

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

A 35-year-old woman with a 3-day history of subacute blurry vision and pain in the right eye also complained of impaired colour vision. The patient has suffered from migraine without aura since the age of 15 years. The clinical workup revealed a visual acuity of 0.4 in the right eye and 1.0 in the left eye. The ophthalmologist suspected optic neuritis and referred the patient to you. Brain MRI was normal. Lumbar puncture produced a cell count of 14 cells per mcl with normal total protein and without CSF-specific oligoclonal bands.

Questions

1. Which of the following MRI sequences is most appropriate to substantiate the diagnosis of optic neuritis?

(Abbreviations: PD: proton density; STIR: short-tau inversion recovery; FLAIR: Fluid-attenuated inversion recovery)

- A Axial PD
- B Axial T2
- C Coronal STIR
- D Sagittal FLAIR

2. Which of the following clinical findings is most suggestive of optic neuritis?

- A Anisocoria
- B Irregular shape of the pupil
- C Pathological swinging flash-light test
- D Pupillotonia

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3. What is the 15-year risk of developing MS after optic neuritis if brain MRI showed one or more lesions suggestive of MS?

- A 10%
- B 30%
- C 50%
- D 70%

4. Which of the following compounds is currently not licensed in patients with Clinically Isolated Syndrome in Switzerland?

- A Interferon Beta 1a
- B Interferon Beta 1b
- C Glatiramer acetate
- D Fingolimod

5. What is the lifelong risk of MS for the offspring if one parent has MS? What is the best answer?

- A 1–5%
- B 10–15%
- C 20–25%
- D 30–35%

6. Over the course of several months our patient's visual acuity did not improve. Six months after optic neuritis the patient developed numbness in both arms and a sensory level at Th4. MRI of the spinal cord is shown in figure 1. What would be the best next diagnostic step?

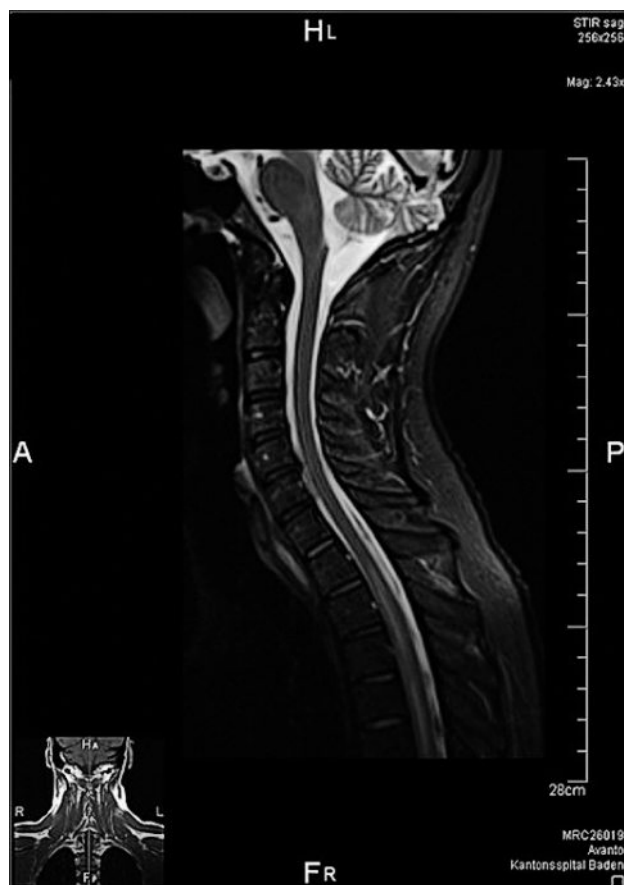
- A Transbronchial lung biopsy
- B Anti-NMO antibodies in serum
- C Borrelia IgG and IgM in serum
- D Treponema pallidum haemoagglutination test in serum

7. Based on this MRI (fig. 1), what is the best next therapeutic step?

- A Natalizumab
- B Glatiramer acetate
- C Azathioprine
- D Fingolimod

Figure 1

Sagittal MRI of the spinal cord after a new episode of numbness in both legs and sensory level at Th4.



Answers and comments

Answer 1: Coronal STIR (C)

Intraorbital fat-suppressing coronal short-tau inversion recovery sequences (STIR) is sensitive for the detection of optic neuritis (fig. 2). Periventricular lesions are best identified on FLAIR images because intraventricular CSF is attenuated and hypointense in this sequence, producing a strong contrast between lesion and surrounding structures.

Answer 2: Pathological swinging flash-light test (C)

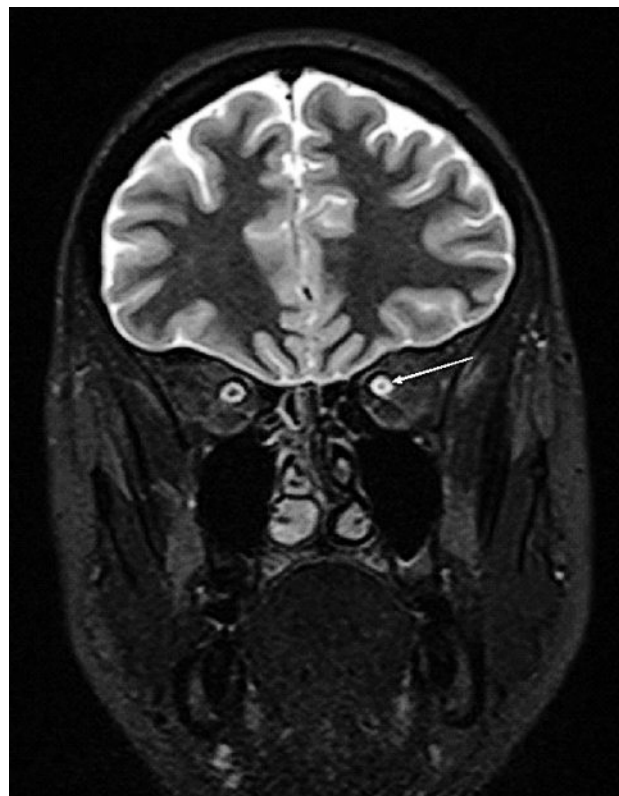
Anisocoria is not typical of optic neuritis. Irregular shape is found in Argyll Robertson pupil. The Argyll Robertson pupil, typically seen in neurosyphilis and rarely in MS, is a small pupil, often of irregular shape, that constricts poorly to direct light but briskly on accommodation (light-near dissociation). Pupillotonia is the most common pupil abnormality and in most cases a benign finding. The lesion is in the ciliary ganglion. The swinging flash-light test is the most important clinical test in patients with optic neuritis.

Answer 3: 70% (D)

Patients with optic neuritis and with one or more lesions in brain MRI suggestive of MS are at approximately 70% risk of clinically definite MS in the subsequent 15 years. Without lesions in brain MRI the risk is only 25% (mean values [1]). Other studies investigating not only optic neuritis pa-

Figure 2

STIR sequence of a patient with left-sided optic neuritis.



tients but CIS patients in general found even higher conversion rates in patients with abnormal brain MRI (85% within 10 years [2]).

Answer 4: Fingolimod (D)

Fingolimod is the only treatment option in the list that is not currently licensed for Clinically Isolated Syndrome in Switzerland.

Answer 5: 1–5% (A)

If one first-degree relative has MS, the index person's risk is 10–20 times higher than the average risk in the population (2–4% vs 0.2%). In monozygotic twins or when both parents are affected, the risk is about 25–30% [3].

Answer 6: Anti-NMO antibodies in serum (B)

Figure 1 shows a spinal cord lesion extending over six vertebral segments. This finding is suggestive of neuromyelitis optica (NMO). NMO is an inflammatory demyelinating CNS disease that is distinct from MS with respect to clinical, laboratory, neuroimaging and prognostic characteristics. The classical presentation is optic neuritis and typically transverse myelitis. In comparison with MS the disease course of untreated NMO is significantly worse, with residual disabilities from relapses as in our patient. Visual acuity did not improve. Within 5 years more than half of the patients with relapsing NMO are blind in at least one eye or require ambulatory help [4]. In Europe the prevalence of NMO is lower than that of MS, but it makes up a substantial proportion of demyelinating central nervous system (CNS) disorders in non-Caucasian populations such as East Asians (up to 48%) [5]. An Italian study estimates that NMO may account for about 1% of the cases seen in tertiary MS clinics [6]. CSF inflammation during NMO relapses can be extreme, especially in severe myelitis. CSF pleocytosis greater than 50 cells/UL, as in our patient, has been reported in 13–35% of patients and increased protein levels in 46–75% of cases [7]. White blood cells are predominantly polymorphonuclear, in contrast to MS where CSF usually shows mild lymphocytic pleocytosis. CSF oligoclonal bands, which are detectable in about 80% of MS patients, are found in only 20–30% of NMO patients. Autoantibodies (Anti-NMO-IgG) targeting aquaporin-4 are specific for NMO. Anti-NMO antibodies in serum is the best next diagnostic step and has a sensitivity of 47–91% and specificity of 85–100% depending on the underlying study population [8]. The clinical presentation and MRI of our patient are not sugges-

tive of neurosarcoidosis, although this is a general differential diagnosis of spinal cord lesions. Neuropathies of cranial nerves are the most common manifestation of neurosarcoidosis, being seen in approximately 50–75% of patients, and are most commonly caused by granulomatous basal meningitis [9, 10].

Answer 7: Azathioprine (C)

Although controlled studies are still lacking, current evidence suggests that MS-disease-modifying therapies such as interferon beta and glatiramer acetate are ineffective in NMO. Sometimes interferons may even worsen the course. General immunosuppressive treatment (e.g., azathioprine or mycophenolate mofetil) or B-cell depletion (e.g., rituximab) seem to improve the natural history of NMO. Azathioprine exerts its full immunosuppressive effects only after 4–6 months. Hence some authors recommend that azathioprine treatment should initially be combined with oral methylprednisolone (0.5–1.0 mg/kg per day) for at least 4 months [11].

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