Neurologist-in-training

The aim of this section is to prepare the neurologist-in-training for the FMH examination, to confront her or him with specific problems of everyday neurological practice and to give him or her updates on recent controversies in clinical neurology.

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Neurological MCQ

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Select the one correct answer.

1 Select the correct statement regarding optic neuritis:

A Long-term incidence of multiple sclerosis is decreased if optic neuritis is treated with corticosteroids.
B Long-term incidence of multiple sclerosis is decreased if certain beta-interferons are given after optic neuritis in patients with asymptomatic lesions on brain MRI.
C Optic neuritis is usually painless.
D Optic disc shows oedema or inflammation in most patients with acute optic neuritis.
E Long-term visual acuity is better if optic neuritis is treated with corticosteroids.

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2 Which statement is wrong about neuro-ophthalmological findings?

A Lisch nodules are only seen in patients with neurofibromatosis.
B Kayser-Fleischer ring is detected equally well by visual inspection of the conjunctiva as by slit-lamp biomicroscopy.
C Pigmentary retinopathy is associated with mitochondrial disease, ceroid lipofuscinosis and abetalipoproteinaemia.
D Arterialisation of the conjunctival veins is characteristic of arteriovenous fistulas involving the cavernous sinus.
E Choroid haemangiomas and leptomeningeal angiomas are usually ipsilateral to the naevus flammeus in Sturge-Weber syndrome.

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3 Which statement is true about Horner's syndrome?

A Is usually due to a Pancoast's tumour.
B Visual acuity is decreased on the side of the Horner's syndrome.
C If the lesion is central, it is usually contralateral to the Horner's syndrome.
D Anisocoria is more pronounced in the dark.
E In the absence of anhidrosis the lesion is always peripheral.

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4 All of the following are seen in narcolepsy except:

A Prolonged night-sleep duration
B Hallucinations that may occur while falling asleep or when awakening
C Disturbed nocturnal sleep (such as sleep walking)
D Automatic behaviours
E Twitching of limbs or face, resembling epileptic seizures

5 Daytime sleepiness is associated with all of the following except:

A obstructive sleep apnoea
B periodic limb movement disorder
C insomnia associated with anxiety
D narcolepsy-cataplexy
E circadian rhythm disorders

6 What is wrong regarding the treatment of insomnia?

A Some SSRIs may increase insomnia.
B Melatonin has been shown to be effective in controlled trials for jet lag.
C Stimulus control should be tried as a standard therapy.
D Sleep restriction has been shown to be effective in controlled trials.
E Cognitive interventions are clearly more effective than pharmacological interventions.

(For correct answers, see page 370)

References

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Neuroradiology/Neuroanatomy

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This 55-year-old patient with a congenital scoliosis and chronic skin lesions developed over 8 months gait problems, distal leg paraesthesias and loss of erections. On neurological examination he can still walk despite a spastic paraparesis. There is a Th-10 sensory level.

Figure 1: bony reconstructions of the thoracic CT, showing severe lower thoracic scoliosis. Figures 2 and 3: thoracic spinal MRI, showing a pathology (P) on the height of thoracic vertebrae 9 and 10.

Describe the anatomical structures (A–C) and the mass (P).

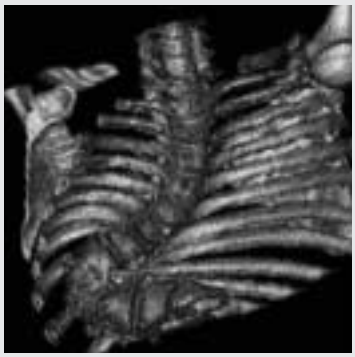

Figure 1

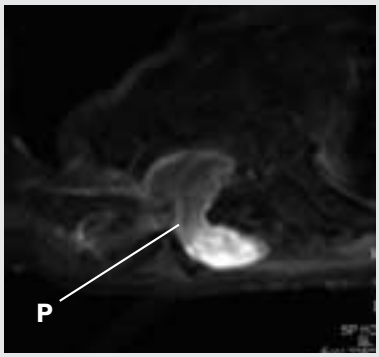

Figure 2

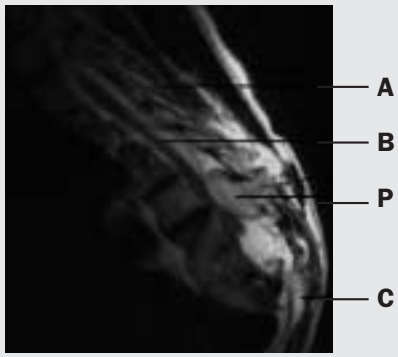

Figure 3

(For correct answers, see page 370)

Read for you

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Parkinson's disease and levodopa therapy

This double-blind randomised placebo-controlled study was designed to address the issue of levodopa neurotoxicity in Parkinson's disease (PD) patients. The primary outcome was the change in parkinsonism severity measured by total unified Parkinson's disease rating scale (UPDRS). 361 PD patients were randomised to receive either placebo or levodopa at 3 different dosages for 40 weeks. A subset of patients underwent [^{123}I]β-CIT SPECT scans.

At the end of the study, after a washout period, severity of parkinsonism had increased significantly more in the placebo group than in patients on levodopa. During treatment there was a dose-dependent improvement in parkinsonism in the levodopa group. The mean decrease in striatal [^{123}I]β-CIT uptake was greater among subjects on levodopa.

These results do not support a neurotoxic effect of levodopa. Persistence of a significant difference after the washout period even suggests that levodopa might be neuroprotective. One can argue that the washout period was too short (2 weeks), but no further worsening of UPDRS was found in a subset of 38 patients in whom it was extended to 4 weeks. The SPECT data are difficult to correlate with the clinical results, as they would suggest a neurotoxic effect of levodopa. Therefore, the clinical and radiological data seem contradictory and further nourish the debate on the role of imaging techniques in Parkinson's disease.

There is another interesting aspect to this study: it is the first randomised controlled study of levodopa despite the fact that levodopa has been prescribed for over 30 years and remains the most effective and most frequently prescribed treatment for Parkinson's disease. It convincingly demonstrates – if necessary – a strong dose-dependent symptomatic effect.

Reference

1 Levodopa and the progression of Parkinson's disease. The Parkinson study group. N Engl J Med 2004;351:2498–508.

Parkinson's disease genetics – two new genes in 2004

PARK6 – PINK1

The locus named PARK6 has already been described by linkage in a very rare form of recessively inherited early onset Parkinson's disease, but Valente et al. found two homozygous mutations affecting the PTEN-induced putative kinase 1 (PINK1) domain in three consanguineous families, two from Italy and one from Spain. Cell culture studies suggest that PINK1 may exert a protective effect on the cell, abrogated by the mutations, resulting in increased susceptibility to cellular stress.

PARK8 – LRRK2

Another gene was cloned by two different groups and the results published together, with missense mutations segregating with PARK8 locus, known to cause dominantly inherited typical levodopa-responsive Parkinson's disease phenotype.

In the work by Paizan-Ruiz et al. two mutations were identified in the gene coding for a protein the authors named *dardarin* (from the Basque word for tremor). Although the precise role of *dardarin* is unknown, it could be involved in the phosphorylation of central proteins. After this paper, the name PARK8 was abandoned and the gene renamed LRRK2 (leucine-rich repeat kinase 2). This paper is very exciting in that mutations in the new gene LRRK2 encoding *dardarin* could be implicated not only in familial Parkinson's disease but also in its "sporadic form", first because they were found in a substantial number of patients unrelated to the five families studied (although a founder effect is possible since all patients were of Basque origin), and second because the maximum onset was 79 years, raising the possibility of underestimating the "familiality" of the disease, since patients might die before symptoms' onset.

In the work by Zimprich et al. two large families with dominantly inherited late-onset Parkinson's disease with linkage to the PARK8 locus were shown to bear mutations in the LRRK2 gene.

In family D, all patients were heterogygous, and two presymptomatic subjects were found (mutation carriers, but without Parkinson's disease phenotype). The authors identified six independent mutations in 34 families with dominantly inherited Parkinson's disease. The striking pathologic heterogenicity suggests a central role of LRRK2 in neurodegeneration. Potentially, LRRK2 may be responsible for the phosphorylation of both α-synuclein and tau, and its kinase activity could be a crucial event in the accumulation and aggregation of these unfolded proteins within degenerating neurons.

References

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Neurologist-in-training

Answers to MCQ

1 B **2** B **3** D **4** A **5** C **6** E

Answers to Neuroradiology/Neuroanatomy

A Processus spinosus
B Spinal cord (thoracic level)
C Thecal sac (containing cauda equalis)
P Neurofibroma with dumbbell (hourglass) shape

Comment

This patient was already diagnosed in his teens with neurofibromatosis type 1 (NF-1, von Recklinghausen's disease) because of familial occurrence (paternal grandfather, father, both sons), skin neurofibromas and café-au-lait spots. He did not have Lisch nodules (iris hamartomas), freckling in the axillary or inguinal regions, nor optic gliomas. NF-1 constitutes 90% of all types of the neurofibromatoses. Skeletal abnormalities, such as craniofacial bone (sphenoid) dysplasia and thinning of long-bone cortex with or without pseudoarthrosis, are well known in NF-1. Less frequently, there is short stature, macrocephaly, gigantism of digits, hands or extremities, or scoliosis, as seen in this patient. NF-1 is also associated with a tendency to develop certain types of central and peripheral nervous system tumours, including optic pathway gliomas, brainstem and spinal gliomas, cerebellar astroglial tumours, benign or malignant schwannomas, and neurofibrosarcomas. There is also an increased incidence of non-neural tumours like pheochromocytoma, carcinoid, and adenocarcinoma of the duodenum.

Although clinically one may think that this patient's severe scoliosis (fig. 1) could be at the origin of a spinal cord syndrome, it was rather a thoracic neurofibroma that compressed the lower thoracic cord (fig. 3, high-intensity signal in the cord at the site of compression). This neurofibroma also grew through the intervertebral foramen to take a dumbbell (hourglass) shape, characteristic of neurofibromas of the spine. The patient underwent lower thoracic laminectomy and resection of the neurofibroma and recovered well. On histology some malignant cells were found, classifying the lesion as a neurofibrosarcoma.

References

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