Mitochondrial ataxia: the Italian experience

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INTRODUCTION

Both prevalence and clinical features of ataxia in adults with primary mitochondrial disease (PMD) are unknown. Based on the database of the "Nation-wide Italian Collaborative Network of Mitochondrial Diseases", we reviewed the clinical, neuroimaging neurophysiological and genetic data of patients with late onset (age>16) PMD (n=764) where ataxia was part of the clinical phenotype.

In this retrospective study, we evaluated the prevalence and features of ataxic syndrome in a cohort of 764 patients with either a genetic or clinical diagnosis of late-onset PMD.

METHODS

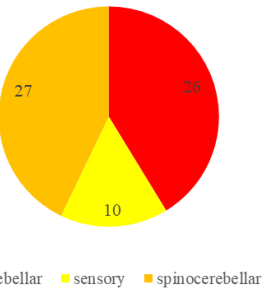
The source was the data uploaded on the "Nation-wide Italian Collaborative Network of Mitochondrial Diseases". We reviewed clinical, neurophysiological, neuroimaging and genetic data.

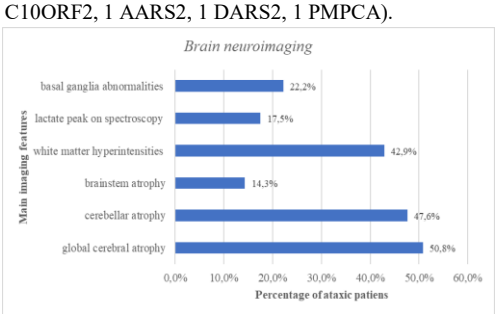
Number of patients	63
Female	33
Male	30
Age of onset of PMD	36.38 (mean)
Age of onset of ataxia	39.86 (mean)
Patients with ataxia before the diagnosis of PMD	7
Onset of ataxia coinciding with diagnosis of PMD	28

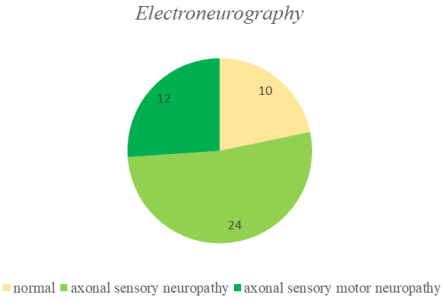
RESULTS

Ataxia was present in 63 subjects (33 females). Mean age of onset of the PMD in ataxic patients was 36.38 (+/-13.74), while age of onset of ataxic syndrome was 39.86 (+/-16.03). In 7 cases ataxia was present before the diagnosis of PMD, and in 28 cases the onset of ataxic symptoms coincided with diagnosis of PMD. We observed cerebellar ataxia in 26 patients, pure sensory ataxia in 10 and spinocerebellar ataxia in 27 cases.

Electroneurography presented an axonal sensory neuropathy pattern in 24 patients and an axonal sensory motor involvement in 12, while it was normal in 10 cases. Most frequent MRI findings were cerebellar (47.6%), brainstem (14.3%) and global cerebral atrophy (50.8%), white matter hyperintensities (42.9%), lactate peak on spectroscopy (17.5%) and basal ganglia abnormalities (22.2%). It was normal in 3 patiens. 25 patients harbored mtDNA variant (mainly the m.8344A>G in MT-TK and m.3243A>G in MT-TL1) and 3 a single mtDNA deletion. The other patients presented a nDNA gene variant (17 POLG1, 3 OPA1, 2 C10ORF2, 1 AARS2, 1 DARS2, 1 PMPCA).







Gene (nDNA)	POLG1	OPA1	C10ORF2	AARS2	DARS2	PMPCA1	multiple del
N° of patients	17	3	2	1	1	1	1

Unknown	9

Gene (mtDNA)	MT-TK	MT-TL1	MT-TS1	MT-TF	MT-CO1	Single del
N° of patients	13	8	2	1	1	3

CONCLUSIONS

Given the growing prevalence of PMDs and the relative frequency of ataxic syndrome in these patients, which often occurs at the onset of the disease, it is important to consider mitochondrial etiology in adult-onset ataxia diagnostic flowchart. Early identification of this etiology can be crucial for addressing any concurrent medical conditions that may arise in PMDs patients, as well as for potential target therapies.

REFERENCES

Lax NZ, Hepplewhite PD, Reeve AK et al (2012) Cerebellar ataxia in patients with mitochondrial DNA disease: a molecular clinicopathological study. J Neuropathol Exp Neurol 71(2):148–161
Musumeci O, Oteri R, Toscano A (2020) Spectrum of movement disorders in mitochondrial diseases. J Transl Genet Genomics 4:221–237
Gorman GS, Chinnery PF, DiMauro S et al (2016) Mitochondrial diseases. Nat Rev Dis Prim 2:16080

DISCLOSURE

The authors have no conflict of interests to declare

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