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Oculomotor Nerve Palsy (CN 3)

Signs and Symptoms

The primary symptom is **diplopia** caused by misalignment of the visual axes, the pattern of image separation (horizontal, vertical, oblique) is the key to diagnosing which particular ocular motor cranial nerve (and extraocular muscle) is involved.

With a complete unilateral third cranial nerve palsy, the involved eye is deviated "down and out" with partial or complete ptosis.

- Pupillary dilatation (involvement) can cause:
- Anisocoria (greater in the light)
- Symptomatic glare in bright light
- Blurred vision for near objects – due to accommodation deficit

A painful pupil-involved oculomotor nerve palsy may result from a life-threatening intracranial aneurysm. Prompt diagnosis of an oculomotor nerve palsy is critical to ensure appropriate evaluation and management.

Pathophysiology

The clinical features of a CN 3 palsy are due to the anatomical relationship of the various branches of the oculomotor nerve and the location of the problem causing the palsy. These anatomical sites can be broken down into:

- **Nuclear portion:** The axons start on each side of the midbrain. Each of the axon origination within the midbrain that travel to a specific extraocular and intraocular muscle can be further classified into a subnucleus.
- **Fascicular intraparenchymal midbrain portion:** This portion of the oculomotor nerve travels courses ventrally (forward) from the nucleus, through the red nucleus, and emerges medially from the cerebral peduncle.
- **Subarachnoid portion:** The nerve then travels in the subarachnoid space anterior to the midbrain and near the **posterior communicating artery**. An aneurysm at the junction between the posterior communicating artery and the internal carotid artery is one of the critical reasons to differentiate a pupil involved CN 3 palsy.
- **Cavernous sinus portion:** The oculomotor nerve then runs through the lateral and superior aspect of the cavernous sinus. Due to the CN 3 proximity to the interclinoid and petroclinoid ligaments (which can compress CN 3), tumors and other masses that can infiltrate cavernous sinus from within the sella turcica (pituitary issues) frequently cause CN 3 palsy prior to involvement of the other cranial nerves in the cavernous sinus.

INTRAOCULAR INNERVATION

The pupil and ciliary muscle neurons derive from the Edinger-Westphal subnucleus, which is in the midline in the most anterior and rostral part of the CN 3 nucleus. These autonomic pathways are all ipsilateral.

- **Orbital portion:** CN 3 enters the orbit through the **superior orbital fissure** near CN 4. CN 3 then branches into superior and inferior divisions, typically within the posterior orbit (occasionally - branching occurs as far posteriorly as the cavernous sinus segment).
 - **Superior division:**
 - levator palpebrae
 - superior rectus muscles
 - **Inferior division:**
 - Medial rectus
 - Inferior oblique
 - Inferior rectus
 - Iris sphincter

Differential diagnosis of acquired 3rd nerve palsy include:

- Trauma
- Tumor
- Aneurysm
- Microvascular

Treatment and Management for CN 3 Palsy

- Incomplete or Pupil Involved:
 - MRI and CTA – Immediate
- Complete AND Pupil Spared
 - Monitor if:
 - Age >40
 - Known microvascular disease
 - No other neurological findings
 - No new symptoms on follow up
 - Resolution by 3 months
 - Otherwise:
- Otherwise:
 - Consider microvascular disease
 - Blood pressure, blood sugar, A1C
 - Consider Inflammatory/infectious causes
 - CRP, ESR, RPR, FTA-ABS, Lyme titer
 - Testing for myasthenia gravis
 - Testing for multiple sclerosis
 - Consider orbital disease
 - Orbital CT
 - Consider cavernous sinus and brainstem disease
 - Brain MRI and CTA

CROSSED

The axons for most of the muscles are not crossed.

Exceptions:

1. Levator palpebrae come from both sides of the central caudal subnucleus via bilateral (ipsilateral and contralateral) pathways.
2. Superior rectus muscle come from the superior rectus subnucleus on the **contralateral side**.

Trochlear Nerve Palsy (CN 4)

Signs and Symptoms

The primary symptom of a CN 4 palsy is vertical or oblique diplopia, occasionally with a torsional component. CN 4 innervates the superior oblique (SO) muscle:

- During primary gaze the mechanism of action of the SO is **intorsion**
- During ADduction, the SO is a **depressor**
- The SO also can aid with **ABduction**

Pathophysiology

Congenital

It is unknown if congenital CN 4 palsy arise from abnormal development of the nucleus or abnormalities in CN 4 itself, most will also have abnormal SO tendons [1]. The result is that patients with congenital CN 4 palsy will typically have the following characteristics:

1. Long standing head tilt (away from the involved eye)
2. Large vertical vergence ranges (typically > 5 pd)
3. Fuller face on the same side as the involved eye
4. No torsional diplopia

Acquired Trochlear Nerve Palsy

As CN 4 leaves the nucleus in the midbrain it decussates posteriorly and travels to the contralateral SO. This long course makes CN 4 susceptible to traumatic injury. There is a ridged portion of dura mater that separates the cerebellum from the inferior portion of the occipital lobes, called the tentorium, which lies adjacent to CN 4 and can insult the nerve during head injury.

- Nuclear lesions impact the contralateral superior oblique
- Midbrain trauma/compression or ischemia can produce bilateral superior oblique palsy See the image below.

Differential diagnosis of acquired 4th nerve palsy include:

- Trauma
- Tumor
- Aneurysm
- Microvascular

While an isolated CN 4 palsy is typically congenital or traumatic, the following clinical pictures should increase ones suspicion of more serious underlying causes:

- Suspect a nuclear lesion when CN 4 palsy is associated with a contralateral Horner syndrome or an ipsilateral relative afferent pupillary defect. The sympathetic pathways in the dorsolateral tegmentum of the midbrain and the pretectal afferent pupillary fibers that run through the superior colliculus near CN 4.
- Multiple neurological symptoms/signs
- Papilledema is also present (typically if increased intracranial pressure will cause a CN palsy it will be CN 6, however, it can also cause CN 4 palsy)

Treatment and Management for CN 4 Palsy

- Park's 3 Step
 1. Which eye is hyper in primary gaze?
 2. Which direction of gaze maximizes the double vision (hyper)?
 3. Which direction of head tilt maximizes the double vision (hyper)?

Example: Pt has a right hyper in primary gaze. The hyper worsens on gaze left (head turn right), and worsens on head tilt right. Which muscle is involved?



- Monitor if:
 1. Age >40
 2. Known microvascular disease
 3. No other neurological findings
 4. No new symptoms on follow up
 5. Resolution by 3 months
- Otherwise:
 1. Consider microvascular disease
 - Blood pressure, blood sugar, A1C
 2. Consider Inflammatory/infectious causes
 - CRP, ESR, RPR, FTA-ABS, Lyme titer
 - Testing for myasthenia gravis
 - Testing for multiple sclerosis
 3. Consider orbital disease
 - Orbital CT
 4. Consider cavernous sinus and brainstem disease
 - Brain MRI and CTA

Abducens Nerve Palsy (CN 6)

Signs and Symptoms

The primary symptom of a CN 6 palsy is horizontal diplopia and signs are an esotropia that is worse when looking in the direction of the involved eye. Often these patients will present with a head turn toward the involved eye, which will minimize/eliminate the double vision.

Pathophysiology

CN 6 innervates the ipsilateral lateral rectus (LR), so defects to CN 6 will lead to convergent strabismus. CN 6 leaves the pons and makes a bend around the petrous ridge of the temporal bone. This makes it susceptible to changes in intracranial pressure.

- Isolated peripheral lesions should result in, no vertical or torsional diplopia, but may result in a contralateral adduction defect (see LR and MR Connection sidebar)
- Nuclear lesions should not cause a contralateral adduction defect.

Differential diagnosis of acquired 6th nerve palsy include:

- Idiopathic Intracranial Hypertension (IIH)
- Tumor
- Microvascular

Treatment and Management for CN 6 Palsy

- Monitor if:
 - Age >40
 - Known microvascular disease
 - No other neurological findings
 - No new symptoms on follow up
 - Resolution by 3 months
- Otherwise:
 - Consider microvascular disease
 - Blood pressure, blood sugar, A1C
 - Consider Inflammatory/infectious causes
 - CRP, ESR, RPR, FTA-ABS, Lyme titer
 - Testing for myasthenia gravis
 - Testing for multiple sclerosis
 - Consider orbital disease
 - Orbital CT
 - Consider cavernous sinus and brainstem disease
 - Brain MRI and CTA

LR AND MR CONNECTION

40% of CN 6 neurons project into the ipsilateral medial longitudinal fasciculus (MLF) then decussate to the contralateral side and ascend to innervate that contralateral medial rectus subnucleus to participate in contralateral eye adduction. This communication leads to accurate yolked eye movements.

IIH-CN VI ASSOCIATION

According to the modified Dandy criteria CN VI palsy (and rarely CN VII Palsy), papilledema are the only localizing neurological defects that can be present in a patient with the diagnosis of IIH [28].

Facial Nerve Palsy (CN 7)

Signs and Symptoms

Patients with a CN 7 palsy can present with varying degrees of lower facial muscle weakness. The key is to differentiate between lower motor neuron weakness and supranuclear weakness is:

- Lower motor neuron weakness (Bell's): Entire side of the face does not function appropriately
 - Can't wrinkle forehead
 - Can't puff out cheeks
 - Can't close eye completely
- Supranuclear lesions (stroke/tumor): Will typically spare the upper portion of facial function so the patient **can wrinkle their forehead**. This is due to the fact that there is both contralateral and ipsilateral input into superior portion of CN 7 that innervates the forehead, upper eyelid and eyebrow.

Pathophysiology

CN 7 moves the face and also provides sensory input from the anterior 2/3 of the tongue for taste, it also provides parasympathetic functions for salivation and lacrimation. A CN 7 palsy can be complete or partial. Typically, a partial palsy will lead to a greater chance of complete recovery.

The paralysis is secondary to an axoplasmic disruption that may be the result of:

- Idiopathic
 - Bacteria
- Infectious
 - Viral
 - Lyme
- Traumatic
- Tumor
- Iatrogenic

Treatment and Management for CN 7 Palsy

- Treatment CN 7 Palsy
- Most will resolve without treatment
- Consider other neurological impairment (6/8)
 - Brain MRI
- Consider oral steroid – discussed later
- Consider oral antiviral – discussed later

Literature Update

Which CN palsy is LEAST likely to be microvascular?

- Among 109 patients enrolled in the study, 22 had cranial nerve III palsy, 25 had cranial nerve IV palsy, and 62 had cranial nerve VI palsy. A cause other than presumed microvascular ischemia was identified in 18 patients.
- **15/18 of these patients either had CN 3 palsies, only 3 patients with isolated fourth and sixth cranial nerve palsies were from other causes than microvascular.** [2]

How often are **acquired** trochlear nerve palsies due to tumors?

- In a series of 190 patients treated surgically for superior oblique palsy at the section of pediatric ophthalmology, the cause of superior oblique palsy was as follows [3]:
 - Congenital: 137
 - **Acquired: 53**
 - Trauma: 29
 - Iatrogenic: 12
 - Vascular: 7
 - **Tumor: 5**

Which microvascular risk factors is MOST likely to cause a CN palsy?

- Of the 54 patients, 16 (29.6%) developed a third nerve palsy, 19 (35.2%) a fourth nerve palsy, and 19 (35.2%) a sixth nerve palsy.
- **The risk factors of diabetes mellitus, hypertension, and hyperlipidemia were significantly more prevalent than other risk factors of heart disease, LVH, and smoking.**
- The mean number of risk factors was 2.3 ± 0.6 in the third nerve palsy group, 1.7 ± 0.9 in the fourth nerve palsy group, and 1.6 ± 1.0 in the sixth nerve palsy group.
- Patients with 2 or more risk factors showed a longer recovery period (9.0 ± 5.1 weeks) than did patients who had 1 risk factor (6.1 ± 2.2 weeks) [4].

Is aspirin effective at preventing CN palsies?

- Aspirin use was not associated with a reduced rate of ischemic third, fourth, sixth, and seventh nerve palsies among patients with diabetes mellitus and hypertension.
- **Aspirin appears to be ineffective in preventing ischemic third, fourth, sixth, and seventh cranial nerve palsies** [5].

What is the treatment of choice for a patient with an acute onset of Bell's Palsy?

1. A double-blind, placebo-controlled, randomized, factorial trial involving patients with Bell's palsy who were recruited **within 72 hours after the onset of symptoms**. Patients were randomly assigned to receive 10 days of treatment with [6]:
 - Prednisolone 25 mg PO BID + Placebo
 - Acyclovir 400 mg PO 5x/day + Placebo
 - Prednisone 25 mg PO BID + Acyclovir 400 mg PO 5x/day
 - Placebo + Placebo

Final outcomes were assessed for 496 of 551 patients who underwent randomization.

Resolution at 3 months:

- 83.0% prednisolone group
- 63.6% no prednisolone
- 71.2% acyclovir group
- 75.7% no acyclovir
- 79.7% both prednisolone and acyclovir

Resolution at 9 months:

CN Palsy Update for the Primary Care OD

- 94.4% for prednisolone group
- 81.6% for no prednisolone
- 85.4% for acyclovir group
- 90.8% for no acyclovir
- 92.7% both prednisolone and acyclovir

No serious adverse events in any group.

Clinical Take-home: **use prednisolone but not acyclovir.**

2. A double-blind, placebo-controlled, randomized, factorial trial involving patients with Bell's palsy who were recruited **within 7 days after the onset of symptoms and confirmatory PCR examinations (to rule out Zoster)**. Patients were randomly assigned to receive the following treatment [7]:

- Pred 60 mg/D x 5 day, 30 mg/D x 3 day, 10 mg/D x 2 day + Placebo
- Pred 60 mg/D x 5 day, 30 mg/D x 3 day, 10 mg/D x 2 day + Valacyclovir 1000 mg PO QD x 5 day

Final outcomes were assessed for 221 patients.

Resolution at 6 months:

- 95.7% both valacyclovir + prednisolone
- 86.6% prednisolone + placebo

No serious adverse events in any group.

Clinical Take-home: **use prednisolone AND valacyclovir.**

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