Mitochondrial A3243G Mutation With Manifestation of Acute Dilated Cardiomyopathy

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A 35-year-old woman (body mass index, 16 kg/m²; height, 140 cm) presented to the emergency ward with severe dyspnea of acute onset. The medical history was noteworthy for bilateral hypacusis treated with a hearing aid.

On admission, the laboratory results revealed an N-terminal prohormone of brain natriuretic peptide level of 10 219 ng/L (normal <200 ng/L). Thoracic CT scan excluded pulmonary embolism but showed cardiomegaly with pericardial and bilateral pleural effusion suggesting the presence of acute heart failure. Cardiac MRI (CMR) demonstrated a severely reduced left ventricular ejection fraction (LVEF, 13%) and severe right ventricular dysfunction (Figure 1A and 1B, baseline); LV mass index was normal. Late gadolinium enhancement images demonstrated extensive subepicardial lesions in inferior and lateral LV segments (Figure 1C, baseline). The angiogram excluded a coronary pathology, and myocardial histology was without histological signs of infiltrative or active inflammatory disease. The ECG was noteworthy for a shortened PQ interval, but supraventricular tachycardia was not revealed during long-term ECG monitoring. Otherwise, the patient showed a hyperglycemic fast, whereas lactate level was normal at rest (2 mmol/L; normal 0.4–2.2 mmol/L), a rapid increase to 4.3 mmol/L was noteworthy for bilateral hypacusis treated with a hearing aid.

Short stature, bilateral hypacusis, retinal dystrophy, cerebellar atrophy, cardiomyopathy with conduction abnormality, hyperglycemia, and a history of hypacusis and ocular maculopathy in the maternal family suggested mitochondrial disorder. Genetic analysis revealed the presence of A3243G mutation in 30±10% of the mitochondrial DNA extracted from the patient’s leukocytes. This mutation occurs in 80% of individuals with MELAS syndrome (mitochondrial encephalopathy, lactic acidosis, stroke-like episodes), which is observed with a prevalence of 13 in 100 000 in the European population.1 The clinical presentation of MELAS syndrome is variable, with severe forms showing myopathy, ophthalmoplegia, stroke-like episodes, and left ventricular hypertrophy (LVH), whereas mild forms may be limited to adult-onset diabetes mellitus or neurosensory hearing loss.2 The heterogeneity of the clinical phenotype is based on the variable burden of the mutation in different tissues and varying resistance of affected organs toward the characteristic sequelae of mitochondrial disorder being energy depletion, increased oxidative stress, and apoptosis.3 Cardiac manifestation of MELAS has been associated clinically with LVH,4 and a correlation between the severity of LVH and the burden of mutant heteroplasmy has been shown.4 The patient presented a high burden of mutant heteroplasmy in myocardial tissue (90–95%); however, LVH was absent in CMR studies at baseline and at follow-up. This suggests that a high heteroplasmy burden in the heart can favor the development of acute dilated cardiomyopathy in analogy to a transgenic mouse model, in which increased mitochondrial oxidative stress was associated with a similar cardiac phenotype.2

In summary, this case of MELAS shows an association with acute dilated cardiomyopathy and clinical improvement of heart failure with standard heart failure treatment.

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Disclosures

None.
**References**


**KEY WORDS:** heart failure, mitochondrial disease, cardiac magnetic resonance

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**Figure 1.** Top row: Left ventricular (LV) ejection fraction is severely reduced at baseline, as shown in the 3-chamber cardiac MR views (A and B). C. Late gadolinium enhancement demonstrates fibrosis in the LV myocardium (between *arrows*) and in the right ventricle. Fibrosis is minimal in the interventricular septum. *Pleural effusion and + pericardial effusion are noted. Bottom row: Follow-up after 18 months of heart failure treatment. LV ejection fraction is improved and pericardial and pleural effusions are absent (D and E), whereas fibrosis remains unchanged (F).
Figure 2. Cerebellar atrophy on T₁-weighted sagittal (left) and T₂-weighted axial MRI.
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