East African Scholars Journal of Medical Sciences
Abbreviated Key Title: East African Scholars J Med Sci
ISSN 2617-4421 (Print) | ISSN 2617-7188 (Online) |
Published By East African Scholars Publisher, Kenya

OPEN ACCESS

DOI: 10.36349/easms.2019.v02i03.011 Volume-2 | Issue-3 | March-2019 |

Letter To The Editor

Subclinical Cardiac Involvement in M.3243A>G Mutation Carriers

Josef Finsterer, MD, PhD.[1], Sinda Zarrouk-Mahjoub, PhD.[2]

[1]Krankenanstalt Rudolfstiftung, Messerli Institute, Veterinary University of Vienna, Vienna, Austria
[2]University of Tunis El Manar and Genomics Platform, Pasteur Institute of Tunis, Tunisia

*Corresponding Author
Finsterer J, MD, PhD

Keywords: Myocardium, mtDNA, mitochondrial, cardiac, arrhythmia, deformity, strain.

In a recent article, Koene *et al.*, (2017) reported about a study of 23 patients carrying the m.3243A>G mutation who were retrospectively investigated for cardiac involvement by 2D speckle tracking echocardiography (Koene, S. *et al.*, 2017). We have the following comments and concerns.

Results of 2D speckle tracking echocardiography may strongly depend on the presence or absence of coronary heart disease (Caspar, T. *et al.*, 2017). How many of the 23 patients from which GLS and a follow up investigations were available had undergone coronary angiography, myocardial scintigraphy, or stress testing prior to the investigations? The number of patients with risk factors for atherosclerosis was high (Koene, S. *et al.*, 2017). Since eighteen had diabetes, 10 a history of smoking, and five arterial hypertension, it is quite likely that at least some of the 23 included patients had coronary heart disease. In these cases it cannot be decided if abnormal longitudinal strain reflects myocardial involvement in the underlying genetic defect or results from atherosclerosis. The situation is even more complicated since some of the cardiovascular risk factors, such as diabetes, hyperlipidemia, or arterial hypertension are a frequent manifestation of a MID.

The authors mention in the introduction that the m.3243A>G mutation is maternally inherited. We have to keep in mind that this is not the case in all cases. Up to 25% of the heteroplasmic mtDNA mutations are sporadic (de novo) (Sallevelt, S. C. *et al.*, 2017). In how many of the 30 patients did other family members carry the mutation as well? How many of these manifested in the heart as well? In how many of the 30 patients was the family history negative for the disease? How many of the mothers of the included patients did not carry the mutation or were clinically unaffected?

A frequent cardiologic abnormality in mitochondrial disorders (MIDs) is left ventricular hypertrabeculation, also known as non-compaction (LVHT) (Finsterer, J. *et al.*, 2017). LVHT may occur even in patients carrying the m.3243A>G mutation (Finsterer, J. *et al.*, 2007). How many of the 30 included patients had LVHT on echocardiography or cardiac MRI? It is important to recognise LVHT since it may be complicated by heart failure, ventricular arrhythmias, or cardio-embolic events (Finsterer, J. *et al.*, 2017).

The m.3243A>G mutation may not only manifest in the myocardium but also in the cardiac conduction system (Wortmann, S. B. *et al.*, 2007). Cardiac conduction abnormalities and arrhythmias in m.3243A>G carriers include QT-prolongation [6], WPW-syndrome (Malfatti, E. *et al.*, 2013), atrial fibrillation (Malfatti, E. *et al.*, 2013), asystoly (Malfatti, E. *et al.*, 2013), atrial or ventricular premature beats (Anan, R. *et al.*, 1995), paroxysmal atrio-ventricular block (Reato, S. *et al.*, 2015), ST-depression (Anan, R. *et al.*, 1995), T-wave inversion (Anan, R. *et al.*, 1995), or sudden cardiac death (Taniguchi, A. *et al.*, 2002). In how many of the included patients were ECG abnormalities recorded?

One major problem of the study is that the results of the applied technique were not compared with a golden standard. The authors mention the feasibility to document abnormal myocardial deformity by cMRI, but it was not applied in the present study. To confirm the reliability of results they should be confirmed by a

Quick Response Code

Journal homepage:
http://www.easpublisher.com/easjms/

Article History
Received: 18.02.2019
Accepted: 27.02.2019
Published: 14.03.2019

technique which is capable to accurately recognise the abnormality of interest.

Overall, this interesting pilot study would profit from providing supplementary data about the family history, routine and long-term ECG recordings, presence or absence of LVHT, and cMRI data. As long as there is no prospective and controlled study available, the significance of 2D speckle tracking echocardiography for detection of subclinical cardiac involvement in m.3243A>G carriers remains uncertain.

REFERENCES

1. Koene, S., Timmermans, J., Weijers, G., de Laat, P., de Korte, C. L., Smeitink, J. A. M., ... & Kapusta, L. (2017). Is 2D speckle tracking echocardiography useful for detecting and monitoring myocardial dysfunction in adult m. 3243A> G carriers?—a retrospective pilot study. *Journal of inherited metabolic disease*, *40*(2), 247-259.
2. Caspar, T., Samet, H., Ohana, M., Germain, P., El Ghannudi, S., Talha, S., ... & Ohlmann, P. (2017). Longitudinal 2D strain can help diagnose coronary artery disease in patients with suspected non-ST-elevation acute coronary syndrome but apparent normal global and segmental systolic function. *International journal of cardiology*, *236*, 91-94.
3. Sallevelt, S. C., de Die-Smulders, C. E., Hendrickx, A. T., Hellebrekers, D. M., de Coo, I. F., Alston, C. L., ... & Smeets, H. J. (2017). De novo mtDNA point mutations are common and have a low recurrence risk. *Journal of medical genetics*, *54*(2), 73-83.
4. Finsterer, J., Stöllberger, C., & Towbin, J. A. (2017). Left ventricular noncompaction cardiomyopathy: cardiac, neuromuscular, and genetic factors. *Nature Reviews Cardiology*, *14*(4), 224.
5. Finsterer, J., Stöllberger, C., Steger, C., & Cozzarini, W. (2007). Complete heart block associated with noncompaction, nail-patella syndrome, and mitochondrial myopathy. *Journal of electrocardiology*, *40*(4), 352-354.
6. Wortmann, S. B., Rodenburg, R. J., Backx, A. P., Schmitt, E., Smeitink, J. A. M., & Morava, E. (2007). Early cardiac involvement in children carrying the A3243G mtDNA mutation. *Acta Paediatrica*, *96*(3), 450-451.
7. Malfatti, E., Laforêt, P., Jardel, C., Stojkovic, T., Behin, A., Eymard, B., ... & Meune, C. (2013). High risk of severe cardiac adverse events in patients with mitochondrial m. 3243A> G mutation. *Neurology*, *80*(1), 100-105.
8. Anan, R., Nakagawa, M., Miyata, M., Higuchi, I., Nakao, S., Suehara, M., ... & Tanaka, H. (1995). Cardiac involvement in mitochondrial diseases: a study on 17 patients with documented mitochondrial DNA defects. *Circulation*, *91*(4), 955-961.
9. Reato, S., Spartà, S., & D'este, D. (2015). Intraventricular conduction disturbances and paroxysmal atrioventricular block in a young patient with MELAS. *Journal of Cardiovascular Medicine*, *16*, S100-S103.
10. Taniguchi, A., Kitagawa, T., & Kuzuhara, S. (2002). MELAS sudden death due to paroxysmal arrhythmia. *Nihon rinsho. Japanese journal of clinical medicine*, *60*, 606.