SYLLABUS

TC46: Clinical Pearls: Practical tips in the diagnosis and management of spinal and peripheral nerve disorders

Thursday, November 17, 2011 09:00 - 12:30 Hall I

Marrakesh, Morocco, November 12-17, 2011

XXth WORLD CONGRESS OF NEUROLOGY

XXth WCN 2011 MARRAKESH World Congress of Neurology

WFN

SMN SOCIETE MAROCAINE DE NEUROLOGIE

WCN Education Program

Thursday, 17 November, 2011

09:00-12:30

CLINICAL PEARLS: PRACTICAL TIPS IN THE DIAGNOSIS AND MANAGEMENT OF SPINAL AND PERIPHERAL NERVE DISORDERS

Chairperson: **Richard Stark**, *Australia*

ASPECTS OF NERVE ROOT COMPRESSION AND CERTAIN MONONEUROPATHIES
David Perkin, *UK*

PRACTICAL ASPECTS OF SPINAL AND PERIPHERAL NERVE DISORDERS
Gerard Said, *France*

SOME SPINAL SYNDROMES: COMMON AND UNCOMMON
Richard Stark, *Australia*

10:30-11:00 *Coffee Break*

Multifocal neuropathies

Gérard Said, MD, FRCP, Département de Neurologie, La Salpêtrière, Paris

Main causes of Mononeuritis Multiplex

- Infectious disorders
  - Leprosy
  - HIV infection & Cytomegalovirus infection
  - Lyme disease
- Vasculitic neuropathy
- Granulomatous neuropathy: tuberculoid leprosy & sarcoidosis
- Metabolic : diabetes
- Inflammatory: multifocal CIDP
- Malignant infiltration of peripheral nerves
- Familial: HLPP

Leprosy in the world – WHO

number of cases officially declared

Country	1993	2002	2007
Brazil	34 235	38 365	39 125
Madagascar	740	5 482	1 644
India	456 000	473 000	137 685

Total number in the World	265 661 in 2006	258 133 in 2007

Characteristics of the lepromatous (multibacillar) form of leprous neuropathy

- In nearly all cases they are associated with characteristic skin lesions.
- Diffuse, bilateral and generally symmetrical nerve damage
- Negative skin test to lepromin
- The more lepromatous the findings, the less marked are the symptoms.
- Symptomatic neuropathy is always associated with severe axon loss,
- average reduction of nerve fibre density to **5%** of control values in symptomatic neuropathy, versus **25%** in patients with silent hypertrophy of the radial nerve.

Tuberculoid (paucibacillar) leprosy

- Clinically tuberculoid lesions may be single or few, and are distributed asymmetrically in the vicinity of typical hypoesthetic or anaesthetic hypopigmented skin lesions.
- **Nerve damage caused not by the bacilli but by the cell mediated immune response to *M. leprae* antigens.**
  - The basis for the destruction of nerve structure is a **delayed type hypersensitivity reaction (DTH)** with specific helper T cells reacting with ML antigens presented in the endoneurium by macrophages
  - Role of activation of macrophages
  - When a **DTH reaction** occurs in the endoneurium it can lead to **major damage**, and even to **necrosis** and to **intraneural abscesses**.
  - **ML as dangerous dead as alive!**

The reversal or upgrade form of reaction in Leprous Neuropathy

- common during the first year of therapy
- Heightened cell-mediated response mainly in patients with the borderline-lepromatous form of leprosy.
- This reaction is identified by swelling and exacerbation of existing skin and nerve lesions in association with general malaise and fever.
- It occurs also after highly active antiretroviral treatment for HIV infection, when the CD4 level increases.
- Endoneurial granuloma, multinucleated giant cells, lymphocytic infiltration, vasculitis and perineuritis are present on morphological examination.
- Necrosis of the endoneurial content may lead to nerve abscesses. No *M. leprae* are observed in this reaction.
- Improvement of the CMI response in patients under treatment can lead to further damage of nerve trunks.

Peripheral neuropathy in HIV patients

- "Immunocompetent" HIV patients
  - In 4% of the patients, peripheral neuropathy at seroconversion.
  - Different patterns of Guillain-Barré syndrome
  - Multifocal demyelinative neuropathy
  - Facial palsy or diplegia
  - Vasculitic neuropathy (necrotizing arteritis)
  - Neuropathy with lymphocytic proliferation
- At the stage of immunodepression (CD4 T cells < 150/ml)
  - Distal symmetrical sensory polyneuropathy
  - Cytomegalovirus neuropathy
  - Drug induced polyneuropathy (DDI, DDC)

Vasculitic Neuropathy
Patients with NA & neuropathy

75% focal or multifocal neuropathy:

Focal neuropathy (mononeuritis):	16.5%
Multifocal neuropathy (mononeuritis multiplex)	56.5%
Distal symmetrical sensory or sensorimotor polyneuropathy	25%

Vasculitic Neuropathy

Nerve affected	*unilateral*	*bilateral*
Peroneal nerve	62%	33%
Popliteal nerve	27%	5%
Ulnar nerve	25%	8%
Median nerve	21%	3%
Radial nerve	8%	3%
Femoral nerve	6%	1%
Sciatic roots:	2%	
Cranial nerves (V, VII)	1%	

Primary Vasculitic Neuropathy
Involvement of other organs

- Skin lesions
  - necrotic cutaneous lesions: 13 %
  - purpuric lesions 11 %
  - reticulate livedo 3 %
  - localised oedema 17%
- Renal involvement 12%
- CNS involvement 2%

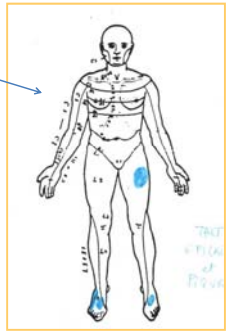
Isolated Neuropathy & Necrotizing Arteritis
The "nonsystemic" vasculitic neuropathy

- PN is the only manifestation of vasculitis; called nonsystemic vasculitis by Dyck et al, 1987
- In our series: In 25% of the 400 patients, peripheral neuropathy was the only manifestation of vasculitis ("non-systemic")
- Mean age: 61 years; 61% females; same neuropathic pattern as in systemic forms.
- ESR: normal in 33% of the patients.
- Diagnosis by nerve and muscle biopsy
- N.A. in the muscle specimens as often as in cases with multisystem involvement, which demonstrates that vasculitis is not restricted to the PNS
- Better prognosis in these forms.

Non-inflammatory vasculitic neuropathy

- M. N...Ray., 38 years; from Beyrouth.
- Good general condition
- Nov 2000 : brown stains over the feet that extended proximally.
- July 2002 : numbness of the dorsal aspect of both feet and of the lateral aspect of the right one associated with oedema of the feet.
- Aug 2002 : improvement of oedema and numbness on corticosteroids.
- Sept 2002 : corticosteroids withdrawn, recurrence of numbness of the feet, which became painful.
- Oct 2002 : Noticed anesthesia of the lateral aspect of the left thigh.

- December 2002: Neurological examination
  - Motor strength: extensor halluci brevis: 4+/5
  - Sensory changes: see
  - Normal tendon reflexes
- Good general condition
- Normal ESR, CRP..., renal function, protein electrophoresis, antinuclear antibodies, HIV, B12, folates...
- Chest radiogram
- EMG: multifocal axonal neuropathy
- Mononeuritis multiplex
- **Conclusion:**
  - Livedo reticularis
    - ► **Polyarteritis nodosa.**



Necrotizing arteritis in non-connective tissue disorders (N-CTD) (Lacroix & Said, J Neurol 2005)

18% of the patients with vasculitic neuropathy

1. Symptomatic viral infection (HIV, HTLV-1, B and C virus chronic hepatitis, CMV)
2. Multifocal diabetic neuropathy
3. Benign monoclonal gammopathy (MGUS)
4. Malignant haemopathy including one with Waldenström and one with multiple myeloma
5. Sarcoid neuropathy

Sarcoid neuropathy

- Regarding the peripheral nervous system, cranial nerves are predominantly affected, and peripheral facial nerve palsy, often bilateral, is the most common neurological manifestation of sarcoidosis.
- Multifocal peripheral neuropathy is a rare event in sarcoidosis. In some cases however, peripheral neuropathy is the presenting manifestation and seemingly the only organ affected.
- Definite diagnosis of sarcoidosis rests on histologic demonstration of sarcoid granulomas in tissue biopsy specimens.
- In patients who present with sarcoid neuropathy nerve biopsy and biopsy of other organs affected, especially intrathoracic lymph nodes, can be diagnostic.

Focal and Multifocal Diabetic Neuropathy

- ➔Cranial neuropathy
- ➔Thoracic neuropathy
- ➔Proximal diabetic neuropathy
- ➔Multifocal diabetic neuropathy

Multifocal diabetic neuropathy
Clinical aspects: Said et al. Brain 2003;126:376.

- Subacute onset over 2-12 months.
- Some patients had recurrent neuropathic episodes within 1-3 years, with spontaneous remission after the first episode.
- **Pains and motor deficit of subacute onset and progression** were the most constant complaints.
  - Spontaneous pains, often burning, more disturbing at night, and allodynia had been present for several weeks in 21/22 patients.
  - 13/22 patients required administration of opiates at referral.

- Distal sensory-motor deficit of the lower limbs predominating in the peroneal nerve territory (22/22):
  - Unilateral (7 patients) or asymmetrical (15 patients) plus :
  - Proximal deficit of the lower limbs in 13/22:
    - unilateral: 7 patients; bilateral: 6 patients
  - Thoracic painful neuropathy: 3/22:
    - unilateral: 1 patient; bilateral: 2 patients
  - Upper limbs involvement: 6/22
    - ulnar nerve: 1
    - median nerve: 1
    - radial nerve: 2 patients
    - Overlapping territories in the hands: 2

CIDP – Clinical aspects

- Two main patterns:
  - **Generalised CIDP**: bilateral, roughly symmetrical sensorimotor deficit;
  - **Multifocal pattern**: any nerve root or trunk territorry can be affected with progression or relapses over months.
- Outcome and response to treatments variable

CIDP - Focal and multifocal presentation

Gorson et al, 1999 - 10 patients

- Initially restricted to the ulnar nerve distribution in 3 patients, and median and axillary nerve in 1 patient each, and involved multiple nerves in 5.
- Conduction block detected in the forearm segment of 68% of the median and ulnar motor nerves tested;
- none had anti-GM1 antibodies
- recovery following treatment was greater in patients with generalized CIDP than in those with focal CIDP

Clinical course in CIDP

- **Bouchard et al: 100 Patients followed > 6 y.**
  - **Relapsing course: 15 %**
  - **Progressive course: 41 %**
    - **Many patients have a secondary progressive course**
  - **Patients in relatively stable condition: 44%**
- **McCombe**
  - **Relapsing-remitting: 1/3**
  - **Chronic progressive: 2/3**

Main causes of Mononeuritis Multiplex

- Infectious disorders
  - Leprosy
  - HIV infection & Cytomegalovirus infection
  - Lyme disease
- Vasculitic neuropathy
- Granulomatous neuropathy: tuberculoid leprosy & sarcoidosis
- Metabolic : diabetes
- Inflammatory: multifocal CIDP
- **Malignant infiltration of peripheral nerves**
- Familial: HLPP

Conclusion

- Focal and multifocal neuropathy are often due to treatable causes
- Nerve and muscle biopsy are especially useful in this setting

Outline

- Some points of anatomy & imaging
- Spinal syndromes
  - Classical
  - Less common
- Clinical aspects of
  - disc disease / spondylosis
  - primary and secondary neoplasia
  - vascular disease
  - Infection
  - Radicular syndromes

Anatomy

- Cervical spine: vertebrae C1-C7, roots C1-C8.
- Cervical roots emerge **above**
  - i.e. C6 emerges at **C5/6**
- Thoracic & lumbar roots emerge **below**
  - i.e. L5 emerges at **L5/S1**
  - What syndrome does L4/5 disc usually cause? **L5**
  - When would an L4/5 cause an L4 syndrome? **Very lateral disc protrusion**
- The point is that, usually:
  - C4/5 disc causes C5 radiculopathy, and
  - L4/5 disc causes L5 radiculopathy,
  - **But for different reasons**
- Misleading sensory levels
  - Discrepancy between cord level and vertebral level
  - Remember Lissauer's tract
  - Lamination of tracts

Radiology

- Radiology of lesions by site:
  - Intramedullary
  - Intradural / extramedullary
  - Extradural
- What is a pars defect?
- Why is a pars defect important to a neurologist?

Classical cord lesions

- Extrinsic compression
- Intrinsic cord lesion with sacral sparing
- Central cord lesion with suspended sensory level (syrinx syndrome)
- Brown-Séquard lesion
- Anterior spinal artery syndrome

Some other spinal syndromes

- Traumatic Central cord syndrome
- Foramen magnum / High cervical cord compression
- Posterior column syndromes
- Excessive cord mobility
- Spinal canal stenosis

Traumatic Central Cord Syndrome

- Typically cause by acute extension injury in a patient with pre-existing cervical spondylosis
- Cord is contused against a spondylotic bar
- Typically motor loss arms>legs:
  - "man in a barrel" (whole of upper limb)
  - "flipper hands" (hands predominantly affected)
- Sensory, lower limb motor and sphincter dysfunction are usually relatively spared
  - (sometimes dorsal column loss in hands)

Atypical / “false localizing” signs from high cord compression

- One review: 11 patients with an extradural lesion above C4 (most commonly C3-C4).
- All had a syndrome of **finger and hand dysaesthesias**, **hand atrophy**, and occipital or cervical pain.
- These complaints usually preceded the development of spasticity and gait disturbance.
- Pathophysiology: theories include
  - anterior spinal artery ischemia,
  - **venous obstruction**, and
  - differential decussation of the forelimb and hindlimb fibers of the corticospinal tract.

Hirayama disease

- Affects 1 limb, or if >1 limbs, asymmetrical
  - Upper limb involvement more common
- 2nd or 3rd decade
- M>>F
  - Initial progressive phase 6mo-2 yrs then stabilises over 5 yrs
- Painless atrophy > weakness mainly distally
  - Eg C7, C8 and T1 with sparing of BR and ECR, but involvement of FCU and EIP = “oblique” atrophy
  - Cold paresis
  - Minimyoclonus
  - Reflexes normal or reduced; sometimes hyperactive
- Pathophysiology
  - Anterior displacement of posterior wall of lower cervical dural sac with widening of epidural space and obliteration of subarachnoid space

Lumbar spinal stenosis: symptoms & signs

- The typical clinical feature of severe lumbar spinal stenosis is **neurogenic claudication**
- This consists of back and buttock or leg pain induced by walking or standing and **relieved by sitting** (or flexing the spine in some other way).
- Symptoms in the legs are usually bilateral.
- Unlike vascular claudication, symptoms are often provoked by standing without walking. Focal weakness, sensory loss, or reflex changes may occur when spinal stenosis is associated with radiculopathy. Severe neurologic deficits, including paralysis and urinary incontinence, occur rarely.
- Congenital **lumbar** stenosis often co-exists with congenital **cervical stenosis** resulting in mixed UMN & LMN signs in the legs
- Spinal stenosis can be acquired, congenital, or **due to a combination of the two causes**.

Neoplastic disease

Extradural / Spinal metastases
Intradural / extramedullary
- Meningeal metastases (often tiny)
- Neurofibroma / meningioma

Intramedullary neoplasia

Spinal Metastases: Primary Site

SITE	M/F	Total
Lung	35/8	43
Breast	0/37	37
Miscellaneous rapid	10/6	16
Miscellaneous slow	12/5	17
Undetermined	9/9	18
TOTAL	**66/65**	**131**

Spinal metastases
Patients not known to have cancer

Lung	30/43
Breast	3/37
Miscellaneous	11/33
Undetermined	18/18
TOTAL	**62/131**

Symptoms & Signs of Spinal Metastases

SYMPTOMS		SIGNS	
Axial pain	72%	Spinal tenderness	74%
Radicular pain	41%	Signs in arms	72%
No pain	14%	Sensory level (PP)	16%
Pain before deficit	69%	Power in legs:	
Leg weakness	82%	Grade 5	11%
Arm weakness	14%	Grade 2-4	65%
Sphincter disturbance	63%	Grade 0-1	24%
		"Clinical transection"	11%
		Decreased anal tone	35%

Meningeal cancer: Clinical patterns

1. Encephalopathy
   - Drowsiness, confusion, headache, papilloedema

2. Multifocal lesions, randomly scattered
   - **Nerve roots** **(very common)**
   - **Cranial nerves** **(very common)**
   - **Spinal cord** **(not rare)**

Non-compressive Myelopathy

Intramedullary metastases
Meningeal cancer
Radiation Myelopathy
Paraneoplastic (subacute necrotising myelopathy)
Intrathecal chemotherapy
Spinal Infarction
Unexplained
(Inadequate imaging: actually compressive)
(Pseudo-myelopathy: cerebral parasagittal)

Vascular disease of the spinal cord

Infarct
Haemorrhage
AVM
Dural venous fistula

Mechanisms of spinal cord infarction (remember sites of special susceptibility)

- Hypoperfusion
- Atheroembolism
- Arterial thrombosis or dissection
- Arteritis
- Fibrocartilaginous embolism
- Compression of vessels by cervical spondylosis or tumours
- Decompression sickness
- Surgery, to aorta or spine, angiography
- Spinal anaesthetic or other injection

Miscellaneous Spinal disorders

Infection
After anaesthesia
Radicular syndromes

Spinal epidural abscess

- Stages
  - 1 Back pain
  - 2 Radicular radiation
  - 3 Motor, sensory, sphincter decline
  - 4 Paralysis
- Pitfalls
  - Systemically unwell, obtunded, difficult to examine patient
  - Staph septicaemia treatment without finding cause
  - Accepting vertebral osteomyelitis as sufficient diagnosis
  - Imaging wrong section of spine
  - Misssing second site of epidural abscess
  - Delaying investigations

Radicular syndromes & their differentials

Upper limb

- C5, C6
  - Neuralgic amyotrophy
  - Suprascapular n
- C7
  - Radial nerve
- C8, T1
  - Lower plexus, ulnar n
  - Radiation plexopathy vs infiltration

Lower Limb

- L2, L3, L4 vs
  - Femoral n
  - Lumbar plexopathy
  - Psoas haematoma
- L5 vs common peroneal n
- Special case:
  Foot drop after THR under spinal
  - Peroneal @ knee vs sciatic @ hip vs L5
- S1 vs sciatic n