Author's Reply

A Mitochondrial DNA A8701G Mutation Partly Associated with Maternally Inherited Hypertension and Dilated Cardiomyopathy in a Chinese Pedigree

Ye Zhu[1], Xiang Gu[1], Chao Xu[2]

[1]Department of Cardiology, Clinical Northern People's Hospital, Medical College of Yangzhou University, Yangzhou, Jiangsu 225001, China
[2]Department of Biostatistics and Bioinformatics, Center for Bioinformatics and Genomics, School of Public Health and Tropical Medicine, Tulane University, New Orleans, LA 70112, USA

DOI: 10.4103/0366-6999.186656

Thank you for your valuable comments on our paper, "A Mitochondrial DNA A8701G Mutation Associated with Maternally Inherited Hypertension and Dilated Cardiomyopathy in a Chinese Pedigree."[1] We agree with this conclusion that this case requires profound confirmation of the pathogenicity of the m.8701A>G variant, all patients need to be investigated for multiorgan involvement, and long-term electrocardiograph data need to be presented. However, it is clinically not easy to implement the comprehensive testing for all of the related patients.

There is some evidence to suggest that mitochondrial genome mutation is closely related to hypertension[2] although it is different from the extensive study of nuclear gene effect on hypertension. Further study has also identified that over one-third of maternal inheritance hypertension could be attributed to mitochondrial DNA (mtDNA) variation.[3] It is the main reason that reactive oxidative species produced by mitochondria is related to hypertension. Dilated cardiomyopathy (dCMP) is one of myocardial disorders, which can be inherited as autosomal dominant, X-linked, or mitochondrial inheritance.[4] Parental consanguinity is often assumed to infer an autosomal recessive etiology, which means that mtDNA investigation may be overlooked in the pursuit of a presumed autosomal defect.[5] Recent studies have suggested the heterogeneity in the etiology and pathogenesis of dCMP.[6] Our study showed that the m.8701A>G variant is another candidate causal variation for dCMP in addition to those existing causal variants in nDNA-located genes. In particular, mtDNA single-nucleotide polymorphism A8701G was identified altering mitochondrial matrix pH and intracellular calcium dynamics and suspected to be involved in pathogenesis of diseases. Our data reinforced the previous observation that mitochondrial dysfunction caused by A8701G mutation has the potential to contribute, either singly or synergistically, to the pathophysiology of cardiovascular diseases. So far, there are no multisystem disorders, no typical angina pectoris, and no myocardium noncompaction in this family by our long-term follow-up. Coronary heart disease and secondary hypertension have also been excluded by coronary angiography and much testing at least in patient II/1 and II/3.

In conclusion, we acknowledge that there are some limitations in this study. A detailed examination and investigation will be required to define. The variability in clinical expression can also be explained by many factors, including genetic background, environmental factors, and personal lifestyle. The coaction of the A8701G mutation and genetic factors caused by consanguineous marriage might affect this family with maternally inherited hypertension and dCMP.

References

1. Zhu Y, Gu X, Xu C. A mitochondrial DNA A8701G mutation associated with maternally inherited hypertension and dilated cardiomyopathy in a Chinese pedigree of a consanguineous marriage. Chin Med J 2016;129:259-66. doi: 10.4103/0366-6999.174491.
2. Lu Y, Xiao T, Zhang F, Chen Y, Liu Y, Li Y, *et al.* Effect of mitochondrial tRNALys mutation on the clinical and biochemical characteristics of Chinese essential hypertensive subjects. Biochem Biophys Res Commun 2014;454:500-4. doi: 10.1016/j.bbrc.2014.10.089.
3. Zhu HY, Wang SW, Martin LJ, Liu L, Li YH, Chen R, *et al.* The role of mitochondrial genome in essential hypertension in a Chinese Han population. Eur J Hum Genet 2009;17:1501-6. doi: 10.1038/ejhg.2009.63.
4. McNally EM, Golbus JR, Puckelwartz MJ. Genetic mutations and mechanisms in dilated cardiomyopathy. J Clin Invest 2013;123:19-26. doi: 10.1172/JCI62862.
5. Alston CL, He L, Morris AA, Hughes I, de Goede C, Turnbull DM, *et al.* Maternally inherited mitochondrial DNA disease in consanguineous families. Eur J Hum Genet 2011;19:1226-9. doi: 10.1038/ejhg.2011.124.
6. Kimura A. Molecular genetics and pathogenesis of cardiomyopathy. J Hum Genet 2016;61:41-50. doi: 10.1038/jhg.2015.83.

Address for correspondence: Dr. Xiang Gu, Department of Cardiology, Northern People's Hospital, Medical College of Yangzhou University, Yangzhou, Jiangsu 225001, China
E-Mail: sbyygx@medmail.com.cn