Question 98

A 52 year old retired school teacher with a 20 year history of type 2 (non insulin-dependant) diabetes mellitus and a 10 year history of hypertension presents with a two day history of progressive right sided ptosis and diplopia. Examination reveals signs consistent with an incomplete right third nerve palsy with pupil sparing. The erythrocyte sedimentation rate (ESR) is 45 mm/hour (0-15).

The most likely diagnosis is:
A. Diabetic right third nerve palsy
B. Mucormycosis of the right orbit
C. Right posterior communicating artery aneurysm
D. Giant cell arteritis involving the right third nerve
E. Right mid-brain infarct

Answer:

Learning Issues:
1) Diabetic neuropathies
2) CN III palsy

This is an isolated unilateral painless CN III palsy which spares the pupil
- Suggests a “medical” CN III palsy
- Associated mild-moderately elevated ESR suggesting inflammatory process
- Not secondary a “surgical” CN III palsy (eg ↑ ICP or space occupying lesion) as parasympathetic activity is spared
  o Parasympathetic fibres are superficial and will thus be affected first

Diabetic neuropathy
- Affects 50% of both long-standing T1DM and T2DM
- Related to duration of diabetes and glycaemic control
- Both myelinated and unmyelinated fibres affected
- Management:
  o Improved glycaemic control (improves nerve conduction velocity but Sx may not)
  o Avoid neurotoxins (eg ETOH)
  o Vitamin supplementation if deficient (eg B12/ folate)
  o Look for and treat complications eg ulcers
  o Analgesia
    ♠ Pain of acute neuropathy may resolve in 1 year
    ♣ Chronic pain hard to treat: TCA/ gabapentin/ anti-epileptics (avoid NSAIDS if renal impairment)
    ♠ Pain clinic
<table>
<thead>
<tr>
<th><strong>Polyneuropathy</strong></th>
<th><strong>Distal symmetrical polyneuropathy</strong></th>
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<tbody>
<tr>
<td>- Pain from distal symmetrical subsides as neuropathy progresses</td>
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<td>- Radiculopathy self-limited, spontaneously improves in 6-12 months</td>
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<td>- Most common (glove + stocking)</td>
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<td>- Acute form (&lt; 12 months)</td>
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<td>- Chronic form (usually painful)</td>
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<td>- Spreads distal -&gt; proximal</td>
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<td>- Distal sensory loss + abnormal proprioception</td>
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<td>- Loss of ankle jerks</td>
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<td>- Numbness/ tingling/ burning</td>
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<td>- Present at rest, worst at night</td>
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**Diabetic mono/polyradiculopathy**

- Pain in distribution of > nerve roots
- +/- motor weakness
- Amyotrophy: affects lumbar flexus with weak hip ext/flexion
- Thoracic radiculopathy less common (debilitating band-like pain, often had extensive GIT Ix)
- Usually self-limited within 6-12/12

**Mononeuropathy**

- Usually does not improve
- May improve with glycaemic control

**Diabetic mononeuropathy**

- Isolated cranial or peripheral nerve dysfunction: pain and motor weakness
- Less common than polyneuropathy
- ? Vascular phenomenon (unclear aetiology)
- Cranial nerves
  - CN III most common
  - Also affects IV, VI and VII (Bell’s)
- Peripheral nerves
  - Common peroneal nerve palsy -> foot drop

**Mononeuritis multiplex**

- > 1 named peripheral or cranial nerve affected
- Less common
- Main ddx: vasculitis (need to exclude)

**Autonomic Neuropathy**

- Difficult to treat
- Usually does not improve with time
- May improve with glycaemic control

**Affects cholinergic, adrenergic and peptidergic (peptides eg substance P) systems**

**Multi-system**

- Cardiovascular
  - Resting tachycardia
  - Postural hypotension
  - Sudden death case reports
- GIT
  - Gastroparesis (↑ transit time with Sx in absence of obstruction, closely related to retinopathy and nephropathy)
  - Enteropathy (constipation +/- diarrhoea)
- Genitourinary tract
  - Bladder dysfunction
- Sympathetic
Hyperhidrosis upper limbs
Anhidrosis lower limbs
\( \downarrow \) counter-regulatory hormone release (hypoglycaemic unawareness)

- Pathogenesis of diabetic amyotrophy suggestive of inflammation (from muscle and nerve root biopsies consistent with immune complex and complement deposition) -> some patients improved with steroids +/- IV immunoglobulin. However, most improved spontaneously with time anyway

Back to the question:
A. Correct. As described, CN III isolated palsy is commonest diabetic mononeuropathy.
- CN III (oculomotor) supplies:
  - Extra-ocular muscles (SR, MR, IR and IO): motor and proprioception
  - Parasympathetic (via ciliary ganglion)
    - Sphincter pupillae -> pupillary constriction
    - Ciliary muscles of lens -> accommodation (\( \uparrow \) convexity for near vision)
- Emerges from mid-brain -> pierces dura -> runs in lateral wall of cavernous sinus
- Enters orbit via superior orbital fissure
- Within fissure: divides into superior (SR and levator palpebrae) and inferior division (IR, MR and IO + parasympathetic fibres)
  - Parasympathetic fibres run from Edinger-Westphal nucleus to ciliary ganglion for synapses
  - Post synaptic fibres then pass to eyeball
- Classically:
  - Diplopia
  - Ptosis (paralysis of levator palpebrae)
  - Ophthalmoplegia (eyeball down and out – unopposed action of SO and LR)
    - Normal pupillary constriction to light (NO interruption of parasympathetic fibres to the iris, so dilator pupillae muscle opposed)
  - Accommodation of the lens still present

B. Incorrect. Patient is too well and has no other classic features. Moreover, if entire orbit involved, parasympathetic fibres will be involved.

Mucormycosis is a devastating fungal infection by zygomycetes
- Ubiquitous especially decaying vegetation and soil
- Enzyme ketose reductase allows them to thrive in acidic, glucose rich environment
- Infection starts from inhalation of spores
- Immunocompetent -> cleared
- Immunosuppressed -> starts at nasal turbinates -> spreads to orbits and brain
- Mucors are angio-invasive, so infarction of infected tissues is the hallmark
- Usually fast-paced infection
- Presents with fevers, headache, purulent nasal discharge and sinus pain
- All sinuses involved -> contiguous structures eg palate, orbit and brain
- If orbit involved -> peri-orbital oedema, proptosis and blindness
- Facial pain common from infarction of sensory nerves of trigeminal nerve
- Other CN palsies possible when spread to cavernous sinus, sinus thrombosis and involvement of carotid artery
- Rarely it seeds to other organs via haematogenous spread (usually neutropenic)

C. Aneurysms of the posterior cerebral artery (or its branch posterior communicating artery) and superior cerebellar artery can exert pressure on CN III as it passes in between them. However, the superficial parasympathetic fibres should also be involved.
D. Giant cell arteritis (temporal arteritis) is chronic vasculitis of large or medium sized vessels – artery supplying CN III not classically affected; in any case, the parasympathetic function should also be impaired.
- May be generalised but commonly affects cranial branches of arteries originating from the aortic arch
- Symptoms: headache, jaw claudication, visual symptoms, fever, polymyalgia rheumatica
- Visual symptoms from ischaemia due to occlusion or thrombosis of posterior ciliary arteries that supply the optic nerve, or the ophthalmic artery itself
- ESR usually substantially elevated and only rarely < 40 (unless on steroids)

E. Right midbrain infarct (supplied by posterior circulation ie vertebral arteries) will affect CN IV ie trochlear nerve and the Edinger-Westphal nucleus.