

Neurologist-in-training

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Case vignette

A 29-year-old woman presented with subacute onset of pain in her proximal right leg that sometimes radiated to the lateral part of the foot. Additionally, she realised a foot drop on the right side and a few days later on the left side as well. Light touch sensitivity was reduced at the dorsum of the right foot. In addition, neurological examination revealed a reduced sensitivity at the dorsum and sole of the contralateral left foot. Ankle reflex was normal on the right side and missing on the left. No other focal neurological signs were detected, the patient felt healthy and had no fever. Personal history was remarkable regarding a similar but less severe episode of pain and foot drop on the right side almost exactly one year previously. These symptoms had resolved without specific treatment after approximately 6 weeks apart from persistent numbness of the dorsum of the right foot.

Questions

1. Which test or investigation is the least appropriate to order at this stage?
 - A Lumbar puncture
 - B MRI of the lumbar region
 - C MRI of the brain
 - D Electroneurography and electromyography (ENG/EMG)
 - E Laboratory tests

The appropriate investigations confirm the clinical diagnosis of a mononeuritis multiplex. Electrophysiologic studies confirm an axonal neuropathy of both peroneal nerves (motor and sensory) as well as the left tibial nerve and the left sural nerve. In addition, there are signs of acute, subacute and more chronic neuropathic changes on electromyographic examination. Laboratory tests including CSF reveal normal results as well as spinal MRI studies. The only pathological result in laboratory testing is a slightly elevated ANA titer of 1:160.

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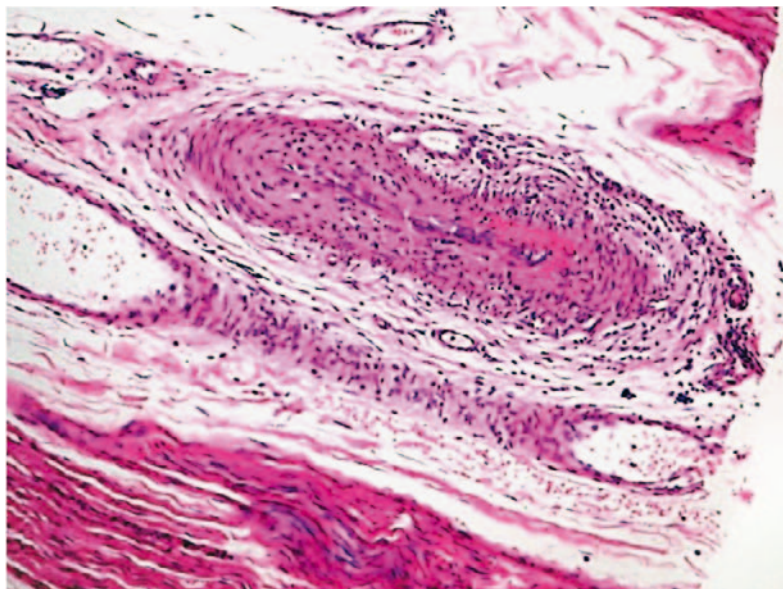
2. Which is the most likely cause of the symptoms in this young patient?
 - A Transverse myelitis of the conus
 - B Amyotrophic lateral sclerosis
 - C Guillain-Barré syndrome
 - D Hereditary Neuropathy with Pressure Palsy (HNPP)
 - E Vasculitis of the peripheral nervous system
3. Which diagnostic test is the best to confirm your suspected diagnosis?
 - A Sural nerve biopsy
 - B Genetic testing
 - C Muscle biopsy of the tibialis anterior
 - D Motor-evoked potentials
 - E None

While awaiting the results of these diagnostic tests, the clinical diagnosis is likely enough to start therapy in order to prevent progression of the disease and reduce symptoms.

4. Which is the first therapeutic option in this situation?
 - A Azathioprin
 - B Oral prednisone
 - C Intravenous immunoglobulin (IVIG)
 - D Plasma exchange therapy
 - E Rituximab

After a few days on therapy, the patient reports some improvement of strength in both feet. The results of the sural nerve biopsy reveal a vasculitis of the small epineural vessels (fig. 1), reflecting the pathological diagnosis of microscopic polyangiitis (MPA) [1]. This diagnosis should lead to further investigations to rule out a systemic disease, as the diagnosis of an isolated vasculitis of the peripheral nervous system is quite rare [2]. In this patient, all additional investigations revealed negative results. Even though prognosis of isolated vasculitis of the peripheral nervous system is better than that in systemic disease, therapeutic regimes usually need to be expanded to other drugs in order to reduce the dose of cortisone in long-term treatment.
5. Which is the most common drug used as the next therapeutic step in this situation?
 - A Rituximab
 - B Mycophenolate mofetil
 - C Natalizumab
 - D Intravenous immunoglobulin (IVIG)
 - E Cyclophosphamide

Figure 1 Biopsy of the sural nerve showing perivascular invasion of leucocytes reflecting vasculitis of small epineural vessels (microscopic polyangiitis).



Answers and comments

Answer 1

C is correct.

The clinical syndrome is suggestive of a mononeuritis multiplex. All clinical signs indicate that the cause of the symptoms must be located in the peripheral nervous system. An MRI of the brain is not likely to contribute significantly to the correct diagnosis. All other tests or investigations can be helpful at this stage: EMG/ENG can confirm the peripheral nature of the disease and give important information on kind and time course of the neuropathy. Lumbar MRI and lumbar puncture can exclude an infectious or compressive process that affects the lumbar nerve roots. Finally, laboratory tests are mandatory to demonstrate if there are signs of systemic inflammation, a rheumatologic disease or an infectious disease like HIV.

Answer 2

E is correct.

An axonal neuropathy in a young patient, especially with such a patchy pattern reflecting the clinical diagnosis of a mononeuritis multiplex is mainly suggestive of a systemic or focal vasculitis. If there were no sensory symptoms, multifocal motor neuropathy would be an important differential diagnosis, too. Very important is the history with pain in the primarily affected limb. The relapsing and remitting course is also very typical for some types of vasculitis. A myelitis of the conus usually presents more acutely with additional clinical signs like reduced urinary and bowel continence and anaesthesia of the perianal region. Amyotrophic lateral sclerosis can be ruled out because of the prominent loss of sensitivity and missing signs of the first motor neuron. Guillain-Barré syndrome could present in a similar fashion. However, the time course and localisation of the symptoms

is very atypical, electrophysiological studies usually should show a primarily demyelinating disease and in most cases there is an elevated protein on lumbar puncture, but protein content can be within normal limits in the acute stage making complicating the differential diagnosis. Finally, hereditary causes should always be considered in a young patient with neuropathy. However, the time course is atypical for HNPP, and electrophysiological studies usually confirm demyelinating lesions with conduction block at more or less typical sites of compression.

Answer 3

A is correct.

To finally confirm the suspected diagnosis of vasculitis of the peripheral nervous system, it is usually necessary to proceed to biopsy. This invasive procedure is justifiable because of important therapeutic consequences. In this patient, clinical and electrophysiological signs show an involvement of the left sural nerve, making it the best nerve to study. Muscle biopsy could only be helpful to show a more widespread vasculitic process or to rule out differential diagnoses, but not in establishing the suspected clinical diagnosis. Genetic testing as well as MEPs will not contribute to the right diagnosis.

Answer 4

B is correct.

The first therapeutic option still remains oral prednisone in a dose of 1mg per kg. In severe cases an intravenous administration of high dose steroids might be discussed as well [3]. Some clinicians start with combined therapy of prednisone and cyclophosphamide, but usually cyclophosphamide will be started later in order to reduce steroid doses. The other options are either not indicated or limited to selected cases as second line treatment.

Answer 5

E is correct.

In cases that show adequate response to steroid treatment but relapse under steroid tapering, cyclophosphamide is the best next therapeutic agent [4]. It can be given orally or intravenously and should always be accompanied by uromitexan for bladder protection. IVIG might be considered in cases without good response to steroid treatment. The other options are second-line treatments or not indicated at all.

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