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Quick Response Code:

Correspondence

Unmasking fibromyalgia as a mitochondrial disorder requires search for more than a single variant or single mtDNA deletions

Sir,

With great interest, we read the article by Danda *et al*[1] about 30 female patients with fibromyalgia syndrome (FMS) who were tested for the presence of mtDNA variant m.3243A>G and for single mtDNA deletions. Neither the m.3243A>G variant nor a single mtDNA deletion was detected in any of the 30 females[1]. We offer the following comments and concerns:

The main shortcoming of the study was that FMS patients were tested only for a single mtDNA point mutation and for single mtDNA deletions. Since the mtDNA carries 37 different genes and the nDNA carries about 1500 genes involved in mitochondrial metabolism or function, it is conceivable that the included 30 patients carried mutations other than the two for which they were investigated.

Another shortcoming was that the 30 FMS patients were not tested for hyper-CKemia and that they did not undergo the lactate stress tests[2]. Since many mitochondrial disorders (MIDs) manifest with mitochondrial myopathy, it is quite likely that creatine kinase (CK) was elevated. Since all patients presented with fatigue and exercise intolerance, it is conceivable that they reacted with lactate elevation under standardized workload below the anaerobic threshold[2]. Unfortunately, CK values were not presented and lactate was measured only at rest.

Chronic fatigue and myalgias may also occur in patients with a beta-oxidation defect[3]. Thus, FMS patients should be investigated not only for MIDs but also for lipid storage disease. Workup for lipid storage disease should include muscle biopsy which was not done in the 30 presented patients.

Since fatigue and myalgias may also occur in lysosomal storage disease, it is crucial that these types of differential diagnoses are excluded as well. Thus, it is essential that lysosmal disorders are ruled out in all FMS patients.

MIDs are frequently multisystem disorders[4], thus, it is crucial that FMS patients are prospectively investigated for the affection of organs or tissue other than the muscle. Organs involved in MIDs include the brain, eyes, ears, endocrine system, myocardium, gastrointestinal tract, kidney, and bone marrow. Since involvement of the brain and the myocardium has the strongest impact on the prognosis and outcome of a MID, we should be particularly informed about the results of cerebral and cardiologic investigations.

Missing in this study is also the family history. Since mtDNA single point mutations and single mtDNA deletions are transmitted *via* a maternal trait of inheritance in 75 and 4 per cent of the cases, respectively[5], it is crucial to know if any of the first-degree relatives presented with a phenotype suggestive of a MID.

Overall, this interesting study could have been more meaningful if heteroplasmy rates were provided, if variants in genes other than the ones reported were also investigated, if an extensive family history was provided, if the multi-organ nature of MIDs was addressed and if muscle biopsy was carried out in all 30 patients.

***Conflicts of Interest*:** None.

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