A NEW PLA2G6 MUTATION IN A FAMILY WITH INFANTILE NEUROAXONAL DYSTROPHY

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INTRODUCTION

Infantile neuroaxonal dystrophy (INAD) is an autosomal recessive disease caused by mutations in PLA2G6 gene . It is a severe progressive psychomotor disorder with infantile onset and characterized by the presence of axonal spheroids throughout the central and peripheral nervous system. Brain magnetic resonance imaging (MRI) shows cerebellar atrophy and sometimes iron accumulation in globi pallidi and substantia nigra. In this study we perform a PLA2G6 screening mutation analysis in a consanguineous Senegal's family with INAD.

PATIENTS AND METHODS

The proband is a 5 years-old child with a typical INAD phenotype : psychomotor regression and optic atrophy. His healthy parents are first cousins. Genomic DNA of all patients was extracted by peripheral blood with standard method and PCR purified products were analysed on 3500 Genetyc Analyzer.

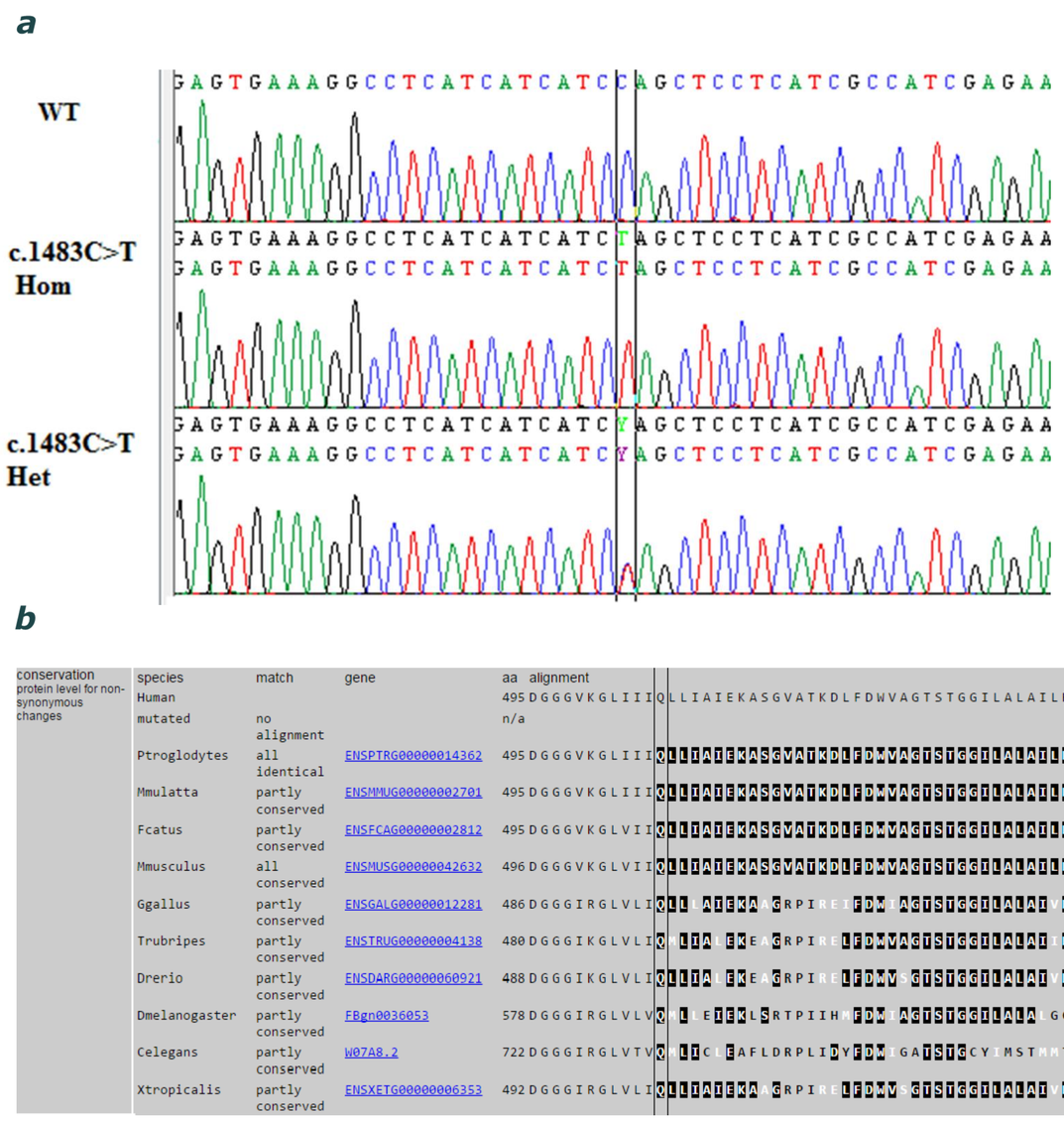

Figure 1 a. Electropherogram b. Conservation protein level

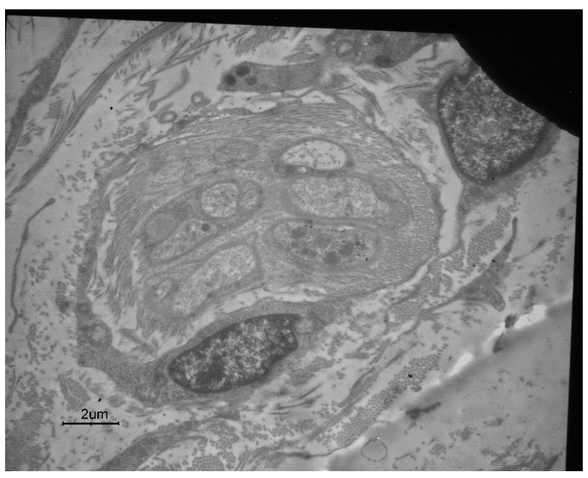

Figure 2. Spheroid bodies on skin biopsy

RESULTS

PLA2G6 mutation screening revealed a new nonsense mutation (c.1483C>T) in homozygous form in the proband (Figure 1a). His Neuroimaging study shows cerebellar atrophy while electron microscopy on skin biopsy revealed spheroid bodies suggesting axonal dystrophy (Figure 2). Naturally we found the same mutation in heterozygous form in his parents. This mutation was not found in a 150 healthy control population and in Exome Variant Server.

CONCLUSION

PLA2G6 gene encodes iPLA2-VI, a calcium-indipendent phospholipase essential for cell membrane homeostasis in the nervous system. The homozygous nonsense variant in exon 11 introduces a previous stop codon at an highly conserved protein position p.Q495* (Figure 1b). As predicted by Mutation Taster and Sift this mutation is probably damaging. It is a loss-of-function mutation, m RNA will be degradated by nonsense-mediated m RNA decay (NMD) or just generating a truncated protein. Genotype-phenotype correlates shows that the mutation c.1483C>T in homozygous form is associated with the INAD profile of early onset and rapid progression, according to literature data.
This study confirm the correlation between gene defects and INAD clinical features and greatly extends the spectrum of PLA2G6 mutations in INAD patients.

REFERENCES

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