tumour was removed with an ultrasonic aspirator. A thin layer of tumour remained attached to the conus. A good plane of dissection between the tumour and the surface of the conus could not be safely achieved.

Postoperatively, she made a slow but steady recovery. She was relieved of low back and radicular pain. At follow up four months after surgery, there was an area of numbness in the L4 dermatome on the right. She had returned home, where she looked after herself.

The tumour specimen was an irregular, soft, greyish portion of tissue 2·2 × 1·5 × 0·7 cm in size. Microscopically it displayed a multinodular structure, in which pale, sparsely cellular islands were separated by connective tissue septa or bands of more compactly cellular neoplastic tissue (figure, c). The pale nodules had a myxomatous appearance composed of stellate or elongated cells in a strongly alcianophilic, mucoid matrix. The tumour cells in the intervening areas were mostly spindle shaped and had a more bulky eosinophilic cytoplasm. Both components stained positively for S-100 protein (figure, d).

Electron microscopy showed that the tumour cells in the myxomatous nodules and those in the internodular areas had elongated cytoplasmic processes, mostly covered by a continuous external lamina. Wide spaced collagen fibres (Luse bodies) were also identified.

Neurothekeomas most often occur in the skin of the face and arms of young adults. They arise from small cutaneous nerve branches and not from the major peripheral nerves. They are benign lesions which are cured by excision. Rare recurrences have been reported after incomplete resection. Cutaneous neurothekeomas have been classified into cellular and myxomatous subtypes, the second arising at an older age.[3]

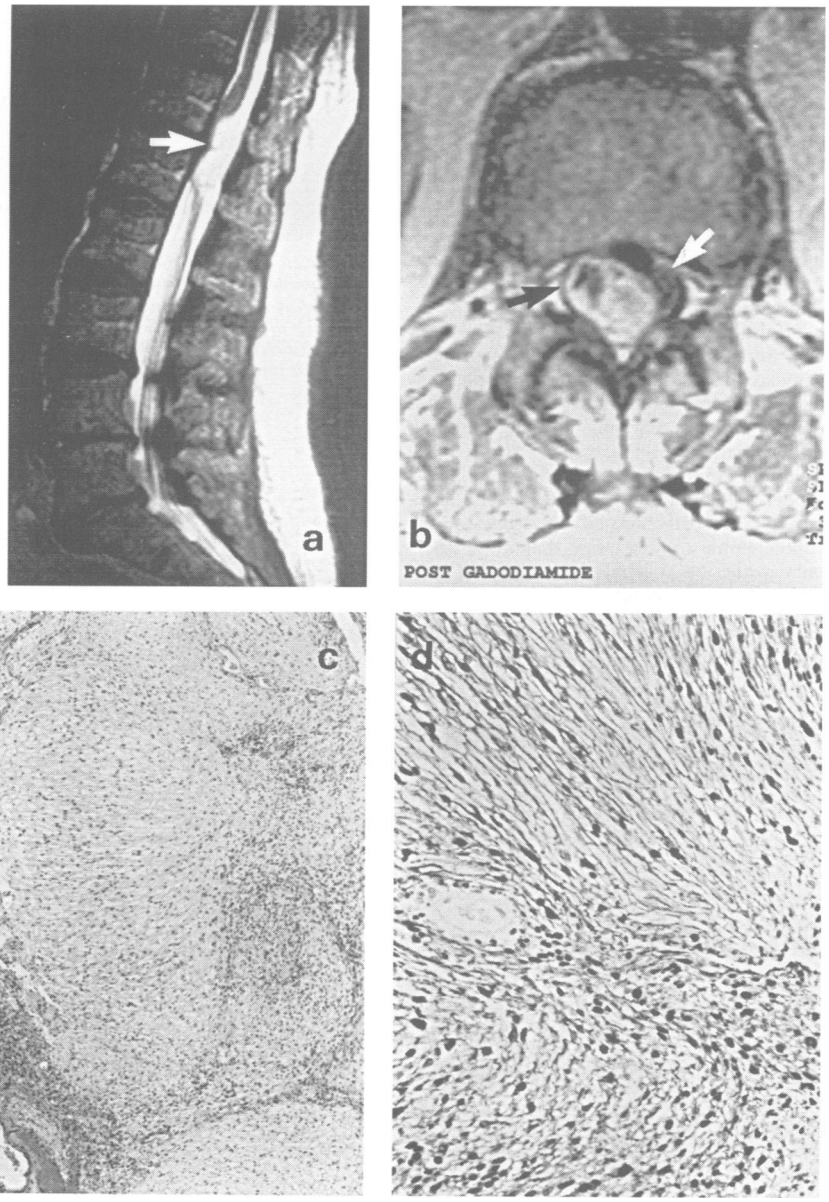
Neurothekeomas have rarely been found intrathecally. There is one report of the tumour arising from a single nerve root in the lower cauda equina.[4] In that case the tumour was completely excised. In the present case complete excision was not possible due to adherence to the conus and multiple nerve roots. The early postoperative course has, however, been satisfactory with relief of pain and restoration of ambulation.

The MRI appearance is similar to that of other intrathecal extramedullary tumours. Ependymoma, neurofibroma, and meningioma were the major differential diagnoses.

Connective tissue myxomas have occasionally been described as arising from paraspinal muscle[5] and from the vicinity of a facet joint.[6] An intramedullary location has also been described.[7] The compact cellular schwannomatous component, the positive staining for S-100 protein, and the ultrastructural appearances clearly distinguish the present tumour from connective tissue myxoma.

GEORGE F KAAR
SAAD H BASHIR
JAMES M N'DOW
Department of Neurosurgery
PHILIP V BEST
Department of Pathology
LESLEY N GOMERSALL
Department of Radiology,
Aberdeen Royal Hospitals NHS Trust,
Aberdeen AB9 2ZB, UK

Correspondence to: Mr G F Kaar, Ward 40, Aberdeen Royal Infirmary, Foresterhill, Aberdeen AB9 2ZB, UK.



(a) Sagittal T2 weighted MR image (TR = 4500 ms, TE = 130 ms) showing tumour distorting the region of the conus (arrow). (b) Postgadodiamide injection T1 weighted MR image (TR = 450 ms, TE = 15 ms), showing tumour (black arrow) displacing conus (white arrow) anteriorly and laterally. (c) Photomicrograph (haematoxylin and eosin × 10) showing pale myxomatous nodules separated by narrow septa. (d) Photomicrograph (× 40) of the tumour stained with the immunoperoxidase method to demonstrate S-100 protein. Note the dark (positive) staining in nuclei and cytoplasmic strands.

1 Webb JN. The histogenesis of nerve sheath myxoma: report of a case with electron microscopy. *J Pathol* 1979;**127**:35–7.
2 Angervall L, Kindblom LG, Haglid K. Dermal nerve sheath myxoma. A light and electron microscopic, histochemical, and immunohistochemical study. *Cancer* 1984;**53**:1752–9.
3 Barnhill RL, Mihm MC Jr. Cellular neurothekeoma. A distinctive variant of neurothekeoma mimicking melanocytic tumours. *Am J Surg Pathol* 1990;**14**:113–5.
4 Paulus W, Jellinger K, Perneczky G. Intraspinal neurothekeoma (nerve sheath myxoma). A report of two cases. *Am J Clin Pathol* 1991;**95**:511–6.
5 Tahmouresie A, Farmer PM, Stokes N. Paraspinal myxoma with spinal cord compression. Case report. *J Neurosurg* 1981;**54**: 542–4.
6 Bell WO, Gill A, Babiak T, *et al.* Epidural myxoma causing compression of the cauda equina. Case report. *Neurosurgery* 1983;**12**: 325–6.
7 Pasaoglu A, Patiroglu TE, Orhon C, Yildizhan A. Cervical spinal intramedullary myxoma in childhood. Case report. *J Neurosurg* 1988;**69**:772–4.

Voluntary facial palsy with a pontine lesion

Emotional voluntary dissociation is not uncommon in patients with central facial palsies.[1-3] The neuroanatomical basis of this dissociation is not well understood. A recent case report in this *Journal* suggested that a pontine stroke could result in unilateral voluntary facial palsy.[4] We have recently had the opportunity to study a very similar syndrome.

A teacher aged 57 was referred three days after the onset of progressive neurological symptoms and signs that had included, in order, unsteadiness, dysarthria, dysphagia, and weakness of the right arm, leg, and face. On admission, the patient was awake, dysarthric but not aphasic, and had normal vision and oculomotor function. He complained of impaired swallowing and right facial weakness. Neurological examination disclosed a right central facial palsy for vol-

untary innervation. The patient could neither whistle nor smile on command. By contrast, the patient had normal emotional facial expression when smiling or laughing (fig 1). Voluntary and emotional innervation of the upper facial muscles were spared on either side, consistent with a central facial palsy. There was a prominent central hemiparesis of right arm and leg. Sensory examination was normal.

Brain MRI showed a single, semilunar lesion of the left pons that was hyperintense on T2 weighted images and hypointense on T1 weighted images (fig 2). The lesion was sharply delineated medially by the pontine raphe which was slightly bulged to the right due to mild oedematous swelling. The lateral border of the lesion was convex and reached the surface of the anterior brainstem, sparing the midpontine tegmentum. No additional cerebral lesions were detected. The involved area corresponds to the territory of the anteromedial and anterolateral group of the pontine arteries which are branches derived from the basilar artery. The localisation of the lesion is consistent with an affection of the corticonuclear and corticospinal tracts, pontine nuclei, and pontocerebellar fibres as well as the medial lemniscus on the midpontine level.

A voluntary unilateral facial palsy with intact emotional expression may result from lesions of the motor cortex or corticonuclear tract. An emotional facial palsy with preserved voluntary facial innervation has been associated with lesions in the basal ganglia, thalamus, temporal lobes, frontal white matter, or supplementary motor cortex.[3] Bilateral voluntary facial palsy with preserved emotional expression is typical of the Foix-Chavany-Marie anterior operculum syndrome.[5] The present study confirms that voluntary facial palsy can result from a pontine lesion[4] and seems to prove that the fibre tracts subserving voluntary and emotional facial innervation are still anatomically distinct in the upper pons—that is, just above the level of the motor facial nucleus.

The pathways for voluntary facial innervation are fairly well understood.[6,7] After preprocessing of the motor impulses—for example, within the basal ganglia and the thalamus, the executive pathway for voluntary facial movements projects from the lateral motor cortex (area 4) *via* the genu of the internal capsule and the cerebral peduncle to interneurons within the pontine motor facial nucleus which synapse on facial motor neurons. This corticonuclear pathway projects bilaterally to neurons that innervate periorbital and frontal muscles and mainly contralaterally to neurons innervating perioral and buccal muscles. As unilateral brain stem lesions in the upper pons cause contralateral voluntary facial paresis (this study and that of Töpper *et al*[4]) the level of crossing of corticonuclear fibres is probably just above or at the level of the motor facial nucleus.

The pathways for emotional innervation of the face are less clear. Reviewing the pertinent medical literature,[1,3] we conclude that probably all patients with unilateral emotional facial palsy had lesions in the *contralateral forebrain*. This excludes as possible pathways for emotional facial innervation those previously implicated which involve ipsilateral or bilateral projections and do not include thalamic and cortical centres: (*a*) from centromedial amygdala and bed nucleus of stria terminalis *via* stria terminalis or ventral amygdalofugal projection to hypothalamic preoptic region or mamillary nuclei, on to ipsilateral motor facial nucleus through the brain stem reticular formation *via* dorsal longitudinal fascicle or median forebrain bundle;[6,8-10] (*b*) directly from the amygdaloid complex to the lateral reticular formation in the ipsilateral pontine tegmentum, which in turn innervates the ipsilateral facial motor nucleus.[11-13] By contrast, we think that emotional facial innervation originates in the amygdaloid complex and associated limbic structures, travels through basal ganglia *via* the thalamus to the supplementary motor area or premotor cortex and from there, possibly partially *via* the *external* rather than internal capsule, to the contralateral motor facial nucleus.[14-16] This model is compatible with contralateral emotional facial palsy caused by lesions of the supplementary motor area, thalamus, external capsule, basal ganglia, rostromedial temporal lobe, and frontal lobe white matter,[3] as well as with isolated voluntary facial paresis after lesions of the contralateral motor cortex (area 4) or internal capsule.

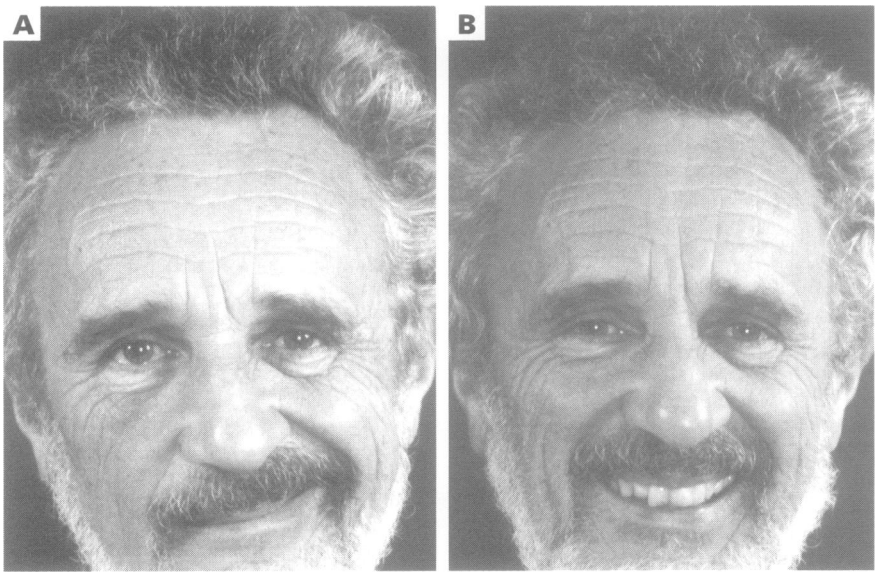


Figure 1 Dissociated right central facial palsy with preserved emotional innervation five days after the onset of symptoms. The patient exhibits voluntary facial palsy when trying to smile on command (left) but has normal innervation on involuntary laughing (right) (with permission).

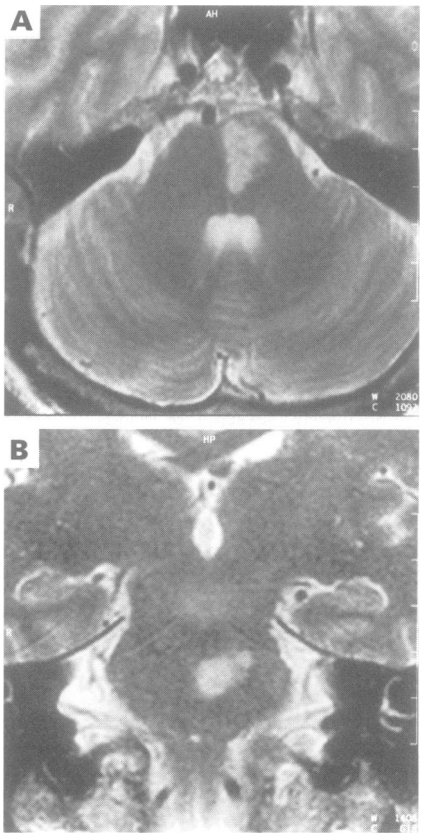


Figure 2 Detection of a single left paramedian midpontine ischaemic lesion by MRI (1·5 Tesla, fast spin echo sequence) four days after the onset of symptoms. (A) axial T2 weighted images (TR/TE 3000/85 ms); (B) coronal T2 weighted images (TR/TE 3000/85 ms).

MARTIN TREPEL
MICHAEL WELLER
JOHANNES DICHGANS
Department of Neurology
DIRK PETERSEN
Department of Neuroradiology,
University of Tübingen, Medical School,
Tübingen, Germany

1 Monrad-Krohn GH. On the dissociation of voluntary and emotional innervation in facial paresis of central origin. *Brain* 1924;**47**: 22–35.
2 Karnosh LJ. Amimia or emotional paralysis of the face. *Diseases of the Nervous System* 1945; **6**:106–8.
3 Hopf HC, Müller-Forell W, Hopf NJ. Localization of emotional and volitional facial paresis. *Neurology* 1992;**42**:1918–23.
4 Töpper R, Kosinski C, Mull M. Volitional type of facial palsy associated with pontine ischaemia. *J Neurol Neurosurg Psychiatry* 1995;**58**:732–4.
5 Weller M. Anterior opercular cortex lesions cause dissociated lower cranial nerve palsies and anarthria but no aphasia: Foix-Chavany-Marie syndrome and "automatic voluntary dissociation" revisited. *J Neurol* 1993;**240**: 199–208.
6 Brodal A. *Neurological anatomy in relation to clinical medicine.* New York: Oxford University Press, 1981:498;733.
7 Jenny AB, Saper CB. Organization of the facial nucleus and corticofacial projection in the monkey: a reconsideration of the upper motor neuron palsy. *Neurology* 1987;**37**: 930–9.
8 De Olmos JS. Amygdala. In Paxinos G, ed. *The human nervous system.* San Diego: Academic Press, 1990:583–710.
9 Heimer L. *The human brain and spinal cord.* New York: Springer, 1995.
10 Holstege G. Some anatomical observations on the projections from the hypothalamus to brain stem and spinal cord: an HRP and autoradiographic tracing study in the cat. *J Comp Neurol* 1987;**260**:98–126.
11 Hopkins DA, Holstege G. Amygdaloid projections to the mesencephalon, pons and

medulla oblongata in the cat. *Exp Brain Res* 1978;**32**:529–47.
12 Price JL, Amaral DG. An autoradiographic study of the projections of the central nucleus of the monkey amygdala. *J Neurosci* 1981;**1**:1242–59.
13 Isokawa-Akesson M, Komisaruk BR. Difference in projections to the lateral and medial facial nucleus: anatomically separate pathways for rhythmical vibrissa movement in rats. *Exp Brain Res* 1987;**65**:385–98.
14 Kuypers HGJM. Corticobulbar connections to the pons and lower brain stem in man. An anatomical study. *Brain* 1958;**81**:364–88.
15 Russchen FT, Bakst I, Amaral DG, Price JL. The amygdalostriatal projections in the monkey. An anterograde tracing study. *Brain Res* 1985;**329**:1242–59.
16 Graybiel AM. The basal ganglia and the initiation of movement. *Rev Neurol* 1990;**146**: 570–74.

Brainstem involvement in Leber's hereditary optic neuropathy: association with the 14 484 mitochondrial DNA mutation

Leber's hereditary optic neuropathy (LHON) is a maternally inherited disease leading to severe bilateral visual loss. It has recently been associated with several mitochondrial DNA (mtDNA) point mutations. Three major primary pathogenic mutations are located at nucleotide positions 11 778, 3460, and 14 484. Whether two other mutations at positions 4160 and 15 257 are primary pathogenic mutations remains controversial.[1]

An association between LHON and various other neurological diseases has long been suggested. However, non-fortuitous combinations of neurological disorders and genetically established LHON seem to be rare. Most of them are cases of "multiple sclerosis-like" illness in patients with LHON with the 11 778 or 3460 mtDNA mutations.[2] We report a case of brainstem involvement in a patient with LHON harbouring the 14 484 mtDNA mutation, and none of the other above mentioned mutations.

A 30 year old man (IV-5) had a strong family history of LHON. This disease was diagnosed by academic ophthalmologists in six other members of his family (fig 1). Four of them (III.2, III.4, III.5, IV.3) were young at onset (9 to 14 years of age) and had good recovery of vision. None had a neurological complaint. Patients III.4 and IV.1 were personally seen: neurological examination and brain MRI were normal in both.

At the age of four years, the patient had bilateral visual loss, which never recovered. At the age of 16, he had vertigo, dizziness, and vomiting that were diagnosed as "central vestibular disorder" at the local hospital. Symptoms resolved spontaneously, but recurred 10 years later. In April 1992, he experienced difficulty in looking down, progressing over 48 hours. Vertical gaze palsy was noted by local neurologists. Cranial CT was normal. The diagnosis of multiple sclerosis was suspected and the patient received intravenous methylprednisolone, with no benefit. He was admitted to our department in July 1992. Visual acuity was 1/10 OD and 4/10 OS. There was bilateral optic atrophy. He had a combined vertical gaze ophthalmoplegia, bilateral eyelid ptosis, and bilateral gaze evoked nystagmus. His neurological examination was otherwise normal.

Brain MRI showed a symmetric area of increased signal on T2 weighted images in the dorsal midbrain (fig 2), and no other abnormalities. Brainstem auditory evoked potentials (BAEPs) and somatosensory evoked potentials were normal. Results from analysis of CSF were normal. Standard blood tests showed a mild previously known increase in liver function. Because of a past transient drug addiction, viral serological tests were performed and were negative for hepatitis B and HIV, but positive for hepatitis C. Serum thiamine concentration was normal.

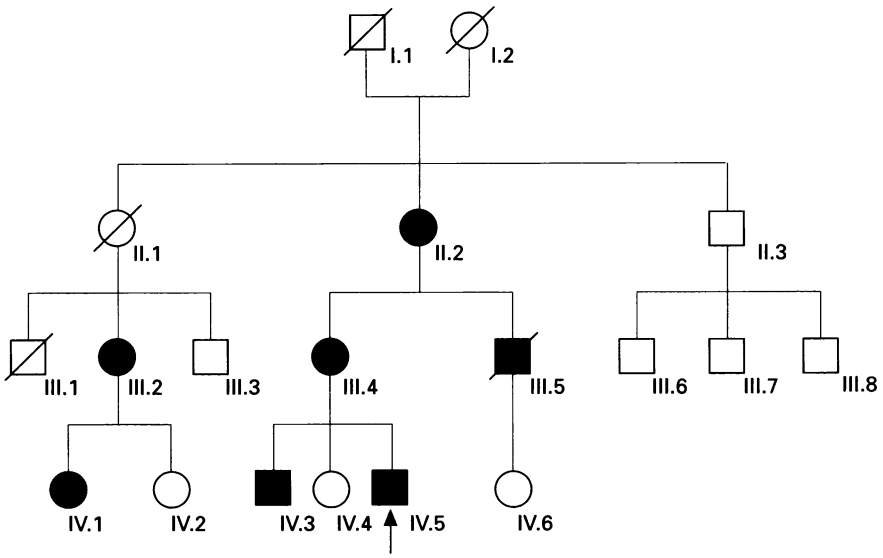


Figure 1 Pedigree of the LHON family, showing a clear maternal transmission of the optic neuropathy. Circle = female; square = male; oblique lines = deceased; filled symbols = affected; open symbols = unaffected; arrow = patient.

In September 1992 and January 1993, he had subacute worsening of his symptoms, leading eventually to global gaze palsy and bilateral tinnitus. The brainstem lesion was larger on MRI (fig 2). His BAEPs showed prolongation of the I-III interpeak interval. Other investigations were normal. During the subsequent months, symptoms improved spontaneously. In January 1994, he complained of stiffness of both legs. On examination, he had a moderate spastic ataxia. Tendon reflexes were very brisk in all limbs and there was bilateral ankle clonus. Plantar responses were flexor. He still had combined vertical gaze ophthalmoplegia. Brain MRI showed a pronounced decrease in the size of the brainstem lesion. Results from cervical and dorsal spinal cord MRI were normal. Again, symptoms improved progressively, and six months later ataxia had partly resolved, tinnitus had almost disappeared, and ophthalmoplegia was limited to a downgaze paresis. One year later, clinical features and brain MRI were unchanged.

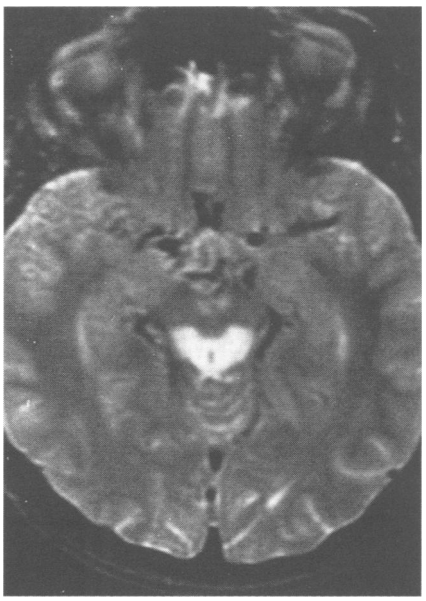


Figure 2 Axial T2 weighted MRI, showing a symmetric lesion of the dorsal midbrain (maximum size, January 1993).

DNA was extracted from venous blood by standard techniques and analysed for the mtDNA mutations at positions 3460, 4160, 11 778, and 15 257 using the polymerase chain reaction (PCR) and restriction endonuclease digestion, as previously described.[3] The T to C mutation at position 14 484 was detected using PCR amplification of a 115 bp segment spanning the mutation site, with oligonucleotide primers 14 390–14 419 (forward) and 14 513–14 486 (reverse). The reverse primer was modified by introduction of a mismatch (substitution of A for C at position 14 487) in the wild type sequence. This creates a restriction site for Bsr I in mutant mtDNA. The patient harboured the 14 484 mutation and was heteroplasmic for it (~70% of mutant mtDNA). He did not harbour any of the four other mutations. Members III.4 and IV.1 were tested for the 14 484 mutation. They were also heteroplasmic (~70% of mutant mtDNA in both).

In the present family, four of the seven affected members had a young age of onset and good recovery of vision, whereas three did not recover. A good recovery of vision has often been reported in patients with LHON harbouring the 14 484 mutation.[1] It seems to be strongly correlated with an early age of onset and not with the degree of heteroplasmy in affected members. Paradoxically, our patient had the earliest age of onset but did not recover. He was the only one that experienced symptoms of CNS involvement. In fact, it is the first time that the 14 484 mutation has been unequivocally associated with CNS involvement in a patient with LHON, although this mutation has already been reported in an LHON pedigree with neurological features. A large