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Pancreatitis in mitochondrial disorders

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Dear Editor, with interest we read the article by Zhiping *et al*. about 5 patients from a Chinese family with MELAS due to the m.3243A>G mutation of whom 2 also had pancreatitis in the absence of a *PRSS1* mutation [1]. We have the following comments and concerns.

We do not agree with the statement that only six patients carrying an mtDNA mutation have been so far reported with pancreatitis (Table I) [1]. Pancreatitis was reported in at least 16 other MID patients (Table I) [2]. Interestingly, pancreatitis has not been reported in association with mutations in nDNA located genes. Among MID patients carrying the mtDNA mutation m.3243A>G pancreatitis has been reported in at least 8 patients (Table I).

In the abstract it is stated that 7 members of the family carried the m.3243A>G mutation. However, in the clinical data section, only 5 patients are presented. We should be informed about the reason why 2 patients were excluded from the study. A further discrepancy derives from Figure 1 which shows 9 affected patients. What was the reason why 4 patients were excluded? Another inconsistency concerns the *PRSS1* mutation. In the abstract it is mentioned that it was found in all tissue samples of all 5 included patients. However, in the results section it is mentioned that no mutations were found in the *PRSS1, SPINK1*, and *CFTR* genes [1].

Proband I/2 is indicated as deceased in Figure 1 [1]. How can this subject have been investigated if he is dead?

The authors mention that they also recorded EEGs of all included patients [1]. How many of the 5 included patients and the 9 clinically affected had epilepsy? What types of seizures were reported, which antiepileptic drugs were administered, and what was the quality of the seizure control? Particularly patient III/1 had epilepsy. Was she put on a ketogenic diet, which has been shown beneficial at least in some patients with mitochondrial epilepsy [3]?

The authors mention that a structured questionnaire was applied but no results are reported [1]. What was the purpose of applying such a questionnaire and what were the results and their interpretation?

It is quite unusual to find the same abnormality in all 5 included patients in the light of the variable heteroplasmy rates [1]. Did truly all 5 patients show up with cytotoxic edema in the internal capsule bilaterally as presented in the results?

Since MELAS is characterised by the occurrence of stroke-like episodes (SLEs) it would be interesting to know if the index case or any of the family members carrying the m.3243A>G mutation had a posi-

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Table I. Mitochondrial disorders in which pancreatitis has been reported

Reference	NOP	Age (y)	Sex	Mutation
Ishiyama 2013	2	10	Female	m.8344A>G
		28	Female	m.3243A>G
Duran 2012	1	3	Male	mtDNA deletion
Liu 2012	1	10	Male	mtDNA deletion
Finsterer 2011	1	80	Female	nm
Velinov 2009	1	4	Female	m.9098T>C
Fragaki 2009	1	Newborn	Male	m.15635T>C
Verny 2008	5	nm	nm	m.3243A>G
Debray 2006	1	17	Male	mtDNA deletion
Finsterer 2006	1	58	Male	nm
Finsterer 2004	1	38	Male	m.8381A>G
Toyono 2001	1	10	Female	m.8344A>G
Tsao 2000	1	3 weeks	Male	mtDNA depletion
Schleiffer 2000	1	37	Female	m.3243A>G
Kishnani 1996	1	1.3	Male	m.3243A>G
Oexle 1996	1	nm	Male	m.3254A>G
Montine 1995	1	17	Male	nm (AHD)
Kato 1990	1	10	Male	CIV deficiency

NOP – number of patients, nm – not mentioned, AHD – Alpers-Huttenlocher disease

tive history for a SLE. In this respect we should be also informed about the results of the DWI and the ADC sequences, particularly if there was a vasogenic or cytotoxic edema in the region of the bilaterally symmetric T2-lesions in the internal capsule.

The authors mention hyperlipidemia as a manifestation of the m.3243A>G mutation [1]. Did they regard hyperlipidemia as a result of the mtDNA mutation and if so, how to explain that serum lipids are elevated due to this mutation? Is it conceivable that hyperlipidemia was attributable to their lifestyle or diet?

Overall, this interesting study could profit from clarification of the inconsistencies mentioned above. Also information about the results of all investigations carried out should be provided. Readers should be also informed about the applied treatment of any phenotypic feature and its effect.

Disclosure

Authors report no conflict of interest.

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Editor's Note

Up to December 2016 the authors of the article entitled: "Application of molecular imaging combined with genetic screening in diagnosing MELAS, diabetes and recurrent pancreatitis" did not reply to the comments including in this letter.