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CORRESPONDENCE

First characterization of LHON pedigrees in North Africa

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To the Editor:

Leber Hereditary Optic Neuropathy (LHON, MIM #535000) is a rare blinding disease related to the optic nerve degeneration [1]. In most cases reported in the world, the disease is caused by one of the three primary mutations in the mitochondrial genome: m.3460G>A, m.11778G>A, and m.14484T>C in the ND1, ND4, and ND6 genes, respectively [2]. So far, a large number of LHON pedigrees have been described in Europe, Asia, North, and South America. Meanwhile, just one LHON individual originating from Tunisia and living in Italy has been reported with the m.14484T>C mutation [3]. Here we report two Moroccan LHON pedigrees with multiple affected individuals (Fig. 1). Ophthalmological examination of the proband from the first family (IV.1), aged 17 years at first examination, disclosed an asymmetric alteration of the visual fields, the right eye being more severely affected than the left eye, the latter showing a clear centrocecal scotoma (Fig. 2a). Fundus and retinal autofluorescence examinations disclosed a pallor of the optic nerve head (Fig. 2b) and angiographic picture of the left eye revealed some faint telangectasias located close to the optic nerve rim (Fig. 2c); these features fitting with the consensual LHON clinical description [4]. Ophthalmological examination of the other members of the family I were not performed, nor for the members of the family II, although the bilateral acute loss of vision reported for the second family was suggestive of LHON. Together these clinical data prompted the molecular screening of the mitochondrial genome of the proband from both families. Whole mitochondrial genome sequencing on blood DNA evidenced the m.11778G>A mutation in both individuals, which was present at an almost homoplasmic status (99.2% and 99.1% of mutated copies, respectively). Segregation study by Sanger sequencing disclosed that affected members from Family I had the causative mutation, and that its transmission was compatible with maternal lineage, although some carriers were unaffected, as commonly described for women carrying a LHON mutation. Analysis of the full mtDNA sequence revealed that the first family belongs to the J2b1a1 haplogroup, whereas the second one belongs to the T2a1a haplogroup. Search for the presence of mtDNA deletions using the eKLIPSe software [5] did not evidence genome alteration.

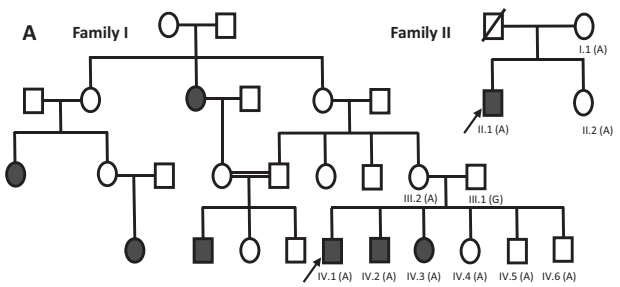

Fig. 1 Pedigrees of the two Moroccan LHON families, with the segregation of the m.11778G>A mutation.

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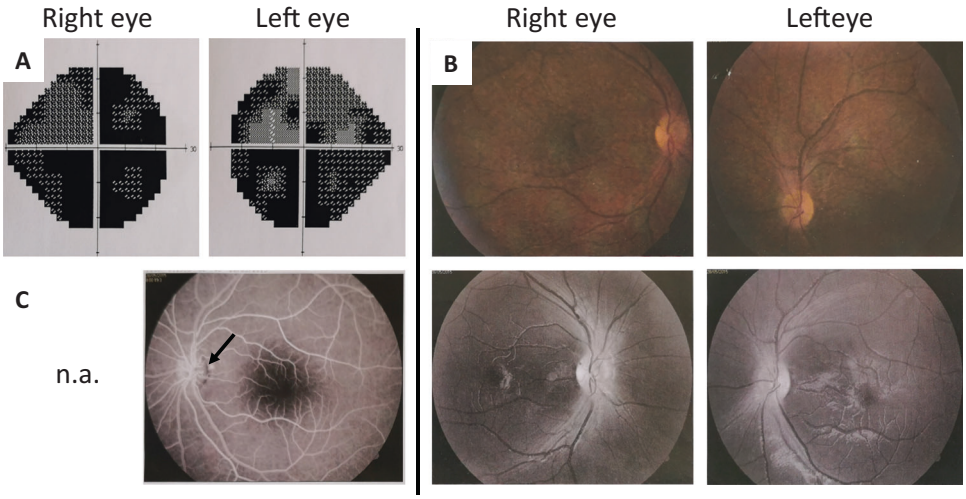

Fig. 2 Results from the ophthalmological examination of the proband from Family I. **a** Visual field evaluation of both eyes, using the Humprey set-up, showing the dramatic visual field loss on the right eye and the centrocecal scotoma on the left eye. **b** Pictures of the eye fundus and of the retinal autofluorescence of the left and right eyes, disclosing a normal retina, but an optic disk pallor. **c** Angiographic picture of the left eye revealing faint telangectasias at the optic nerve rim (black arrow; n.a.: picture not available for the right eye).

Thus altogether, we describe here the first LHON pedigrees from North Africa with the most common m.11778G>A mutation of the mitochondrial genome, witnessing the worldwide distribution of this disease and mutation, whatsoever the family haplogroup.

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Compliance with ethical standards

Informed consent Authors have obtained informed consent from the patients to perform genetic analyses and to publish the results of the ophthalmological examinations.

Conflict of interest The authors declare that they have no conflict of interest.

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