APPROACHING THE ED PATIENT WITH DIPLOPIA

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HISTORY:

CONFIRM BINOCULAR DIPLOPIA

With the exception of hallucinatory diplopia (pallinopsia), diplopia from a (possible) neurological etiology is caused by ocular misalignment causing each eye to perceive a different mages. As such it only occurs in binocular (i.e. both eyes open) conditions. Covering either eye will eliminate one image and eliminate binocular diplopia due to ocular misalignment. If the diplopia persists with either eye covered, the most likely cause is ophthalmic.

EXAMINATION:

EXAMINE HOW THE EYES MOVE INDIVIDUALLY AND TOGETHER

Once it is confirmed that the patient is experiencing binocular diplopia, the next step is to examine the eyes together and separately for movement limitations. Testing of saccades (look at my pen – held to the side), smooth pursuits (follow my pen) and voluntary gaze (look to the right) should be performed with attention to whether each eye moves fully within the eye socket. Comparing between the eyes can be helpful to identify abnormalities in up, down, left and right gaze. If there are any limitations, evaluation of eye movements induced by reflex maneuvers (e.g. vestibulo-ocular reflex using dolls eyes or caloric tests) can be helpful to localize any eye limitation to a supranuclear origin.

Examination of the extent of eye movements may be sufficient to characterize the eye movement disorder causing diplopia. However, it is important to recognize that full extraocular movements DO NOT exclude a neurological disorder causing diplopia.

DETERMINE EYE ALIGNMENT

The goal is to define the relative alignment of the eyes (turned in = esotropia, turned out = exotropia, right eye higher = right hypertropia, left eye higher = left hypertropia) in each direction of gaze (straight ahead, up, down, left, right). This may be obvious based on inspection. If not, one important clue is to ask the patient if they see double as you have them look in each direction of gaze. If they see two images ask them if the images are horizontally, vertically or obliquely oriented with respect to each other and if the images change in orientation/separation distance in different directions of gaze. If both the examiner and the patient are savvy observers - have the patient occlude one eye at a time to determine which image is coming from each eye. Due to the optics of the eye the orientation of the images will be opposite to the orientation of the eyes – for example, if the right eye is higher than the left eye, the right eye image will be lower than the left eye image.

Other methods of eye alignment testing include examining the reflection of light in the pupils for relative displacement off of the center of the pupil (e.g. if the light reflects of the inner iris of one eye this suggests the eyes are relatively turned out). Alternately covering each eye while the patient fixates on an object is an easy bedside test. The examiner observes for the direction of the corrective eye movement as each eye recovers fixation.

HISTORY, NEUROLOGICAL EXAM & LOCALIZE[1]

The logic behind a comprehensive eye movement examination is to facilitate pattern identification to localize the lesion, select appropriate diagnostic testing and institute appropriate empiric management. The eye movement exam is a small part of the cranial nerve exam and must be interpreted in the context of a full neurological examination and history.

COMMON PATTERNS & EXAMPLES OF ETIOLOGIES:

THIRD NERVE PALSY

A non-nuclear third nerve palsy in isolation affects the superior rectus, inferior rectus, medical rectus and inferior oblique (i.e. all EOM except the superior rectus and lateral rectus) to cause oblique diplopia in primary gaze, vertical diplopia in up and down gaze, horizontal diplopia in contralateral gaze and no diplopia in ipsilateral gaze.

Additional localizing signs are a larger ipsilateral pupil and ptosis. A nuclear third nerve palsy typically causes bilateral ptosis and bilateral upgaze deficits in addition to typical ipsilateral CN III signs.

- Can't miss diagnoses:
  - Aneurysm compressing the ipsilateral nerve, requires emergent angiographic imaging[2]
  - Uncal herniation typically associated with altered mental status
  - Brainstem parenchymal event (stroke, demyelination, tumor) including Benedikt syndrome (with contralateral movement disorder), Claude syndrome (with contralateral ataxia), Weber syndrome (with contralateral hemiparesis)
- Other causes: microvascular, trauma (usually severe), compressive from skull base tumor

FOURTH NERVE PALSY

A non-nuclear fourth nerve palsy in isolation affects the superior oblique muscle to cause vertical diplopia that is worse in down gaze, contralateral gaze and ipsilateral head tilt. Due to the torsional action of the superior oblique the image in the affected eye can appear tilted. Patients may adopt a compensatory head tilt. A nuclear fourth nerve palsy causes contralateral superior oblique dysfunction.

- Can't miss diagnoses:
  - Brainstem parenchymal event including with contralateral Horner syndrome
- Other causes: microvascular, trauma, decompensated "congenital", compression from skull based tumor

SIXTH NERVE PALSY

A non-nuclear sixth nerve palsy in isolation affects the lateral rectus muscle to cause horizontal diplopia in ipsilateral gaze that resolves in contralateral gaze. A nuclear sixth nerve palsy causes an ipsilateral gaze palsy (i.e. affecting both eyes and therefore without diplopia).

- Can't miss diagnoses:
  - Elevated ICP (e.g. tumor, venous sinus thrombosis, meningitis) causing 6th nerve palsy as a "false" localizing sign
  - Intracranial hypotension (e.g. CSF leak)
  - Cavernous sinus syndrome: The 6th nerve floats freely within the cavernous sinus and can be affected in isolation by pathologies in this region (see below)
  - Gradenigo syndrome (with pain and otitis media) due to petrous apicitis
  - Brainstem parenchymal event (stroke, demyelination, tumor)
- Other causes: microvascular, trauma

INTERNUCLEAR OPHTHALMOPLEGIA (INO) due to lesion of the medial longitudinal fasciculus

This is characterized by horizontal diplopia that is present in contralateral gaze only. Often there is nystagmus of the abducting (normal) eye and slowed adducting saccade of the affected eye. Adduction of the affected eye is often better during convergence, since this does not use the MLF.

- Can't miss diagnoses:
  - Stroke
  - Demyelination
  - Other brainstem parenchymal lesion
- Other causes: metabolic disorders

SKEW DEVIATION

This is a supranuclear disorder is characterized by vertical diplopia with tilting of images in both eyes. Typically it is associated with other vestibular or cerebellar symptoms and signs.

- Can't miss diagnoses:
  - Stroke
  - Tumor
- Other causes: peripheral vestibular lesions

ORBITAL APEX SYNDROME

Complete or partial involvement of CN III, IV, VI, V1 and the optic nerve localizes to the orbital apex. Focal processes may not cause significant orbital signs and be very difficult to discern on imaging.

- Can't miss diagnoses:
  - Fungal infection[3]
- Other causes: inflammation, tumor, vascular lesion, foreign body

CAVERNOUS SINUS SYNDROME

Complete or partial involvement of CN III, IV, VI, sympathetic pathways (Horner syndrome) V1 and V2 localizes to the cavernous sinus. Any process that elevates venous pressure in the cavernous sinus can transmit this pressure to the orbit to cause significant orbital signs including proptosis and red eyes. Vision can be affected if the process extends superiorly to the optic chiasm or if blood flow to the eye is affected. A standard head CT does not image this region adequately and imaging studies protocolled for the sella or pituitary region are necessary.

- Can't miss diagnoses:
    - Cavernous carotid fistula draining into the orbit is associated with a red, proptotic eye with ophthalmoplegia, possible vision loss and a prominent superior ophthalmic vein on orbital imaging
    - Cavernous sinus thrombosis, often associated with adjacent sinus infection can be bacterial or fungal and can progress rapidly to meningitis[4]
    - Cavernous carotid aneurysm[5]
    - Pituitary apoplexy can occur horizontally into one or both cavernous sinuses and is associated with vision loss if it extends superiorly to contact the chiasm or optic nerves. Patients are prone to acute adrenal insufficiency.[6]
- Other causes: neoplasm, inflammation

DIFFUSE DYSFUNCTION (overlaps with isolated dysfunction)

Myopathies and neuro-muscular junction disorders can affect single EOMs or combinations of EOM. The pattern of diplopia depends on which muscles are involved and can imitate eye movement disorders from higher causes. If ocular misalignment does not result, the patient may not have diplopia.

- Can't miss diagnoses:
    - Botulism is associated with systemic weakness, dilated pupils and constipation[7]
    - Wernicke's encephalopathy from B1 deficiency can affect eye movements in isolation as well as associated with ataxia, nystagmus and encephalopathy. Empiric treatment is necessary as blood thiamine levels do not reflect body stores[8]
    - Miller Fisher syndrome, associated with anti-GQ1b antibodies as well as areflexia and ataxia. Imaging is typically normal.[9]
    - Myasthenia gravis is usually associated with ptosis and can be associated with respiratory insufficiency if there is bulbar involvement
    - Inflammatory, infectious, neoplastic meningeal processes
- Other causes: thyroid eye disease (an inflammatory myopathy), orbital pseudotumor (an inflammatory mass lesion), mitochondrial myopathies (e.g. chronic progressive external ophthalmoplegia), gaze palsies from brainstem or hemispheric parenchymal lesions.

TESTING TO CONSIDER

MRI BRAIN is the test of choice to exclude brainstem parenchymal lesions such as stroke, demyelination or tumor as well as mass lesions causing 6th nerve palsy as a false localizing sign. Imaging evidence of meningeal processes of intracranial hypotension can also be captured.

MRI PITUITARY/SELLA provides detailed imaging of the cavernous sinus region and pituitary.

MRI ORBIT provides detailed imaging of the orbits and includes fat saturated images, which are helpful for visualizing T2 hyperintensity or contrast enhancement separate from the background T1/T2 hyperintensity caused by orbital fat.

MRA head or CTA head are useful for evaluating for aneurysms.[10] Catheter angiography may be necessary in cases of high aneurysm or fistula suspicion and for treatment of both.

MRV head is helpful to evaluate venous sinus thrombosis as a cause of sixth nerve palsy and to assess for cavernous sinus disease.

Lumbar puncture is helpful for investigation of subarachnoid based processes and for measurement of opening pressure as a cause of sixth nerve palsy.

EMG can be support the diagnosis of botulism, Miller Fisher syndrome and myasthenia gravis.

Serological testing can be helpful for the diagnosis of Miller Fisher syndrome, botulism, and myasthenia gravis.

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