Queensland LHON family was found to harbour two mtDNA mutations, at positions 14 484 and 4160 (the second being found in this family only). Many family members were affected by a severe neurological disorder, which has not been reported in any other family with LHON until now. To date, the neurological disorder in the Queensland family seems to be related to the presence of the 4160 mutation. The 14 484 mutation is likely to be the cause of the optic neuropathy in this kindred.

The nature of the midbrain lesion found in our patient remains hypothetical. In most cases, patients with LHON and CNS involvement are females affected by a multiple sclerosis-like illness. In our patient, some of the clinical features (global paralysis of gaze, tininnitus), MRI, BAEP, and CSF findings do not support the diagnosis of multiple sclerosis. Involvement of the CNS can occur in drug addicts, but it has never been reported in patients that had stopped taking drugs for years. Hepatitis C infection has not been associated with this kind of brainstem lesion until now. Interestingly, a very similar lesion of the dorsal midbrain has been reported in a German patient with LHON. This male patient had vertical gaze ophthalmoplegia and oculopupillary mydriasis, and harboured the 3460 mtDNA mutation. The brainstem lesion also decreased on successive MRI. The clinical and MRI features shared by this patient and ours suggest the existence of a separate type of CNS involvement in LHON, characterised by clinical symptoms of brainstem involvement (in particular, supranuclear ophthalmoplegia) and a dorsal midbrain lesion on MRI.

We are grateful to Dr Eric Méary for his help in the preparation of the manuscript.

BENOIT FUNALOT
DANIELE RANOUX
JEAN-LOUIS MAS
Service de Neurologie, Hôpital Sainte-Anne, Paris
CHRISTINE GARCIA
JEAN-PAUL BONNEFONT
Laboratoire de Génétique Moléculaire et Unité Inserm 393, Hôpital Neuro-Enfants Maladies, Paris

Correspondence to: Professor J-L. Mas, Service de Neurologie, Hôpital Sainte-Anne, 1 Rue Cabanis, 75674 Paris Cedex 14, France.

1 Riordan-Eva P, Harding AE. Leber's hereditary optic neuropathy: the clinical relevance of different mitochondrial DNA mutations. Med Genet 1995;32:81-7.
2 Riordan-Eva P, Bell S, Kerswill MD, Govan GG, Sweezy MG, Da Costa J, Harding AE. The clinical features of Leber's hereditary optic neuropathy defined by the presence of a pathogenic mitochondrial DNA mutation. Brain 1995;118:319-37.
3 Johns DR, Neufeld MJ. Pitfalls in the molecular genetic diagnosis of Leber hereditary optic neuropathy (LHON). Am J Hum Genet 1993;53:916-20.
4 Howell N, Kובאָكا I, Xu M, McCullough DA. Leber hereditary optic neuropathy: involvement of the mitochondrial ND1 gene and evidence for an intragenic suppressor mutation. Am J Hum Genet 1991;48:935-42.
5 Pausis W, Straube A, Bauer W, Harding AE. Central nervous system involvement in Leber's optic neuropathy. J Neurol 1993;240:251-3.

Pure sensory deficit with crossed oro-crural topography after pontine haemorrhage

Sensory deficits involving one half of the body and restricted to the hand and mouth region or the face are unusual clinical findings associated with contralateral lacunes. or haemorrhages in the pontine tegmentum. We describe the first case of pontine stroke leading to pure sensory deficit with crossed distribution reminiscent of the sensory pattern occurring with Wallenberg's lateral medullary syndrome. A 71 year old man with a history of hypertension and diagnosed as having Charcot-Marie-Tooth disease, suddenly experienced left frontal headache, vomiting, and numbness on the left side of the tongue and peribuccal area, followed by a tingling sensation over the right leg. On admission, there was no weakness of the limbs or ataxia, and cranial nerve palsy was not present. Pain and temperature sensations were diminished on the left side of the tongue and lips, and were abolished on the right side of the body below T12. Response to tactile stimulation and vibration was slightly disturbed on the right leg, but position sense was spared. Brain MRI performed two weeks after the onset of symptoms showed a lesion of high intensity in the left pontine tegmentum on both T1 and T2 weighted images (figure A), the upper part of the medulla being spared. The somatosensory evoked potentials were normal on both sides after median nerve stimulation, and showed symmetric normal latencies with significantly reduced amplitudes when stimulating the posterior tibial nerves (findings considered compatible with Charcot-Marie-Tooth disease). Brainstem auditory evoked potentials and blink reflex studies were normal.

Nine months later, the numbness in the tongue and lips on the left side had gradually reduced, but continuous burning dysesthesia in the right lower limb persisted. The left intraoral and perioral sensory loss had resolved; a considerable decrease in pain and temperature sensations remained in the lower abdomen and leg on the right side, but tactile and proprioceptive sensations were preserved. At this time, T1 and T2 weighted MRI showed pronounced hypointensity in the left lateral pontine tegmentum reflecting haemosiderin deposition (figure B), and no cryptic vascular malformation was detected.

What is most conspicuous in this case is the presence of trigeminal sensory changes ipsilateral to the pontine haemorrhage accompanied by abnormal sensation in the contralateral lower limb. A similar crossed sensory pattern occurs, although not isolated but in combination with other neurological dysfunction, after vascular lesions in the lateral aspect of the pons and medulla. It is noticeable that our patient showed decreased pinprick and temperature sensations without impaired vibration or position senses in a crural distribution. This restricted sensory deficit presumably occurred as the result of damage to the lateral side of the spinothalamic tract where the leg representation area is situated, whereas sensory fibres from the arm are most medi- ally projected. Our patient also had dysaes- thesia and diminished intraoral perception of pinprick sparing facial sensation. The pres- ent case is consistent with the clinical find- ings of Graham et al suggesting that the rostral spinal trigeminal nucleus in thepons

Figure (A) T1 weighted MRI on day 14 shows high signal intensity suggestive of a subacute haemorrhage in the left dorsolateral tegmentum of the middle pons. (B) T2 weighted MRI nine months later shows abnormally decreased signal intensity corresponding to old haemorrhage. (C) Diagram showing the area clinically affected (shaded area). STN = Spinal trigeminal nucleus; STH = spinohalothamic tract; VTT = trigeminothalamic tract; ML = medial lemniscus; CTLS = cervical (C), thoracic (T), lumbar (L), and sacral (S) levels.
plays a major part in the perception of intra-or- oral sensation, whereas facial sensation projects to the medullary portion of this nucleus.

As our case indicates, a small lesion at the lateral pontine tegmentum can cause a pure and crossed oculorossal sensory deficit, by involvement of the rostral spinal trigeminal nucleus and the lateral side of the spinohala- mic tract, where the respective sensory fibres from the mouth and the lower part of the face are immediately adjacent (figure, C).

Correspondence to: Dr O Combarros, Service of Neurology, University Hospital “Marqués de Valdecilla”, Santander, Spain.

1 Shintani S, Tsuuraoka S, Shigai T. Pure sensory stroke caused by a pontine infarct. Clinical, radiological, and physiological features in four patients. Stroke 1994;25: 1512–15.

2 Bassetti C, Bogousslavsky J, Barth A, Regli F. Isolated infarts of the pons. Neurology 1996; 46:165–73.

3 Holtzman RN, Zablocki V, Yang WC, Leeds NE. Lateral pontine tegmental haemorrhage presenting as isolated trigeminal sensory neuropathy. Neurology 1997;37:704–6.

4 Matsumoto S, Okuda B, Imai T, Karneyama M. A sensory level on the trunk in lower lat- teral brainstem lesions. Neurology 1998;38: 1515–19.

5 Graham SH, Sharp FR, Dillon W. Intraoral sensation in patients with brainstem lesions: role of the rostral spinal trigeminal nuclei in pons. Neurology 1988;38:1529–33.

Hereditary neuropathy with liability to pressure palsies with a partial deletion of the region often duplicated in Charcot-Marie-Tooth disease, type 1A

Hereditary neuropathy with liability to pres- sure palsies (HNPP) is an autosomal domi- nant disorder characterised by recurrent peripheral nerve palsies, paraesthesiae, and less often by a prominent symmetric polyneuropathy. Nerve biopsies show thick- enings of myelin called tomaculae. Chance et al1 found such patients to have a large chromosomal deletion located in this region as in Charcot-Marie-Tooth disease (CMT) neuropathy, type 1A. This region contains a gene for peripheral myelin protein 22 (PMP22). The role of this gene in the pathogenesis of HNPP has been shown by the discovery of a frame shift mutation cre- ating a null mutation and resulting in the HNPP phenotype.2 In the case of deletion/ duplication, a gene dosage effect has been proposed.3 In a family affected with HNPP, we found a deletion at locus D17S122 including the PMP22 gene and sparing distal loci (D17S61 and D17S125), hence confirming the expectation that deletion of a smaller region than that previously described, but including PMP22, is capable of causing HNPP, and therefore supporting the role of PMP22 in HNPP.

Patient I.1 developed leg weakness at the age of 30. Since the age of 26, he had noticed episodes of paraesthesiae on multiple nerve trunks, at first transient, then lasting and needing several surgical decompres- sions. At the age of 58, he had bilateral pes cavus, distal weakness, severe muscle atrophy, and areflexia in the lower limbs with normal paraesthesiae and cramps; sensory examina- tion showed hypoaesthesia in the left per- oneal nerve territory. In the upper limbs, only muscle atrophy and mild weakness of interosseous muscles were noted. All tendon reflexes were absent. Motor nerve conduc- tion velocities (MNCVs) were severely slowed in median nerves (42 m/s on the right and 40 m/s on the left) and radically altered in the ulnar nerves (32 m/s on the right and 24 m/s on the left at the elbow). A nerve biopsy showed severe loss of myelinated fibres, some having an othothen myelin sheet. Rare onion bulbs were present. Tomaculae were found in 7% of the 300 internodes studied on teased fibres.

Hereditary neuropathy with liability to pressure palsies (HNPP) is an autosomal dominant disorder characterised by recurrent peripheral nerve palsies, paraesthesiae, and less often by a prominent symmetric polyneuropathy. Nerve biopsies show thickenings of myelin called tomaculae. Chance et al1 found such patients to have a large chromosomal deletion located in this region as in Charcot-Marie-Tooth disease (CMT) neuropathy, type 1A. This region contains a gene for peripheral myelin protein 22 (PMP22). The role of this gene in the pathogenesis of HNPP has been shown by the discovery of a frame shift mutation creating a null mutation and resulting in the HNPP phenotype.2 In the case of deletion/duplication, a gene dosage effect has been proposed.3 In a family affected with HNPP, we found a deletion at locus D17S122 including the PMP22 gene and sparing distal loci (D17S61 and D17S125), hence confirming the expectation that deletion of a smaller region than that previously described, but including PMP22, is capable of causing HNPP, and therefore supporting the role of PMP22 in HNPP.

Patient I.1 developed leg weakness at the age of 30. Since the age of 26, he had noticed episodes of paraesthesiae on multiple nerve trunks, at first transient, then lasting and needing several surgical decompres- sions. At the age of 58, he had bilateral pes cavus, distal weakness, severe muscle atrophy, and areflexia in the lower limbs with normal paraesthesiae and cramps; sensory examina- tion showed hypoaesthesia in the left per- oneal nerve territory. In the upper limbs, only muscle atrophy and mild weakness of interosseous muscles were noted. All tendon reflexes were absent. Motor nerve conduc- tion velocities (MNCVs) were severely slowed in median nerves (42 m/s on the right and 40 m/s on the left) and radically altered in the ulnar nerves (32 m/s on the right and 24 m/s on the left at the elbow). A nerve biopsy showed severe loss of myelinated fibres, some having an othothen myelin sheet. Rare onion bulbs were present. Tomaculae were found in 7% of the 300 internodes studied on teased fibres.

His daughter (patient II.1), had presented since the age of 26 with paraesthesiae and episodes of weakness of one or two weeks' duration in the peroneal, ulnar, or median nerve territories. At the age of 27, she had pes cavus, severe peroneal muscle atrophy, weakness, and distal extraluminal and par- tially lemniscal sensory impairment in the lower limbs. Mild sensory impairment was noticed in the left ulnar and median nerve distribution. Tendon reflexes were all absent. In the upper limbs, MNCVs were normal in 1990, but in 1995 a bilateral entrapment of the ulnar nerve at the elbow and a left carpal tunnel syndrome were diagnosed. In skin cross sections of the sural nerve a slightly reduced large myelinated fibre density, tomaculae, and lesions of remyelination. All the teased fibres presented features of tomaculae and of demyelination and remyelination. Tomaculae were found in 39% of the internodes.

Molecular genetic studies were carried out for both patients by southern blotting analy- sis (figure, A) and pulsed field gel elec- trophoresis (PFGE) (figure, B).

Probe pVAW409R3a (D17S122) dis- closed only one band for both patients whereas probes pBW401HE (D17S61) and pVAW412R3HEc (D17S125) were heterozygous for the second patient. Density scanning showed the presence of a single pVAW409R3a allele in both patients, and the presence of two alleles for the other probes in the first patient. The same tech- nique showed only one copy of the PMP22 gene in the patients (not shown).

In PFGE analysis, hybridisation of Eagl- digested DNA with CMT1A-REP probes usually detects deletion and duplication junction fragments in HNPP and CMT1A, respectively.4 No such junction fragments were found for our patients with HNPP.