OPA1 gene mutation mimicking MS: diagnostic pitfalls.

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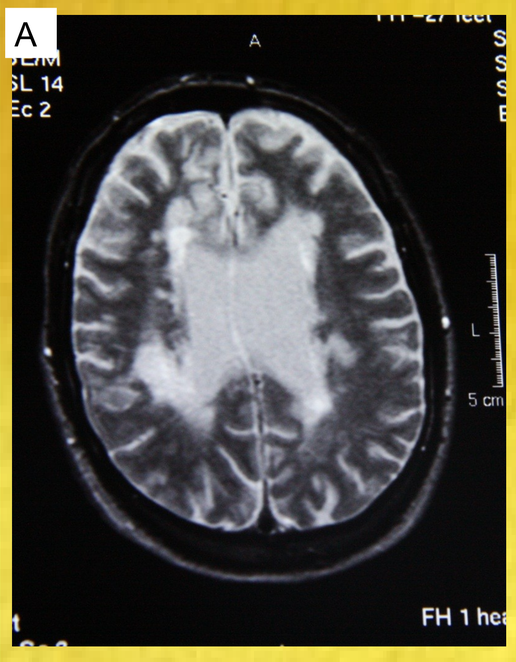
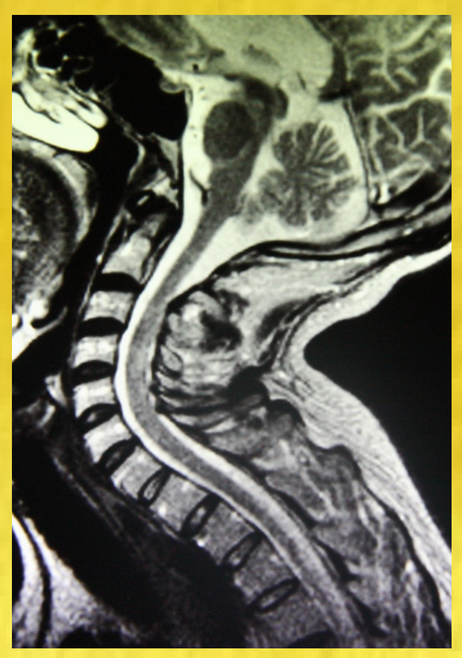
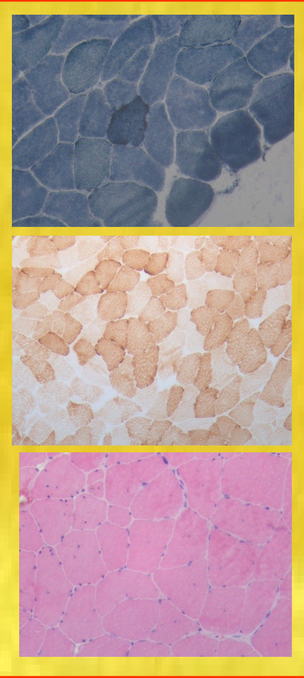
Background. Mitochondrial diseases can sometimes mimic MS MRI and clinical features. Until recently, many of these were unknown. The number of involved mutations in nuclear and mitochondrial DNA is constantly growing. For these reasons, in particular cases, there is a risk of misdiagnosis of MS.

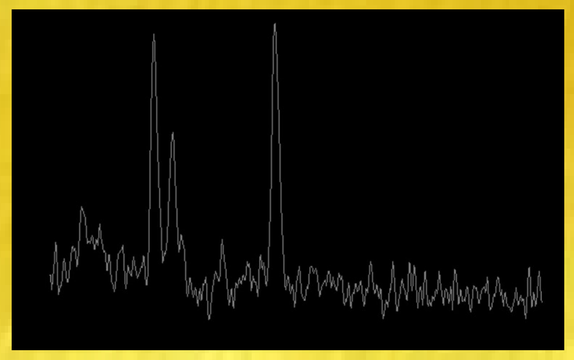
Case History. Here we report two familiar cases of OPA-1 mutations diagnosed as MS for years. The onset for male child (A) was at 21 years old with ambulatory instability. The MRI (1989) was positive for MS. He experienced relapses in the following years characterized by instability and dizziness. His father (B) had suffered by visual loss and deafness since his youth. At 56 years old, B experienced progressive left leg weakness and the MRI (1998) was typical for MS. The two patients were re-evaluated in 2009, the EDSS was 2.5 and 5.5, respectively. In both subjects, ***visual, brainstem and somatosensiorial evocated potentials*** were altered, ***brain and spinal cord MRI*** showed lesions, a ***muscular biopsy*** was compatible with mitochondrial myopathy, the ***muscular MRI*** was normal, ***the audiometric evaluation*** showed sensorineural deafness, and the ***electroencephalography*** was abnormal. B had chronic neurogenic sufferance of his legs at ***electromyography***. The ***ophthalmic examination*** showed bilateral optic atrophy in B. Crystalline lens abnormalities and papillary pallor were present in both patients at ***optical coherence tomography*** examination, but were more evident in B. ***Cerebrospinal fluid analysis*** was negative for OB in A, positive in B. ***MRI spectroscopy*** showed increased lactates and creatine in A, and a lactates increase in B. ***Leber's mutations*** were negative (MTND4 nt.G11778A, MTND1 nt.G3460A, MTND6 nt.G14459A, MTND6 nt.T14484C). A and B both had a punctiform mutation (c.1756T>C) in the exon 18 in OPA-1 gene, in hetero and homozygous, respectively. This mutation causes the amino acidic change p.Arg586Trp.

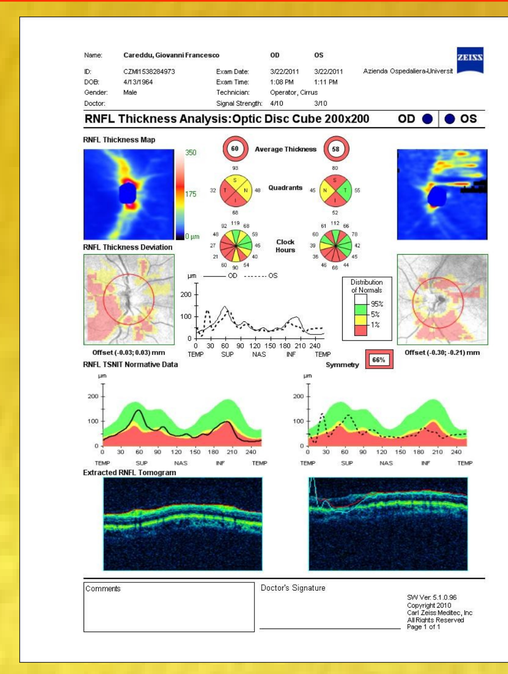
A











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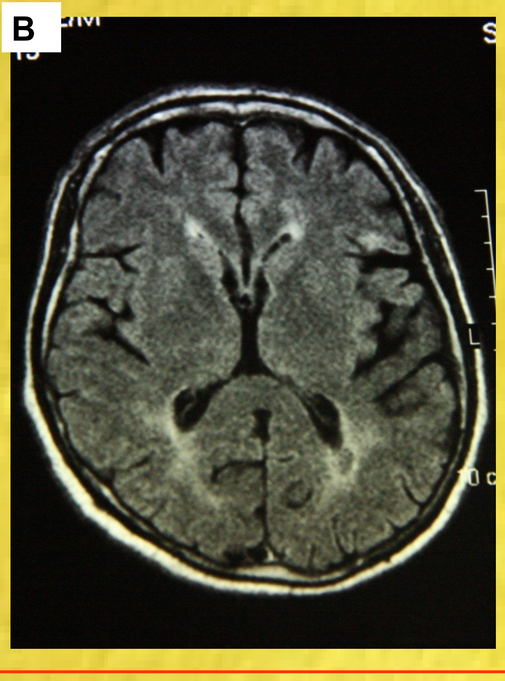

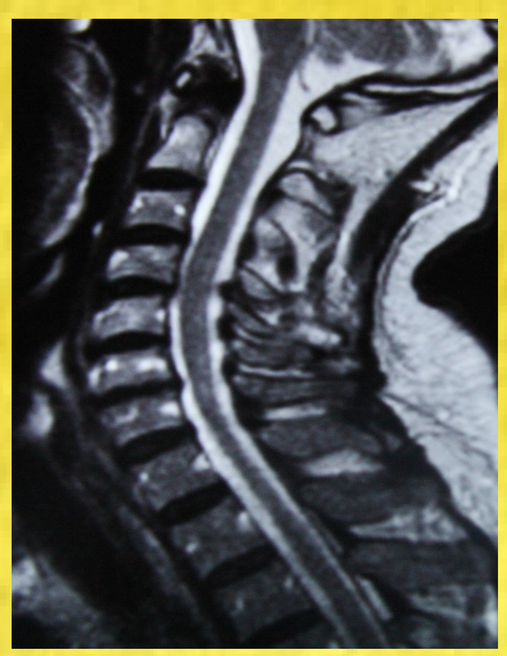

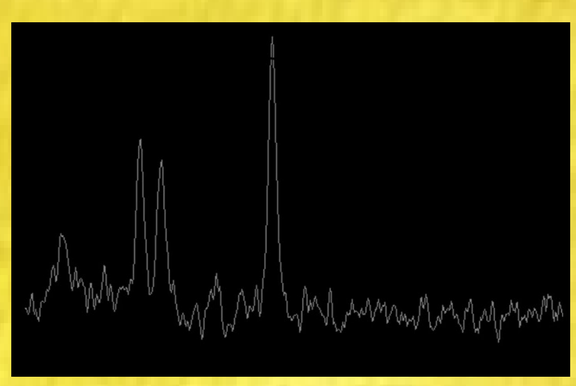

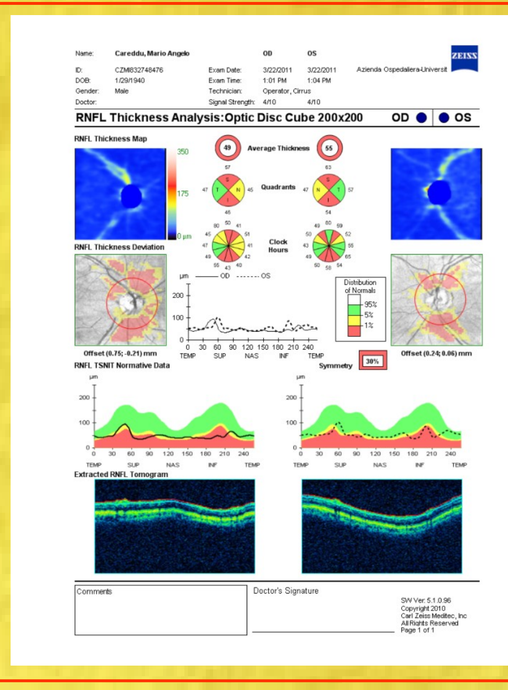

Discussion and conclusions. OPA-1 is a nuclear gene encoding a mitochondrial dynamic-related protein. Its autosomic dominant mutation causes mitochondrial DNA instability and the phenotype could be complex. (1) This mutation could be responsible for the optic atrophy "plus" phenotype. (2) Only one case has previously been reported in which optic atrophy was associated with neurological and MRI features mimicking MS. (3) It is important re-evaluate for OPA-1 the MS patients with particular symptoms, such as deafness and optic atrophy, in particular if there are cases in the same family.

References:
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3. Verny C, et al. Neurology. 2008;25;70(13Pt2):1152-3