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, tinnitus, 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 palsy, homonymous hemianopsia, and ocular扑lal myoclonus, 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 Mearé for his help in the preparation of the manuscript.

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Pure sensory deficit with crossed orocrural 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 consistent 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 dysaesthesia 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 senses 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 medially projected. Our patient also had dysaesthesia and diminished intraoral perception of pinprick sparing facial sensation. The present case is consistent with the clinical findings of Graham et al suggesting that the rostral spinal trigeminal nucleus in the pons...
plays a major part in the perception of introral 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 orocural sensory deficit, by involvement of the rostral spinal trigeminal nucleus and the lateral side of the spinthalamic tract, where the respective sensory fibres from the mouth and the lower part of the body are immediately adjacent (figure, C).

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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 pressure palsies (HNPP) is an autosomal dominant disorder characterised by recurrent peripheral nerve palsies, paraesthesiae, and less often by a prominent symmetric polynuropathy. Nerve biopsies show thickening of myelin called tomaculae. Chance et al 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. In the case of deletion/duplication, a gene dosage effect has been proposed.

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 decompressions. At the age of 58, he had bilateral pes cavus, distal weakness, severe muscle atrophy, and asestheic insensate areas with transient paraesthesiae and cramps; sensory examination showed hypoaesthesia in the left peroneal nerve territory. In the upper limbs, only muscle atrophy and mild weakness of interosseous muscles were noted. All tendon reflexes were absent. Motor nerve conduction 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 overthin myelin sheet. Rare onion bulbs were present. Tomaculae were found in 7% of the 300 interneurones 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 extraneuronal and partial 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 present. Further thinning in transverse sections of the sural nerve showed a slightly reduced large myelinated fibre density, tomaculae, and lesions of remyelination. All the teased fibres presented features of demyelination and demyelination. Tomaculae were found in 39% of the interneurones.

Molecular genetic studies were carried out for both patients by southern blotting analysis (figure, A) and pulsed field gel electrophoresis (PFGE) (figure, B). Probe pVAW4099R3a (D17S122) disclosed only one band for both patients whereas probes pEW401HE (D17S61) and pVAW412R3HEc (D17S125) were heterozygous for the second patient. Density scanning showed the presence of a single pVAW4099R3a allele in both patients, and the presence of two alleles for the other probes in the first patient. The same technique showed only one copy of the PMP22 gene in the patients (not shown).

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