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Anti-mitochondrial antibody–mediated myopathy with cardiac involvement: reply

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We would like to thank Finsterer[1] for his interest in our article.[2] In his letter,[1] the importance of differential diagnosis including the other muscular disorders was emphasized.

In our case, presence of myopathy was evidenced by pathological changes in muscle biopsy samples.[1] Of note, we routinely perform a full battery of histochemistry for all muscle biopsy samples, including succinate dehydrogenase (SDH), cytochrome c oxidase (COX), SDH/COX double stain, as well as more than 20 different antigens for immunohistochemistry, including a variety of proteins deficient in muscular dystrophies. In our case, there were no findings suggestive of mitochondrial abnormalities, such as ragged red fibres, COX-negative fibres, and strongly SDH-reactive blood vessels, and all muscular dystrophy-associated proteins were normally expressed. Further, there were no findings of fatty replacement on muscle imagining analysis, which is one of the features suggesting hereditary myopathy.[3] Blood test showed positive anti-mitochondrial M2 antibody (AMA) and normal lactate level (0.9 mmol/L). There were no findings indicating dysfunction of the other organs based on physical examination, blood tests, and imaging studies. The information on detailed family history showed no histories of muscular or cardiac disorders, pacemaker implantation, or sudden death, except for atrial fibrillation in her mother. These findings ensured an adequate diagnosis of AMA-associated myopathy, and there was no clear indication for genetic testing.

We are afraid that his suggestion that mitochondrial myopathy should be ruled out seems to be irrelevant for the reasons as follows. First, as mentioned above, there were no clinicopathological features suggesting mitochondrial disease. Second, AMA has never been associated with mitochondrial myopathy.[4] Although he showed recent meta-analysis,[5] it merely evaluated the diagnostic value of AMA for cardiac involvement in idiopathic inflammatory myopathies (IIMs), not its pathogenicity.

Among a variety of myositis-specific antibodies (MSAs) reported in IIMs, anti-nuclear antibody was positive (×80), but ribonucleoprotein, Sjö gren's syndrome - A, Sjö gren's syndrome - B, and Jo-1 antibodies were all negative in our case. Remarkably, MSAs have the particularity of being mutually exclusive, the co-existence of two or more in the same patient being exceedingly rare (reportedly 0.18%).[6]

We are sure that the other cardiac diseases were adequately ruled out. There were no findings indicating arrhythmogenic right ventricular (RV) cardiomyopathy including electrocardiogram changes, regional RV wall motion abnormalities, or pathological changes in endomyocardial biopsy samples. Amyloidosis was ruled out since Congo red staining was negative both in skeletal muscle and myocardial tissues. Fluor-deoxy-glucose (FDG)-positron emission tomography was performed for suspected sarcoidosis. Although that showed diffuse uptake of FDG in cardiac muscles indicating false positive finding, there were no other lesions (i.e. lymph nodes) with FDG uptake. Biomarkers and gallium scintigraphy demonstrated negative findings. There was no evidence of epithelioid cell granulomas in endomyocardial biopsy samples. From these findings, sarcoidosis was deemed highly unlikely.[1]

In summary, in our case, the diagnosis of AMA-related myopathy was made, and the other cardiac and muscular disorders were ruled out with certainty. The pathogenicity of AMA and mitochondrial derangement in AMA-associated myopathy remain to be elucidated and need further investigation.

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Data availability

Data that are referenced are publicly available.

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