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Summary of the mitochondrial findings in a series of 300 cases

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The Mitomed diagnostic Lab in UCI began to offer mitochondrial diseases tests in 2007. We reviewed 300 serial cases referred for mitochondrial genome and point mutation testing. Around half (51.5%) of our cases were mitochondrial sequencing and another half (48.5%) were for point mutation screening. We identified 34 cases (11.3%) of mitochondrial disease causing mutations among the 300 cases. The most common finding was the classic 3243A > G mutation in 14 cases (41.2%), associated with multiple phenotypes. These patients had typical mitochondrial diseases syndromes like Leigh Syndrome, Mitochondrial Encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS), maternally inherited diabetes and deafness (MIDD), sensorineural hearing loss (SNHL), seizures, developmental delay, learning disabilities, mental retardation, muscle pain, cardiomyopathy, fibromyalgia and neurological disorder. The second most common mutation was 11778G > A mutation (10.3%) associated with Leber's Hereditary Optic Neuropathy (LHON) and progressive dystonia. Other indentified mutations included 827A > G (5.9%), 5567T > C (5.9%) and 9 other rare mutations (2.9%).

We will focus on the rare 3302A > G mutation that was found in two siblings and their mother. The 33-year-old sister had severe limb-girdle muscle weakness, neck extensor muscle weakness and diaphragmatic insufficiency and respiratory failure. An EKG showed right ventricular conduction delay and a very short P-R interval. Her 35-year-old brother had the similar, but less severe symptoms, and their mother with similar clinical features died at age 29 of cardiopulmonary complications. Heteroplasmy levels of ~80–90% were observed in the muscle sample of this patient and her brother and comparable heteroplasmy level was found in blood and urine sample with lower levels in buccal sample. This case suggests that the 3302A > G heteroplasmic substitution can lead to a syndrome similar to limb-girdle muscular dystrophy, with prominent respiratory, cardiac and neck extensor muscle weakness.

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