Yu FK, Kang LM
- 6353 Global strategy for prevention of gastric cancer
Kotelevets SM
- 6358 Enhancing ulcerative colitis treatment with traditional Chinese medicine
Hao WR, Cheng CY, Cheng TH

MINIREVIEWS

- 6361 Overview of emerging therapies for demyelinating diseases
Medina R, Derias AM, Lakdawala M, Speakman S, Lucke-Wold B

ORIGINAL ARTICLE**Retrospective Study**

- 6374 Hematological picture of pediatric Sudanese patients with visceral leishmaniasis and prediction of leishmania donovani parasite load
Elnoor ZIA, Abdelmajeed O, Mustafa A, Gasim T, Musa SAM, Abdelmoneim AH, Omer IIA, Fadl HAO
- 6383 Deep neck infections mortal complications: Intrathoracic complications and necrotising fasciitis
Bal KK, Aslan C, Gür H, Bal ST, Ustun RO, Unal M

Clinical and Translational Research

- 6391 Functional investigation and two-sample Mendelian randomization study of primary biliary cholangitis hub genes
Yang YC, Ma X, Zhou C, Xu N, Ding D, Ma ZZ, Zhou L, Cui PY

LETTER TO THE EDITOR

- 6407** Additional comments on foot reflexology treatment for sensorineural hearing loss in infant
Zhang Y, Pei H, He BJ
- 6410** Beyond the imaging evaluation of fractures of the lateral process of the talus: Let's not forget concomitant injuries
Lindner C, Reyes P, Molina E, Olave A
- 6413** Percutaneous transhepatic cholangiography: An effective option for endo-biliary radiofrequency ablation before stent insertion in unresectable biliary cancer?
Karagiannakis DS
- 6417** Clinical characteristics of renal anastomotic hemangioma
Huang K
- 6420** Addressing mucosal ulcers during orthodontic treatment: An urgent call for preventive strategies
Ardila CM

ABOUT COVER

Peer Reviewer of *World Journal of Clinical Cases*, Yao Christian Hugues Dokponou, MD, Department of Neurosurgery of Mohammed V Military Teaching Hospital, Rabat 10000, Morocco. dokponou2407@gmail.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 PubMed, PubMed Central, *Reference Citation Analysis*, China Science and Technology Journal Database, and Superstar Journals Database. The 2024 Edition of Journal Citation Reports® cites the 2023 journal impact factor (JIF) for *WJCC* as 1.0; JIF without journal self cites: 0.9; 5-year JIF: 1.1; JIF Rank: 168/325 in medicine, general and internal; JIF Quartile: Q3; and 5-year JIF Quartile: Q3.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Zi-Hang Xu*, Production Department Director: *Xu Guo*, Cover Editor: *Jin-Lai 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, Salim Surani, Jerzy Tadeusz Chudek, George Kontogeorgos, Maurizio Serati

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

PUBLICATION DATE

October 26, 2024

COPYRIGHT

© 2024 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>



Rethinking Kawasaki disease diagnosis: Continuing the search for new biomarkers

Yan Pan, Fu-Yong Jiao

Specialty type: Immunology

Provenance and peer review:

Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade A

Novelty: Grade A

Creativity or Innovation: Grade B

Scientific Significance: Grade A

P-Reviewer: El Deriny G

Received: May 18, 2024

Revised: August 14, 2024

Accepted: August 19, 2024

Published online: October 26, 2024

Processing time: 108 Days and 12.8 Hours



Yan Pan, Department of Pediatrics, The First Affiliated Hospital of Yangtze University, Jingzhou 434000, Hubei Province, China

Fu-Yong Jiao, Shaanxi Kawasaki Disease Diagnosis and Treatment Center, Children's Hospital, Shaanxi Provincial People's Hospital of Xi'an, Jiaotong University, Xi'an 710000, Shaanxi Province, China

Corresponding author: Fu-Yong Jiao, MD, Research Scientist, Shaanxi Kawasaki Disease Diagnosis and Treatment Center, Children's Hospital, Shaanxi Provincial People's Hospital of Xi'an, Jiaotong University, No. 256 Youyi West Road, Beilin District, Xi'an 710000, Shaanxi Province, China. 3105089948@qq.com

Abstract

Recent findings by Yamashita *et al* report a Kawasaki disease (KD) case with normal biomarker levels, challenging traditional diagnostic paradigms. This editorial explores the implications of such atypical KD presentations, emphasizing the need for novel biomarkers and revised diagnostic guidelines. The case underscores the limitations of current biomarkers, the importance of clinical judgment, and the necessity for comprehensive research to identify new diagnostic tools. Emerging technologies in proteomics and genomics offer potential avenues for discovering reliable biomarkers. Revisiting clinical guidelines to incorporate flexibility for atypical presentations is crucial. Ensuring timely and accurate KD diagnosis, even without elevated traditional biomarkers, prevents severe complications. Future advancements should focus on novel biomarkers to improve patient outcomes.

Key Words: Kawasaki disease; Diagnostic criteria; Guide line; Biomarker; Technologies

©The Author(s) 2024. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: A recent case report challenges this paradigm by presenting a Kawasaki disease (KD) case with normal biomarker levels, emphasizing the need for novel biomarkers. This editorial discusses the limitations of current biomarkers, the importance of clinical judgment, and the necessity for comprehensive research to identify new diagnostic tools. Emerging technologies in proteomics and genomics may offer promising avenues for discovering reliable biomarkers, ensuring timely and accurate KD diagnosis, even in atypical KD.

Citation: Pan Y, Jiao FY. Rethinking Kawasaki disease diagnosis: Continuing the search for new biomarkers. *World J Clin Cases* 2024; 12(30): 6346-6348

URL: <https://www.wjgnet.com/2307-8960/full/v12/i30/6346.htm>

DOI: <https://dx.doi.org/10.12998/wjcc.v12.i30.6346>

INTRODUCTION

Diagnosis of Kawasaki disease (KD) has traditionally relied on clinical criteria supported by elevated inflammatory biomarkers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). KD is typically diagnosed based on clinical presentation. Classic KD is defined by the presence of at least four of the following five major clinical features: Fever, oral changes, ocular changes, rash: Polymorphous rash, and cervical lymphadenopathy[1]. However, a recent case report by Yamashita *et al*[2], presents a case of KD with normal inflammatory biomarker levels. This editorial aims to discuss the implications of these findings and the need for new inflammatory biomarkers.

CASE ANALYSIS

Yamashita *et al*[2] describe a 1-year-old boy presenting with five of the six principal symptoms of KD (fever, bilateral bulbar conjunctival injection, rash, changes in the peripheral extremities, and nonsuppurative cervical lymphadenopathy) but with normal levels of CRP, ESR, and serum amyloid A. Despite the atypical laboratory findings, the diagnosis was confirmed based on clinical features. The patient was treated with intravenous immunoglobulin (IVIG) and aspirin but demonstrated resistance to initial treatments, necessitating additional IVIG doses. Throughout treatment, inflammatory biomarkers remained within normal ranges, and levels of the novel biomarker leucine-rich alpha-2-glycoprotein 1 (LRG1) were not elevated. This case underscores the necessity of re-evaluating the diagnostic approach to KD, particularly in cases where traditional biomarkers fail to indicate the disease.

The diagnosis of KD has always been predominantly clinical, guided by the presence of fever lasting at least five days and at least four of the five principal features: Bilateral conjunctival injection, changes in the lips and oral cavity, polymorphous exanthema, changes in the extremities, and cervical lymphadenopathy. Laboratory tests, including elevated levels of CRP and ESR, have been auxiliary but crucial in supporting the clinical diagnosis and monitoring treatment response. The case presented by Yamashita *et al*[2] raises critical questions about the reliance on these biomarkers. Untreated KD has been proven to lead to serious cardiovascular complications, including coronary artery aneurysms. Thus, early and accurate diagnosis is paramount. However, as demonstrated, normal inflammatory markers do not necessarily rule out KD, posing a significant diagnostic challenge. This highlights the potential for underdiagnosis or delayed treatment in atypical cases, risking severe outcomes.

The limitations of current biomarkers require exploration of novel diagnostic tools. LRG1, as mentioned in the case report, has shown promise as a biomarker for the acute phase of KD. However, its normal levels in this patient indicate that LRG1 alone may not be sufficient as a standalone diagnostic tool. Comprehensive research is required to identify additional biomarkers or a combination thereof that can reliably diagnose KD, particularly in atypical presentations. Emerging technologies, such as proteomics and genomics, offer promising avenues for discovering new biomarkers. High-throughput screening and advanced data analytics can help identify molecular signatures specific to KD. Additionally, integrating clinical data with genetic and biomarker profiles could pave the way for more precise and personalized diagnostic criteria.

Given the findings of Yamashita *et al*[2], there is a pressing need to revisit and potentially revise clinical guidelines for KD diagnosis. The American Heart Association and other leading bodies provide comprehensive guidelines for KD management, which heavily rely on clinical presentation and traditional biomarkers[3]. However, incorporating flexibility to account for cases with normal biomarker levels is essential. Clinicians should maintain a high index of suspicion for KD in patients with compatible clinical features, regardless of inflammatory marker status. Furthermore, risk stratification tools like the Kobayashi score, which predict IVIG resistance, may need re-evaluation. The reported case had a low Kobayashi score but still required intensified treatment, indicating that current risk stratification methods might not adequately capture KD presentations[4].

CONCLUSION

The case report by Yamashita *et al*[2] provides valuable insights into the complexity of KD diagnosis and the limitations of current biomarkers. It underscores the importance of clinical judgment and the need for novel diagnostic tools to ensure early and accurate identification of KD, especially in atypical cases[5]. Future research should focus on identifying and validating new biomarkers. Ensuring all patients with KD receive timely and appropriate treatment is crucial for preventing long-term cardiovascular complications and improving patient outcomes.

FOOTNOTES

Author contributions: Jiao FY designed the research study; Pan Y designed the research study, performed the research, contributed new reagents and analytic tools, analyzed the data, wrote the manuscript, read and approve the final manuscript.

Supported by The Hubei Pediatric Alliance Medical Research Project, No. HPAMRP202117.

Conflict-of-interest statement: All the authors declare no conflict of interest.

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 of origin: China

ORCID number: Yan Pan 0000-0003-0240-7085; Fu-Yong Jiao 0000-0002-8306-2543.

S-Editor: Liu JH

L-Editor: A

P-Editor: Xu ZH

REFERENCES

- 1 Pan Y, Jiao F. Application of artificial intelligence in the diagnosis and treatment of Kawasaki disease. *World J Clin Cases* 2024; **12**: 5304-5307 [DOI: [10.12998/wjcc.v12.i23.5304](https://doi.org/10.12998/wjcc.v12.i23.5304)]
- 2 Yamashita K, Kanazawa T, Abe Y, Naruto T, Mori M. Kawasaki disease without changes in inflammatory biomarkers: A case report. *World J Clin Cases* 2022; **10**: 13038-13043 [PMID: [36569014](https://pubmed.ncbi.nlm.nih.gov/36569014/) DOI: [10.12998/wjcc.v10.i35.13038](https://doi.org/10.12998/wjcc.v10.i35.13038)]
- 3 McCrindle BW, Rowley AH, Newburger JW, Burns JC, Bolger AF, Gewitz M, Baker AL, Jackson MA, Takahashi M, Shah PB, Kobayashi T, Wu MH, Saji TT, Pahl E; American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young; Council on Cardiovascular and Stroke Nursing; Council on Cardiovascular Surgery and Anesthesia; and Council on Epidemiology and Prevention. Diagnosis, Treatment, and Long-Term Management of Kawasaki Disease: A Scientific Statement for Health Professionals From the American Heart Association. *Circulation* 2017; **135**: e927-e999 [PMID: [28356445](https://pubmed.ncbi.nlm.nih.gov/28356445/) DOI: [10.1161/CIR.0000000000000484](https://doi.org/10.1161/CIR.0000000000000484)]
- 4 Chiang WN, Huang PY, Kuo HC, Huang YH, Chang LS. Evaluation of Formosa score and diagnostic sensitivity and specificity of four Asian risk scores for predicting intravenous immunoglobulin resistance in Kawasaki disease: a bivariate meta-analysis. *Front Cardiovasc Med* 2023; **10**: 1164530 [PMID: [37378410](https://pubmed.ncbi.nlm.nih.gov/37378410/) DOI: [10.3389/fcvm.2023.1164530](https://doi.org/10.3389/fcvm.2023.1164530)]
- 5 Pan Y, Jiao FY. Relationship between Kawasaki disease and abdominal pain. *World J Clin Cases* 2024; **12**: 2932-2934 [PMID: [38898859](https://pubmed.ncbi.nlm.nih.gov/38898859/) DOI: [10.12998/wjcc.v12.i17.2932](https://doi.org/10.12998/wjcc.v12.i17.2932)]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Telephone: +1-925-3991568

E-mail: office@baishideng.com

Help Desk: <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

