The rs6505162 C>A polymorphism in the *miRNA-423* gene exhibits a protective element of coronary artery in a southern Chinese population with Kawasaki disease

Jiawen Li[1,*], Jinxin Wang[1,*], Xiaoping Su[1], Zhiyong Jiang[2], Xing Rong[1], Xueping Gu[2], Huixian Qiu[1], Lanlan Zeng[3], Hao Zheng[3], Xiaoqiong Gu[4,&], Maoping Chu[1,&]

[1]Children's Heart Center, Institute of Cardiovascular Development and Translational Medicine, the Second Affiliated Hospital and Yuying Children's Hospital, Wenzhou Medical University, Wenzhou, China;
[2]Department of Blood Transfusion and Clinical Lab, Guangzhou Institute of Pediatrics, Guangzhou Women and Children's Medical Center, Guangzhou Medical University, Guangzhou, Guangdong, China
[3]Department of Clinical Lab, Guangzhou Institute of Pediatrics, Guangzhou Women and Children's Medical Center, Guangzhou Medical University, Guangzhou, Guangdong, China
[4]Department of Blood Transfusion, Clinical Biological Resource Bank and Clinical Lab, Guangzhou Institute of Pediatrics, Guangzhou Women and Children's Medical Center , Guangzhou Medical University, Guangzhou, Guangdong, China
*These authors contributed equally to this work

[&] **Correspondence to: Xiaoqiong Gu**, Department of Blood Transfusion ,Clinical Biological Resource Bank and Clinical Lab, Guangzhou Institute of Pediatrics, Guangzhou Women and Children's Medical Center ,Guangzhou Medical University, Guangzhou 510623, Guangdong, China**,** Email:guxiaoqiong@163.com; **or Maoping Chu**, Children's Heart Center, The Second Affiliated Hospital and Yuying Children's Hospital, Institute of Cardiovascular Development and Translational Medicine, Wenzhou Medical University, 109 West Xueyuan Road, Wenzhou 325027, Zhejiang, China, Email:chmping@hotmail.com.

Abstract

Background: Manifesting as acute rash, fever and vasculitis, belonging to autoimmune syndrome, Kawasaki disease(KD) is prone to occur in infants and young children. Males and females is affected by KD at a ratio of 1.4 to 1.7 : 1. KD is known to own many common clinical manifestations and complications, like coronary artery lesion(CAL) and coronary artery aneurysm(CAA). Polymorphisms of the rs6505162 locus in the *miRNA-423* gene are associated with enhancive susceptibility to coronary artery disease and the alterations of the four cytokines IL-4. , IL-10, IL-21, IL-22 in the early stages of diabetes. However, no researcher has reported whether rs6505162 is related to KD susceptibility or no. Therefore, we carried out the trial concentrating on the connection between *miRNA-423* rs6505162 C>A polymorphism and KD susceptibility.

Methods: To obtain the genotypes of rs6505162 *in* objects enrolled by 532 KD children and 623 control, we applied Taqman real-time PCR and all statistical analyses was carried out by SAS.

Results: The comparison between all cases and all controls hinted that the rs6505162C>A polymorphism has no relationship with KD susceptibility. Nevertheless, a subgroup analysis revealed that the CA/AA genotypes of rs6505162 could reduce the occurrence of CAA (Adjusted age and gender odds ratio=1.30, 95%CI=1.02-1.67, *P*=0.037) and CAL (Adjusted OR=1.56, 95%CI=1.19-2.03, *P*=0.001)in KD patients.

Conclusion: Our final results stated clearly that *miRNA-423* rs6505162 polymorphism appears to be a protective element of CAL and CAA in southern Chinese suffers with KD.

Keywords:*miRNA-423* rs6505162, Kawasaki disease, polymorphism, coronary artery lesion, coronary artery aneurysm

Running head:*miRNA-423* rs6505162 and Kawasaki disease

Introduction

In the year of 1967, the illness named Kawasaki disease(KD) was detected by Dr. Kawasaki.(1) Manifesting as acute rash, fever and vasculitis, belonging to autoimmune syndrome, Kawasaki disease(KD) which trigger acquired heart disease at most in non-developing countries is prone to occur in infants and young children.(2) In recent years, 18. 4% suffers are subjected to coronary artery disease and 20-25% untreated sick children suffered from coronary artery dilatation. The phenomenon above-mentioned could give rise to myocardial ischemia, and some of them develop into coronary aneurysm which perhaps rupture, even gigantic coronary aneurysms.(3, 4) KD can occur at any age including adults and neonate.(5-7) In patients with KD, complications of coronary artery disease which Initial corticosteroid therapy can prevent are related to the duration of disease before treatment.(8) The incidence of KD in most international areas such as Korea

have been increasing slowly year by year, with a sex ratio of 1.4 to 1.7.(9-11)

The cause of KD is not totally clear and definite so far, and the exploration for the pathogen also has been upset.(12) According to the epidemiology and pathogenesis, the majority of human approve of the standpoint that the vasculitis of this illness is caused by the unsuitable immune reaction in individuals with hereditary susceptibility encountering one or more infectious irritants.(12, 13) In the culture of endothelial cells, somebody found that KLF4-miR-483 axis could be restrained by Kawasaki disease serum to speed up the development of Endothelial-to-Mesenchymal Transition(EndMT) which can injure vessel in KD patients.(14) Damage of endothelial cell homeostasis might concern the unusual circumstance of coronary artery in KD.(15) In a network analysis regarding protein interaction, the close contact between these genes concerning KD was verified to tell the pathogenesis of KD.(16) Several genes in the hypermethylated region were studied by Chen, and the correlation between the hypermethylated CpG locus and the pathogenesis of KD was mentioned for the first time. (17) These are some of the mechanisms of KD above.

Non-coding miRNAs, of which length are ~22 or so nucleotides, are produced by substances in the nucleus and cytoplasm and affect the course of genetics expression.(18) miRNA having a connection with plenty of mechanism and disease, include inflammatory response, severe asthma, diabetes mellitus, congenital heart disease, coronary artery disease(CHD). (19-23) Colorectal carcinoma whose potential biomarker might be *miR-423* rs6505162 has been studied by Jia, W.(24) Jha, Chandan K detected that The gene mutation in *microRNA-423* was in connection with enhancive susceptibility to CHD.(25)The *miRNA-423* rs6505162 having a certain relationship with CHD in prognosis, as studied in this article, is associated with HDL.(26) However, the connection of the *miRNA-423* rs6505162 C>A polymorphism with KD susceptibility has not been investigated so far. On the foundation of the medical center we employing resources from 532 KD patients and 623 controls implemented a new case-control study to appraise the relationship between the *miRNA-423* rs6505162 C>A polymorphism and the risk of KD in Han children from southern China at the point.

Materials and methods

Ethics declaration

The present study satisfying the standard of the Declaration of Helsinki was implemented in Guangzhou Women and Children's Medical Center(2014073009), of which Review Committee acknowledged this study. And we ought to gather the written informed consent which legal guardians of participants endorsed.

Study sample

A majority of participators coming from southern China have been recruited in the trial. All of participants who were from January 2012 - January 2017were Chinese Han with unrelated blood relationship. There were a plenty of samples that composed by 532 sufferers with recently diagnosed KD and 623 healthy controls in the research, according to the American Heart

Association (AHA) reference.(27) Each participant offered 2ml fresh blood, of which 200ul was extracted for genomic DNA, and the specimens remained were stored for further study.

Extraction and genotyping in DNA

On the basis of TIANGEN Company's specification, genomic DNA was abstracted from 200ul blood of each participant by making use of TIANamp Blood DNA Kit (Centrifugal column, TIANGEN). Positive and negative samples were put into 384-well plates, which could be beneficial to contrast. Taqman real-time PCR was applied to genotype the *miRNA-423*rs6505162by ABI Q6 (Applied Biosystems).

Statistical analysis in subgroups

In the group of the controls, genotype distributions that ought to be in line with the Hardy–Weinberg equilibrium were checked by a goodness-of-fit χ^2 test. The diversity of selective variables were tested by utilizing two-sidedχ^2 test as well as frequency distributions of the genotype. By means of univariate logistic regression, the relationship between the *miRNA-423* rs6505162 C>A polymorphism and the susceptibility of KD was described by odds ratios(ORs) and 95% confidence intervals (CIs). The adjustment of multivariate analysis was calculated through gender and age. Connections between susceptibility of KD and the genotypes were deeply assessed by stratification, when data were divided into subgroups about age, gender, coronary lesion and coronary artery aneurysm. The groups mentioned above are based on American Heart Association (AHA) and can be concretely grouped according to coronary artery and age.(27, 28)SAS software (version 9.4; SAS Institute, Cary, NC) in motion carried out all Statistical analyses quickly.

Results

Population feature

532 KD children and 623 healthy controls made up the participators in our research. The demographics entire participators possess were exhibited in the Table 1. 28.39 months was the average age of KD participators in onset. The quantity of 365(68.61%) in KD male patients was more than the one of 167(31.39%) in KD female patients. There was no distinct diversity in age (*P*=0.602) or gender (*P*=0.143) between KD children and healthy controls. There were 51(9.59%) patients with coronary artery aneurysm(CAA)when we took notice of the complications of KD. In addition, on the basis of coronary injury, 168(31.58%), 364(68.42%) cases were divided into CAL, NCAL, respectively.

Connection between the *miRNA-423* rs6505162 C>A polymorphism and KD susceptibility

In the groups of KD children and controls, to probe the association between *miRNA-423*

rs6505162 C>A polymorphism and KD susceptibility, we analyzed the genotype frequency distributions. As illustrated in Table 2, the controls satisfied the elements for Hardy-Weinberg equilibrium (P=0.791). The genotype frequency distributions of the *miRNA-423* rs6505162 C>A polymorphisms were 61.06% (CC), 34.97% (CA) and 3.97% (AA) in the KD group and 66.13% (CC), 30.50% (CA) and 3.37% (AA)in the controls. We observing the data from the rs6505162 C>A polymorphism and KD susceptibility, no significant connections was detected.

Stratification analysis in subgroups

Stratifying by age, gender, coronary injury(CAL), and coronary artery aneurysm (CAA)which are closely related to KD ,we explored the connection between rs6505162 C>A polymorphism and KD susceptibility in a deeper level. In Table 3, there are two significant numbers we found. We noticed that the CA/AA genotypes of rs6505162 decreased the occurrence of CAA. (Adjusted OR=1.30, 95%CI=1.02-1.67, *P*=0.037). The CA/AA genotypes of rs6505162 could also decrease the occurrence of CAL(Adjusted OR=1.56, 95%CI=1.19-2.03, *P*=0.001). No other notable connections was detected, after we observed other subgroups such as gender and age.

Discussion

The nexus between KD susceptibility and the *miRNA-423* rs6505162 C>A polymorphism in our case-control investigation was further probed. No relevant association between the rs6505162 C>A polymorphism and KD susceptibility was noticed in the sick (Table 2). Using the subgroup analysis, we pointed out that the *miRNA-423* rs6505162 CA/AA genotypes is one of protective factors of CAA and CAL in KD patients (Table 3). These can serve as a basis for studying other relevant matters. Nevertheless, no conclusion that CAA and CAL in KD patients might have certain connection with age and gender has been analyzed in our subgroup research. More samples from KD patients with various age groups ought to be gathered to verify this discovery.

miRNA-423 rs6505162 polymorphisms in KD children is first referred in this study. According to many reports, *miRNA-423* is closely related to heart failure and can also be used as a corresponding indicator, such as BNPs.(29-31) Other finding hinted that *miRNA-423* A allele and CA genotypes could enhance the risk of coronary artery disease(CAD).(25) Hakimzadeh reported that up-regulation of *miR423-5p* could identify the sick with low coronary collateral volume.(32) Alterations in the expression extent of 8 miRNAs including *miRNA-423* participating in the immune pathway might be involved in the immune process in the early stages of diabetes, through the alterations of the four cytokines IL-4. , IL-10, IL-21, IL-22 and three pancreatic autoantibodies IA-2A , ICA, GAD65A.(33) In membranous glomerulonephropathy upregulation of *miRNA-423* had a certain significant association with down regulated IL6.(34)We found that the descending expression of the designated genes on proliferation and differentiation in myoblast was caused by the upregulated *miR-423-5p* suppressing the suppressor of fused homolog in expression.(35) In the polymorphism of *pre-MIR423* rs6505162, genetic mutations, C to A transition, inhibited the function of HEC-1b cell proliferation and migratory.(36) The abduction of EndMT progression accelerating cell proliferation and migratory capacity was caused by KD serum in endothelial cells,

which could be one of the pathogenesis in KD.(14) On the basis of the series of articles above, there is a clear connection between *miRNA-423* and coronary artery and coronary collateral. At the same time, *miRNA-423* is associated with a range of inflammatory factors. Manifesting vasculitis, belonging to autoimmune syndrome, KD refers to inflammatory disease. Finally, the pathway of EndMT can be used to explain that *miRNA-423* can be a protective factor of KD as well as the stability of coronary arteries.

Our nowadays research suggested that the *miRNA-423* rs6505162 C>A polymorphism might not act on the susceptibility to KD in a majority of Han in southern China. KD is known to have many familiar clinical manifestations and complications, such as CAL and CAA.(3) We also noted that the CA/AA genotypes of rs6505162 reduced the occurrence of CAA and CAL in KD children. Nevertheless, our discovery including two positive point is required to affirm by more evidences owing to various factors restricting our study.

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Conflicts of interest

No conflicts of interest have been declared so far.

References

1. Kawasaki T. [Acute febrile mucocutaneous syndrome with lymphoid involvement with specific desquamation of the fingers and toes in children]. Arerugi = [Allergy] 1967: 16: 178-222.
2. McCrindle BW, Rowley AH, Newburger JW et al. 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.
3. Newburger JW, Takahashi M, Burns JC. Kawasaki Disease. Journal of the American College of Cardiology 2016: 67: 1738-1749.
4. Bozorgi A, Shahrzad M, Karbalaei Saleh S. Gigantic coronary aneurysms: a late complication of Kawasaki disease. Kardiologia polska 2014: 72: 989.
5. Fraison JB, Seve P, Dauphin C et al. Kawasaki disease in adults: Observations in France and literature review. Autoimmunity reviews 2016: 15: 242-249.
6. Altammar F, Lang B. Kawasaki Disease in the neonate: case report and literature review. Pediatric rheumatology online journal 2018: 16: 43.
7. Sanlidag B, Balkan C, Bahceciler N. A case report: incomplete Kawasaki disease in a hypogammaglobulinemie child. Archivos argentinos de pediatria 2018: 116: e322-e324.
8. Chen S, Dong Y, Kiuchi MG et al. Coronary Artery Complication in Kawasaki Disease and the Importance of Early Intervention : A Systematic Review and Meta-analysis. JAMA pediatrics 2016: 170: 1156-1163.
9. Cimaz R, Fanti E, Mauro A et al. Epidemiology of Kawasaki disease in Italy: surveillance from national hospitalization records. European journal of pediatrics 2017: 176: 1061-1065.
10. Ha S, Seo GH, Kim KY et al. Epidemiologic Study on Kawasaki Disease in Korea, 2007-2014: Based on Health Insurance Review & Assessment Service Claims. Journal of Korean medical science 2016: 31: 1445-1449.
11. Saundankar J, Yim D, Itotoh B et al. The epidemiology and clinical features of Kawasaki disease in Australia. Pediatrics 2014: 133: e1009-1014.
12. Yim D, Curtis N, Cheung M et al. Update on Kawasaki disease: epidemiology, aetiology and pathogenesis. Journal of paediatrics and child health 2013: 49: 704-708.
13. Takahashi K, Oharaseki T, Yokouchi Y. Pathogenesis of Kawasaki disease. Clinical and experimental immunology 2011: 164 Suppl 1: 20-22.
14. He M, Chen Z, Martin M et al. miR-483 Targeting of CTGF Suppresses Endothelial-to-Mesenchymal Transition: Therapeutic Implications in Kawasaki Disease. Circulation research 2017: 120: 354-365.
15. Ueno K, Ninomiya Y, Hazeki D et al. Disruption of Endothelial Cell Homeostasis Plays a Key Role in the Early Pathogenesis of Coronary Artery Abnormalities in Kawasaki Disease. Scientific reports 2017: 7: 43719.
16. Lv YW, Wang J, Sun L et al. Understanding the pathogenesis of Kawasaki disease by network and pathway analysis. Computational and mathematical methods in medicine 2013: 2013: 989307.
17. Chen KD, Huang YH, Ming-Huey Guo M et al. The human blood DNA methylome identifies crucial role of beta-catenin in the pathogenesis of Kawasaki disease. Oncotarget 2018: 9: 28337-28350.

18. Achour C, Bogard B, Hube F et al. The Non-Coding RNA Journal Club: Highlights on Recent Papers-5. Non-coding RNA 2017: 3.

19. Borghini A, Andreassi MG. Genetic polymorphisms offer insight into the causal role of microRNA in coronary artery disease. Atherosclerosis 2018: 269: 63-70.

20. Chen Y, Mao ZD, Shi YJ et al. Comprehensive analysis of miRNA-mRNA-lncRNA networks in severe asthma. Epigenomics 2019: 11: 115-131.

21. Gao X, Yang L, Luo H et al. A Rare Rs139365823 Polymorphism in Pre-miR-138 Is Associated with Risk of Congenital Heart Disease in a Chinese Population. DNA and cell biology 2018: 37: 109-116.

22. Hashimoto N, Tanaka T. Role of miRNAs in the pathogenesis and susceptibility of diabetes mellitus. Journal of human genetics 2017: 62: 141-150.

23. Wang Z, Wang P, Wang Z et al. MiRNA-548c-5p downregulates inflammatory response in preeclampsia via targeting PTPRO. Journal of cellular physiology 2018.

24. Jia W, Zeng L, Luo S et al. Association of microRNA-423 rs6505162 C>A polymorphism with susceptibility and metastasis of colorectal carcinoma. Medicine 2018: 97: e9846.

25. Jha CK, Mir R, Elfaki I et al. Potential Impact of MicroRNA-423 Gene Variability in Coronary Artery Disease. Endocrine, metabolic & immune disorders drug targets 2019: 19: 67-74.

26. Li Q, Chen L, Chen D et al. Influence of microRNA-related polymorphisms on clinical outcomes in coronary artery disease. American journal of translational research 2015: 7: 393-400.

27. Newburger JW, Takahashi M, Gerber MA et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a statement for health professionals from the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association. Circulation 2004: 110: 2747-2771.

28. Che D, Li J, Fu L et al. The rs1625579 T>G polymorphism in the miRNA-13 gene confers a risk of early- onset Kawasaki disease in a southern Chinese population. Infection and drug resistance 2018: 11: 1055-1060.

29. Schneider S, Silvello D, Martinelli NC et al. Plasma levels of microRNA-21, -126 and -423-5p alter during clinical improvement and are associated with the prognosis of acute heart failure. Molecular medicine reports 2018: 17: 4736-4746.

30. Yan H, Ma F, Zhang Y et al. miRNAs as biomarkers for diagnosis of heart failure: A systematic review and meta-analysis. Medicine 2017: 96: e6825.

31. Tijsen AJ, Creemers EE, Moerland PD et al. MiR423-5p as a circulating biomarker for heart failure. Circulation research 2010: 106: 1035-1039.

32. Hakimzadeh N, Nossent AY, van der Laan AM et al. Circulating MicroRNAs Characterizing Patients with Insufficient Coronary Collateral Artery Function. PloS one 2015: 10: e0137035.

33. Samandari N, Mirza AH, Kaur S et al. Influence of Disease Duration on Circulating Levels of miRNAs in Children and Adolescents with New Onset Type 1 Diabetes. Non-coding RNA 2018: 4.

34. Barbagallo C, Passanisi R, Mirabella F et al. Upregulated microRNAs in membranous glomerulonephropathy are associated with significant downregulation of IL6 and MYC mRNAs. Journal of cellular physiology 2018.

35. Ge J, Zhu J, Xia B et al. miR-423-5p inhibits myoblast proliferation and differentiation by targeting Sufu. Journal of cellular biochemistry 2018: 119: 7610-7620.

36. Su X, Hu Y, Li Y et al. The polymorphism of rs6505162 in the MIR423 coding region and recurrent pregnancy loss. Reproduction 2015: 150: 65-76.

Table 1:Frequency distribution of selected variables for cases and controls.

Variables	Cases (n=532)		Controls (n=623)		P^a
	No.	%	No.	%	
Age range, month	1.00-166.0		0.07-166		0.602
Mean ± SD	28.39 ± 24.68		28.48 ± 25.33		
<12	137	25.75	165	26.48	
12-60	351	65.98	397	63.72	
>60	44	8.27	61	9.79	
Gender					0.143
Female	167	31.39	221	35.47	
Male	365	68.61	402	64.53	
Coronary artery aneurysm					
CAA	51	9.59			
NCAA	481	90.41			
Coronary artery lesion					
CAL	168	31.58			
NCAL	364	68.42			

[a] Two-sided χ^2 test for distributions between cases and controls.

Abbreviations: CAA, coronary artery aneurysm; CAL, coronary artery lesion; NCAA, patients without CAA; NCAL, patients without CAL.

Table 2. Genotype distributions of rs6505162 C>A polymorphism and Kawasaki disease susceptibility

Genotype	Cases (N=529)	Controls (N=623)	*P* [a]	Crude OR (95% CI)	*P*	Adjusted OR (95% CI) [b]	*P* [b]
CC	323 (61.06)	412 (66.13)		1.00		1.00	
CA	185 (34.97)	190 (30.50)		1.25 (0.98-1.61)	0.075	1.25 (0.97-1.60)	0.085
AA	21 (3.97)	21 (3.37)		1.29 (0.69-2.40)	0.425	1.28 (0.69-2.38)	0.443
Additive			0.202	1.20 (0.97-1.48)	0.087	1.20 (0.98-1.48)	0.084
Dominant	206 (38.94)	211 (33.87)	0.074	1.25 (0.98-1.59)	0.074	1.25 (0.98-1.59)	0.071
Recessive	508 (96.03)	602 (96.63)	0.688	1.19 (0.64-2.20)	0.588	1.18 (0.64-2.20)	0.591

[a] χ^2 test for genotype distributions between Kawasaki disease patients and controls

[b] Adjusted for age and gender

Abbreviations: HWE, Hardy – Weinberg equation; KD, Kawasaki disease; OR, odds ratio.

Table 3. Stratification analysis for the association between rs6505162 C>A polymorphism and Kawasaki disease susceptibility

Variables	CC	CA/AA	Crude OR	*P*	Adjusted OR [a]	*P* [a]
	cases/controls		(95% CI)		(95% CI)	
Age, month						
<12	84/107	52/58	1.14 (0.71-1.83)	0.580	1.11 (0.69-1.78)	0.673
12-60	212/263	137/134	1.27 (0.94-1.71)	0.119	1.28 (0.95-1.72)	0.111
>60	27/42	17/19	1.39 (0.62-3.14)	0.426	1.32 (0.57-3.07)	0.514
Gender						
Females	96/148	71/73	1.50 (0.99-2.27)	0.056	1.46 (0.96-2.22)	0.081
Males	227/264	135/138	1.14 (0.85-1.53)	0.393	1.13 (0.84-1.52)	0.425
Coronary artery aneurysm						
CAA	36/412	15/211	0.81 (0.44-1.52)	0.518	0.82 (0.44-1.53)	0.529
NCAA	287/412	191/211	**1.30 (1.02-1.66)**	**0.038**	**1.30 (1.02-1.67)**	**0.037**
Coronary artery lesion						
CAL	122/412	46/211	0.74 (0.51-1.07)	0.112	0.74 (0.50-1.07)	0.112
NCAL	201/412	160/211	**1.55 (1.19-2.03)**	**0.001**	**1.56 (1.19-2.03)**	**0.001**

[a] Adjusted for age and gender. Statistically significant values are exhibited in bold (P<0.05).

Abbreviations: CAA, coronary artery aneurysm; CAL, coronary artery lesion; KD, Kawasaki disease; NCAA, patients without CAA; NCAL, patients without CAL; OR, odds ratio.