Birds of a feather flock together: Maternally inherited diabetes and deafness AND Mitochondrial encephalopathy lactic acidosis and stroke like episodes.

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Introduction:

The mutation at m. 3243 adenine to guanine (A>G) in mitochondrial encoded transfer-RNA Leucine 1 (MTTL1) gene is the single most prevalent disease-causing mitochondrial DNA (MtDNA) mutation, with carrier status of 1:400 in our general population. The distinct disease phenotype is dependent on the level of heteroplasmy of wild-type vs mutation-type mtDNA in the specific target tissues, ranging from Maternally inherited diabetes and Deafness (MIDD) to mitochondrial encephalopathy lactic acidosis and stroke like episodes (MELAS). However, current studies have shown MELAS/MIDD overlap to be present (in up to 6% of the cases) but not without posing diagnostic dilemmas as current clinical criteria are based on classical features of one or the other with the likelihood of missing conditions with overlapping features. The authors describe a similar case of overlap where MIDD was overlooked due to the pre-existing diagnosis of MELAS.

Case History:

A 33-year-old female with a background of MELAS and type 1 diabetes mellitus, admitted because of symptomatic uncontrolled capillary blood glucose levels. She had four admissions in the last three months related to hyperglycaemia and presence of ketones. Despite optimization of her basal bolus insulin regime, it was felt that she was unable to follow advice on self management with probable issues with compliance. She was frequently found to be not listening to staff instructions as an inpatient and kept on repeating the same question regarding when she could go home. Her examination was unremarkable with no evidence of diabetic retinopathy, nephropathy or neuropathy. Her recent investigation were normal other than HbA1c of 86 mmol/mol and high capillary blood glucose readings.

Further exploration and examination revealed sensorineural deafness and a previous genetic testing which had confirmed m. 3243 adenine to guanine (A>G) mutation which was clinically labelled as MELAS six years ago as she was not diabetic at the time. However with her diabetes, sensorineural deafness and forgotten genetic testing all pieced together, a diagnosis of MIDD was made. Her mother was subsequently tested and was also found to have m. 3243 A>G mutation with classical MIDD features. She had been diabetic with sensorineural deafness for over two decades and had adapted to lip syncing and was never referred for hearing evaluation. The identification of MIDD helped arranging necessary follow-up and management for both patients. The case identifies the importance of watching out for mitochondrial diabetes and to remember that clinical overlap of MIDD and MELAS may exist and confuse clinicians who may think of only one spectrum.

Conclusion:

The case highlights the importance of recognizing patients with three of more clinical features of either MIDD or MELAS without the classical presentation and the need for genetic testing in these patients as well as in those with either classical MIDD or MELAS or overlap syndrome or with maternal history of m. 3243 A>G mutation.

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