ACUTE MANIFESTATION OF LHON AND COINCIDENTAL FINDING OF A PITUITARY ADENOMA: A CASE REPORT

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SUMMARY

A patient with Leber Hereditary Opticus Neuropathy (LHON) and a pituitary adenoma is presented. The different ophthalmological signs of LHON are described and illustrated. A definite diagnosis is made by detecting a mitochondrial mutation. A radiological examination revealed a pituitary adenoma.
The pituitary adenoma may be a trigger factor in the penetrance of LHON.

RÉSUMÉ

Les auteurs décrivent le cas d'un patient présentant une neuropathie optique héréditaire de Leber (LHON) et un adénome hypophysaire.
Les différents signes ophtalmologiques de LHON sont décrits et illustrés. Le diagnostic est confirmé par la détection d'une mutation mitochondriale. L'examen radiologique a mis un adénome hypophysaire en évidence.
L'adénome hypophysaire peut avoir joué un rôle dans le déclenchement des symptômes d'atrophie optique de Leber.

KEY WORDS

LHON, pituitary adenoma, case report, mitochondrial mutation 11778

MOTS-CLES

LHON, adénome hypophysaire, mutation mitochondriale 11778

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INTRODUCTION

In 1871 Theodor Leber suggested the existence of a hereditary form of optic neuritis. In the last decennia the disorder has been recognized as a mitochondrial disease with matrilineal inheritance. LHON is manifested as a bilateral, acute or subacute loss of central vision in young adults, predominantely males. Colour vision is affected early, and visual fields demonstrate central or caecocentral defects. The classic ophthalmoscopical findings in acute LHON are (1) circumpapillary telangiectatic microangiopathy, (2) hyperaemic optic discs and swelling of the nerve fiber layer around the disc, (3) absence of leakage from the disc or peripapillary region on fluorescein angiography.

CASE REPORT

An otherwise healthy 24 year old male electronic engineer presented at our department because of visual loss since 10 days. Past medical history was significant only for smoking 20 cigarettes a day. No medications were taken and there were no elements pointing to alcohol abuse.

The visual acuity was 1/10 (Snellen 3) in the right and in the left eye. Slitlamp examination was normal. There was an anisocoria (right pupil 2.5 mm and left pupil 4 mm) and an asymmetric and smaller constriction amplitude in the left eye on light. Colour vision tested with the Ishihara colour plates was severly disturbed on both eyes. Hyperaemic optic discs with peripapillary telangiectasia were seen in fundo (fig.1). Fluorescein angiography showed absence of leakage from the disc and from the papillary region (fig 2). Goldmann perimetry showed a normal peripheral field and automated central static perimetry (Humphrey) revealed a centrocaecal scotoma in both eyes (fig 3). Neurological examination revealed no abnormalities. A CT-scan of the skull and orbitae was normal whereas the MRI showed a suspect sellar region.

FBC, protein electrophoreses, ESR, CRP, liver function tests, kidney function tests, ANCA and TSH were all normal. There was no acute infection with HSV, CMV, Borrelia, Ebstein Barr, VZV and Toxoplasma. The serum levels of folate and vitamin B 12 were normal. A blood-sample was taken to detect possible mutations in mitochondrial DNA.

Considering the clinical picture and the inconclusive results from the technical investigations and laboratory tests, a trial therapy of one gram of intravenous methylprednisolone was administered every day for 5 days. On follow-up examination on the fifth day of the intravenous therapy the visual acuity dropped from 1/10 (Snellen 3) to counting fingers (Snellen 8) in both eyes. The anisocoria and abnormal pupillary light reflexes persisted. Fundoscopic examination demonstrated the same hyperaemic papillae with peripapillary telangiectasia.

The MRI (axial and sagittal views) was reevaluated and because an intracranial process in the sellar region could not be excluded on the first MRI, additional MRI scans were taken, this time completed with coronal views and with contrast injection. Now, the MRI clearly showed a pituitary adenoma with suprasellar extension and discrete compression on the chiasma, mainly on the left side. (fig 4). The endocrinological work up was normal and because there was an intact visual field measured with the Goldmann perimeter a conservative attitude was taken by the neurosurgical departement consisting in a monthly ophthalmological follow-up and a neuroradiological examination every six months.

Some weeks later, the mitochondrial mutation at position 11778 was detected and considering the clinical picture the diagnosis was made of Leber Hereditary Opticus Neuropathy.

On follow-up examination, approximately 3 months after the acute (subacute) onset of visual loss, the visual acuity is counting fingers on 1.5 meter, Snellen 8 at the right eye and counting fingers on 1.5 meter, Snellen 10 at the left eye.

There is still an anisocoria and a smaller constriction amplitude in the left eye on light. The colour vision is severely affected and the optic discs became pale (fig 5). The peripheral visual field with the Goldmann perimeter remains intact and the automatic perimetry with the Humphrey perimeter shows a central scotoma of approximately 30 degrees (fig 6).

Fig 1: Acute stage: hyperaemic discs and peripapillary teleangiectasia

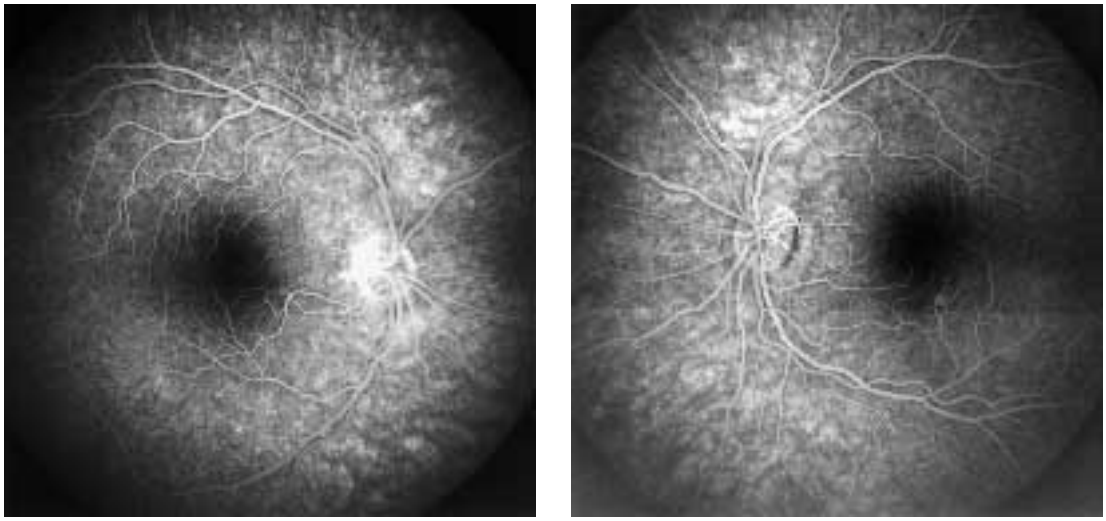

Fig 2: Fluorescein angiography: absence of leakage from the disc and from the papillary region.

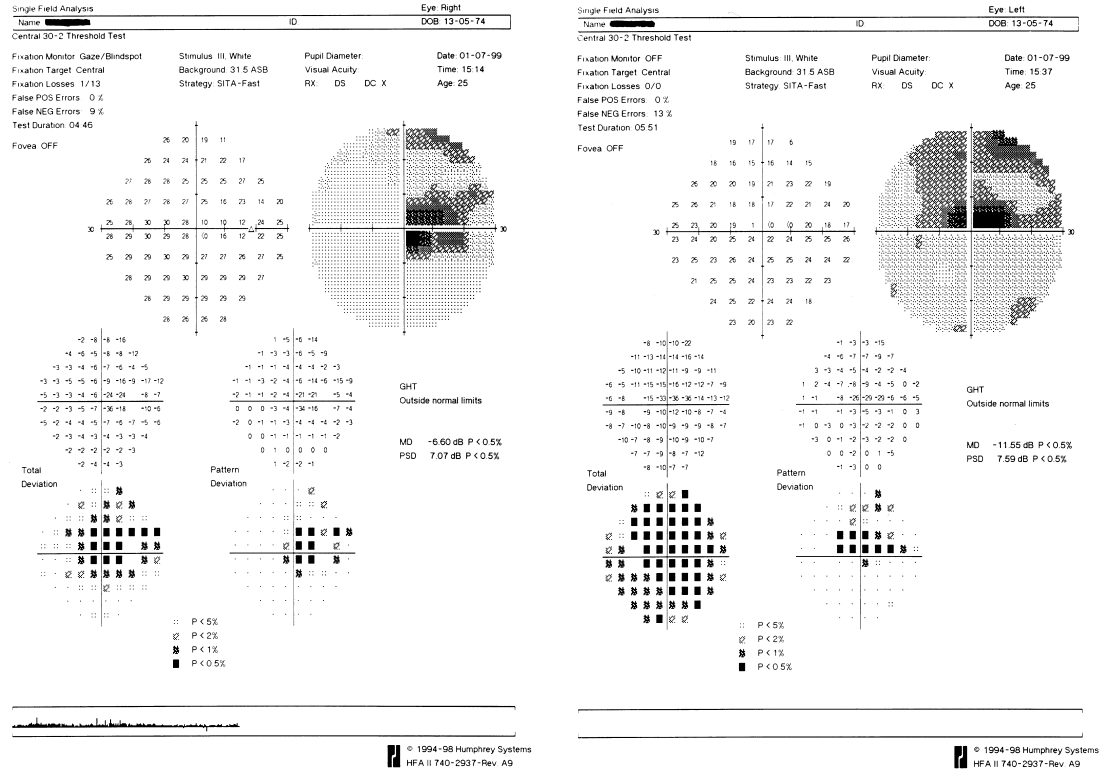

Fig 3: Automated perimetry: centrocaecal scotoma

Fig 4: MRI: Coronal view after contrastinjection (Gadolinium): pituitary adenoma with suprasellar extension and compression on the chiasma

DISCUSSION

In a patient presenting with bilateral painless subacute visual loss, centrocaecal scotomata, disturbed pupillary light reactions and impairment of colour vision different possibilities have to be considered: postinfectious optic neuritis, toxic optic neuropathy, nutritional optic neuropathy and hereditary optic neuropathy (2,4,5). Considering the severe visual loss and the inconclusive results of the laboratory tests and neuro-radiological examination, a trial therapy with intravenous megadose methylprednisolone was administered.

In a postinfectious optic neuritis, intravenous steroids usually cause a dramatic improvement of the visual acuity (4,5). The further impairment of visual acuity after 5 days of megadose cortisone is unusual in case of an optic neuritis or postinfectious optic neuritis. Anamnestically, there were no elements to suspect a toxic optic neuropathy. A nutritional optic neuropathy was excluded anamnestically and by detecting a normal folate and vitamin B12 level in the bloodserum (5). Based on the clinical picture and detecting the mitochondrial mutation at position 11778, the diagnosis of Leber Hereditary Optic Neuropathy was made. Several mutations are now recognized as associated with LHON. The first mutation related to LHON was reported by Wallace in 1988 (15). He described a mutation in the mitochondrial (mt) DNA at position 11778. Since then, about 18 mutations are described associated with LHON. There are the so called, primary LHON mutations because they are believed to be sufficient to cause LHON on their own (11778, 15257, 14484...). The secondary mutations may act in a synergistic manner with primary or with other secondary mutations.

The majority of patients with LHON have the mitochondrial mutation 11778 (7, 9, 13). The 11778 mutation is associated with a poor visual acuity, a very low or no incidence of visual recovery and large absolute central scotoma (5, 7-10). The initial field defect in this case was an enlarged blind spot or caecocentral scotoma that progressed during the months of follow-up to an absolute scotoma of approximately 30 degrees. Although some clinicians found no abnormalities in pupillary light reflexes (3, 11, 14), our patient showed a clearly asymmetric and smaller constriction amplitude in the left eye with the most impaired visual acuity. These findings are consistent with the results of the study done by Ludtke and al (6) and confirm that LHON really is an optic nerve disease.

The first NMR with axial and sagittal views without injection of contrast was doubtful to exclude a tumoral proces in the sellar region. The later MRI, with additional coronal views and with injection of Gadolinium revealed a pituitary adenoma with suprasellar extension and discrete compression on the left side of the chiasma. Considering the normal peripheral visual field measured with the Goldmann perimetry and the normal endocrinological balance a conservative neurosurgical attitude is taken with radiological MRI follow-up every 6 months.

Blindness in this patient is caused by LHON and the finding of the pituitary adenoma is a coincidental finding. The primary mutation (mt DNA 11778) produces a respiratory chain defect in the mitochondria that compromises axoplasmic transport (3). The variable penetrance in the population is explained by an influence of secondary factors such as tobacco and alcohol use, anatomical features (''disk at risk'') and genetic secondary mutations (1, 3, 5, 12). They trigger a more profound slowing of the

Fig 5: 3 months later: atrophic optic discs

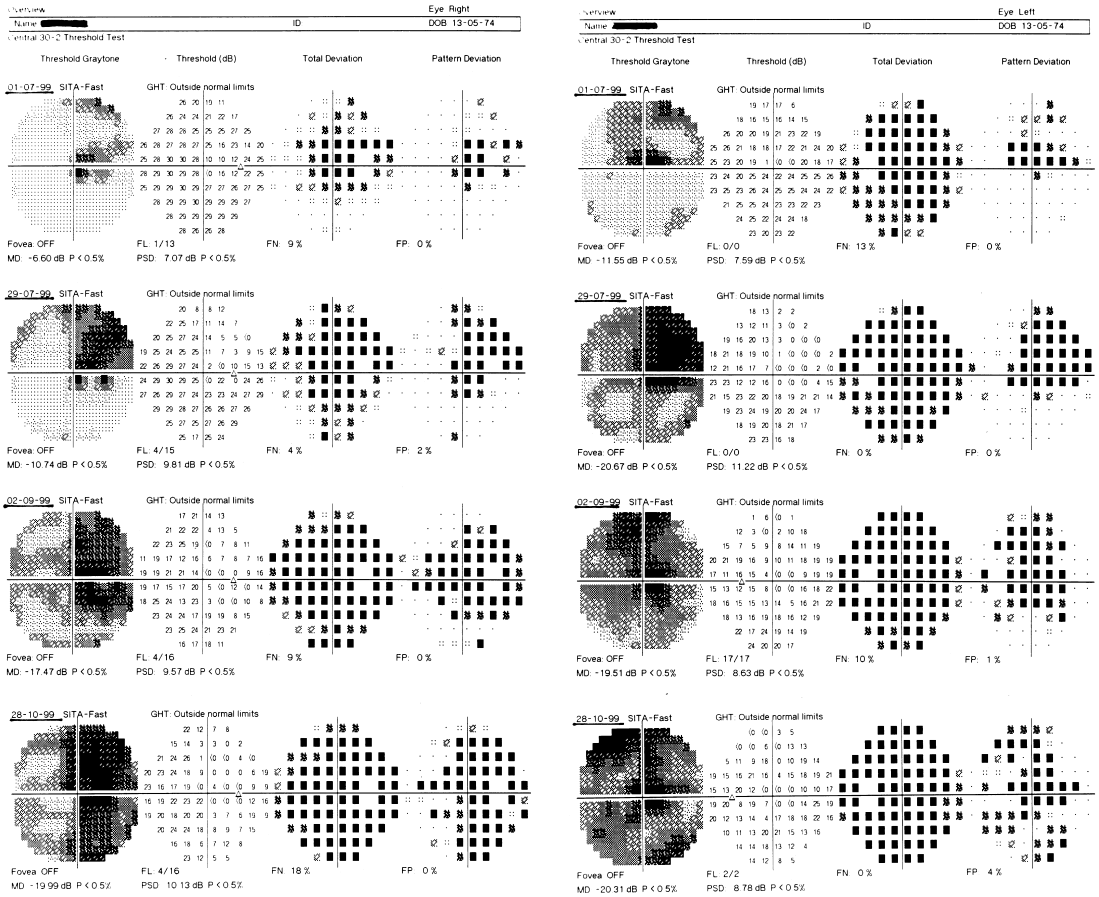

Fig. 6

axoplasmic transport to a level that precludes normal function of the ganglion cells resulting in a clinical expression of the disease.
Compression of the pituitary adenoma could be included in the list of secondary factors triggering LHON in patients with the mitochondrial mutation.

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