Palsy of CN VI:
Approach to binocular diplopia:
with exception of palsies of
Duration of symptoms:
transient and intermittent symptoms
Presentation:
Binocularity:
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Binocularity: binocular double vision indicates misalignment of
eyes; ophthalmologist should confirm that symptoms improve
when patient closes one eye
Presentation: patients may report symptoms other than double
vision, such as skipping lines or blurring, and may spontaneously
assume specific head posture; some patients have significant
neuro-ophthalmologic problems or acquired abnormalities of
eye movements but do not report diplopia, perhaps because of
adaptive head position or disparate eye positions that result
in large distance between 2 images; lesions of orbital apex may
cause double vision but allow patient to ignore second image;
5% of patients have preexisting abnormality of binocular vision,
in which case, patient may be incapable of experiencing diplopia
but have subtle but significant palsy of cranial nerve (CN) III
Duration of symptoms: transient and intermittent symptoms
indicate different conditions; patients with intermittent diplo-
pia often have abnormality of eye movement even if symptoms
absent during examination; examples include hypertropia in
upgaze from disease of thyroid or large fusional amplitude
from congenital palsy of CN IV; transient symptoms suggest
giant cell arteritis (GCA), transient ischemic attack (in elderly
patient), or migraine (in younger patient)
Monocular diplopia: should not be referred to specialist, but
rather evaluated with techniques such as corneal topography
and pinhole; monocular diplopia not associated with neuro-
logic disorders
Approach to binocular diplopia: with exception of palsies of
CN III, most causes not serious; ophthalmologist should assess
alignment before sending patient to neurologist; asking subjec-
tive questions about what patient sees may reveal diagnosis;
subjective assessment of excursions, ductions, and versions
least effective way to assess diplopia, especially vertical dip-
lopia; instead, ophthalmologist should become familiar with
cover testing and Maddox rod; impaired eye movements must
be accompanied by evidence of misalignment
Palsy of CN VI: in absence of papilledema, most cases benign;
may be caused by neoplasms; carotid cavernous aneurysms
not life threatening; other etiologies include inflammation
and GCA; any older patient with CN palsy may have GCA; how-
ever, palsy of CN VI may be concerning in young patients;
among patients <60 yr of age with new palsy of CN VI, 40%
have multiple sclerosis or tumor; imaging — advisable; may
reveal small pontine stroke, intraxial lesion, demyelination,
or skull base neoplasm such as schwannoma or meningioma;
tumors of skull base may be associated with spontaneous
resolution of palsy of CN VI; delay of diagnosis may not
change outcome but likely to be perceived unfavorably by
patient; among 66 patients with isolated CN palsies, 9 had
abnormalities on imaging, including infarction of brainstem
and aneurysm; these patients clinically indistinguishable from
those with normal images
Differential diagnosis: meningioma; chordoma; nasopharyn-
geal carcinoma; tumor of frontal lobe; associated redness of
eye suggests fistula of carotid (often seen in women in sixth
or seventh decade who have hypertension [HTN]; associated
with dilated superior ophthalmic vein); examiner should also
assess CN V and VII and look for Horner syndrome, deaf-
ness, ipsilateral facial weakness, and increased intracranial
pressure; patients with vasculopathic etiologies improve
spontaneously; not all patients with acquired or long-stand-
ing esotropia have palsy of CN VI; in Duane syndrome, eyes
straight in primary position but large abduction deficit and
fissure narrowing seen on addiction; other mimics include
thyroid disease and convergence spasm (patients with con-
vergence spasm often young, with history of head injury);
orbital fracture may mimic palsy of VI; patients with long-
standing strabismus often have abduction deficits that may
cause diplopia; other conditions to consider myasthenia gra-
vis (MG) and adult-onset esotropia due to decompensated
esophoria or divergence insufficiency; esotropia in patients
with head injuries may be due to bilateral palsies of CN IV
with V-pattern strabismus
Palsy of CN III: should be ruled out in patient with adduction
deficit; alternating hypertropia, palsy of CN III, MG, and
internuclear ophthalmoplegia with pontine stroke should be
ruled out using Maddox rod or red glass; if adducting eye has
hypotropia in upgaze and hypertropia in downgaze, problem
may not be simple adduction deficit; if palsy of III and MG
ruled out, problem in brainstem; vertical diplopia — may be
associated with palsy of CN IV or III; skew deviation rarely
isolated and usually secondary to lesion in brainstem; other
etiologies occult thyroid disease, MG, trauma, and nonspe-
cific hyperphoria; patients with diplopia and ptosis have
either MG or palsy of CN III; 30% to 40% of patients with
vasculopathic palsy of CN III have pupillary involvement;
isolated, dilated pupil without ptosis or hypertropia not asso-
ciated with palsy of CN III, except in cases of herniation; in
series of patients with palsy of CN III, 100% had ptosis and
80% had motility defects; careful assessment of eyelid and
motility necessary; pupillary sparing refers to complete palsy

Educational Objectives
The goals of this program are to improve diagnosis and treat-
ment of double vision and interpretation of optical coherence
tomography (OCT). After hearing and assimilating this pro-
gram, the clinician will be better able to:
1. Diagnose a patient with diplopia.
2. Determine when to refer a patient with diplopia to a
neurologist or neuro-ophthalmologist.
3. Choose appropriate imaging studies for patients with
diplopia.
4. Explain the shortcomings of OCT scanners.

5. Choose the appropriate form of OCT to use, based on the
type of eye disease being assessed.

Faculty Disclosure
In adherence to ACCME Standards for Commercial Support,
Audio Digest requires all faculty and members of the planning
committee to disclose relevant financial relationships within
the past 12 months that might create any personal conflicts of
interest. Any identified conflicts were resolved to ensure that
this educational activity promotes quality in health care and
not a proprietary business or commercial interest. For this pro-
gram, members of the faculty and planning committee reported
nothing to disclose.
in presence of normal pupil; imaging — patients should be imaged to make expeditious diagnosis; patients with palsy of CN III and headache have aneurysm until proven otherwise; Tolosa-Hunt syndrome may present with palsy of CN III and intracranial HTN related to cavernous sinus, but many other disorders mimic this and diagnosis often incorrect; aberrant regeneration — patients with vasculopathic etiology do not demonstrate signs of aberrant regeneration, such as eyelid synkinesis (eyelid retraction on downgaze, also called pseudo-Graefe sign); however, patients with trauma or compressive etiologies may have aberrant regeneration; alternating hypertropias — different in upgaze and downgaze; associated with palsy of CN III but also occur when inferior rectus muscle injured in fracture; in cases with alternating hypertropia, bilateral palsy of CN IV should be ruled out.

Skew deviation: associated with strokes low in medulla; in contrast to palsy of CN IV, causes right hypertropia more pronounced in right gaze, and left hypertropia more pronounced in left gaze; differential diagnosis includes MG and thyroid disease

Palsy of CN IV: testing may not be required; in most cases of isolated palsy, patient has history of trauma or vasculopathic disorder; ophthalmologist may follow patient; difficult to diagnose by observing deficit in downgaze on adduction; 3-step test — additional signs present if palsy due to pineal tumors or other lesions; however, schwannoma of CN IV may present as isolated palsy; if 3-step test positive for isolated palsy of CN IV, finding may be congenital, vasculopathic, or due to trauma; intracranial disease rare; test does not detect all palsies of CN IV.

Differential diagnosis: includes thyroid disease, skew deviation with cycloptropia, and MG; bilateral palsy of CN IV characterized by left hypertropia in right gaze and right hypertropia in left gaze, V-pattern esotropia, and torsion >15°; congenital palsy of CN IV — common; may include symptoms suggesting long-standing problem in left or right gaze; examination demonstrates large fusional amplitudes and overaction of inferior oblique; no additional testing required.

Orbital disease: silent sinus syndrome — characterized by erosion of floor of maxillary sinus, large superior sulcus, and hypotropia on affected side; thyroid disease — patients have chronic symptoms; two-thirds report change in appearance of eyes, two-thirds have family history of thyroid disease, 60% have eyelid retraction, and 50% have exaggerated eye movements; ultrasonography or computed tomography (CT) may reveal diagnosis; on orbital ultrasonography, large muscle plus high reflectivity diagnostic for thyroid disease; imaging may distinguish thyroid disease from fibrotic condition of eye muscles seen in elderly patients.

Skew deviation: rare disorder; important to consider setting and ask about other symptoms; diagnosis should not be made unless patient has disease in brainstem; high eye found on same side as midbrain lesion; low eye found on same side as medullary lesion

Myasthenia gravis: most patients report acute symptoms; 90% have ptosis when diplopia first reported; 80% have fatigability, weakness of orbicularis oculi, or eyelid twitch; diagnosed via ice test and antibodies to receptor for acetylcholinesterase; in presence of normal pupil; imaging — patients should be imaged to make expeditious diagnosis; patients with palsy of CN III and internal limiting membrane, width of retinal nerve fiber layer half or two-thirds of that observed clinically; measurement using BMO has higher sensitivity and specificity for glaucoma.

Tips for Interpretation of Optical Coherence Tomography

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Challenges of imaging: clinicians do not always agree on location of margin of disc; new studies with spectral domain optical coherence tomography (OCT) show that clinical examination may not localize disc margin; anatomy of nerve fiber layer around disc varies; reproducibility of time domain OCTs poor; time domain OCT useful for macular disease but not glaucoma; normal parameters and optimal testing strategy need to be defined; quick scan useful for measuring macular edema, but slower scan better for examining posterior pole and assessing changes over time; like visual field test (VFT), OCT ancillary test; clinical decisions should not be based solely on changes in OCT.

Physics of time and spectral domain OCT: spectral domain OCT offers higher resolution and reproducibility; testing protocols should include clinical correlation; Stratus OCT provides slices through macula to allow measurement of its thickness, but slices may not intersect because time domain on time domain OCT slower than saccadic eye movements, so measurement of macular thickness inaccurate; in recent studies, Bruch membrane opening (BMO) most reproducible landmark on spectral domain OCT scans and marks anatomic edge of optic nerve (neuroretinal rim); study showed wide variability among glaucoma specialists in locating optic disc and cup.

Glucoma: characterized by damage to ganglion cells; different instruments used to analyze ganglion cell complex and layer; ideal instrument one that can accurately and reproducibly measure layer.

Optical coherence tomography: similar to ultrasonography, but uses near-infrared light instead of sound; time domain OCT measures time of flight of light; spectral domain OCT measures wave-lengths of back-reflected light and contains spectrometer that can measure all shifted wavelengths at same time, so scanning speed faster and errors not introduced by saccadic eye movements; spectral domain OCT more accurate than time domain OCT; swept source OCT next generation of scanning techniques.

Interpretation of OCT: includes evaluation of mean thickness of global retinal nerve fiber layer; nerve classified by scanning software as normal, borderline, or abnormal; asymmetry should be reviewed; as with VFTs, hemifields may be compared between eyes using OCT; definitive conclusions cannot be made on basis of single test; OCT should be correlated with VFTs and clinical findings.

Important elements of examination: although different examiners do not agree on location of margin of optic nerve, most important issue assessment of amount of rim remaining and determination of whether rim is becoming thinner; where and how to measure rim width, nerve fiber layer, and ganglion cell layer must be considered; on clinical examination of optic nerve, examiner actually looking at horizontal width of margin of rim; measurement from edge of rim to cup may differ significantly from true thickness of retina; on clinical examination, entire horizontal width interpreted as rim for optic nerve; however, when considering shortest distance between BMO and internal limiting membrane, width of retinal nerve fiber layer half or two-thirds of that observed clinically; measurement using BMO has higher sensitivity and specificity for glaucoma.
than measurement of horizontal width of rim or thickness of nerve fiber layer; tilt — on examination of fundus, fovea ≈ 7° lower than center of optic nerve; however, anatomy varies, so fovea lies between 2° above and 18° below horizontal center of nerve; measurements of nerve fiber layers do not account for tilt of nerve; scanners should adjust for tilt based on location of center of nerve as determined by BMO and center of fovea

Software and scanners: next generation of software from Heidelberg adjusts slices for tilt of nerve and anatomically centers posterior pole ganglion cell fitness map on fovea; Op- tovue scanner does not distinguish components of ganglion cell complex (ie, retinal nerve fiber, ganglion cell, and inner plexiform layers) from one another; Zeiss instrument provides ganglion cell analysis, which encompasses ganglion cell and inner plexiform layers; software designed to distinguish each layer currently being developed; due to anatomic variation in distance of nerve fiber layer from disc margin, new software will show 3 different rings (at different distances from center of nerve) which may be followed over time

Future developments: BMO to be used to give reproducible measurement of optic rim; minimum width of rim to be used to determine thickness of nerve fiber layer at head of optic nerve instead of assessing oblique cuts of nerve fiber layer; center of BMO to be aligned with fovea to adjust for tilt of optic nerve and provide more anatomical measurement of ganglion cell layer; >1 ring around optic nerve to be measured to assess nerve fiber layer

Acknowledgments

Dr. Volpe and Dr. Schertzer were recorded at 13th Annual Downeast Ophthalmology Symposium, presented by the Maine Society of Eye Physicians and Surgeons, and held September 19-21, 2014, in Bar Harbor, ME. For information about courses sponsored by the Maine Society of Eye Physicians and Surgeons, visit maineeyemds.com. The Audio Digest Foundation thanks the speakers and the Maine Society of Eye Physicians and Surgeons for their cooperation in the production of this issue.

Suggested Reading

1. In an older patient presenting with transient diplopia, the most important diagnosis to exclude is:
   (A) Thyroid disease
   (B) Congenital palsy of cranial nerve (CN) IV
   (C) Migraine
   (D) Giant cell arteritis

2. Before referring a patient with diplopia to a neurologist, the ophthalmologist should:
   (A) Test the patient for antibodies to acetylcholinesterase
   (B) Ensure that the diplopia is binocular (diplopia resolves with covering either eye)
   (C) Order orbital ultrasonography
   (D) Perform the ice test

3. A 65-yr-old woman presents with redness of the eye and palsy of the sixth nerve. Which of the following is the most likely diagnosis?
   (A) Tumor
   (B) Multiple sclerosis
   (C) Carotid fistula
   (D) Schwannoma

4. A patient with vertical diplopia secondary to a skew deviation is most likely to have which of the following?
   (A) Lesion in brainstem
   (B) Myasthenia gravis
   (C) Trauma
   (D) Giant cell arteritis

5. Until proven otherwise, a patient with a palsy of CN III and headache should be presumed to have:
   (A) Migraine
   (B) Aneurysm
   (C) Giant cell arteritis
   (D) Tolosa-Hunt syndrome

6. Imaging usually is required for patients with a palsy of:
   1. CN III
   2. CN IV
   3. CN VI
   (A) 1,2,3
   (B) 1,2
   (C) 1,3
   (D) 2,3

7. Which of the following is(are) common in patients with diplopia secondary to thyroid disease?
   (A) Retraction of the eyelid
   (B) Change in appearance of the eyes
   (C) Family history of thyroid disease
   (D) All the above

8. Choose the incorrect statement about time domain optical coherence tomography (OCT).
   (A) Has poor reproducibility
   (B) Useful for assessing macular disease
   (C) Useful for assessing glaucoma
   (D) Time domain is slower than saccadic eye movements

9. Which of the following is the most reproducible landmark for examining the optic nerve on spectral domain OCT?
   (A) Bruch membrane opening
   (B) Margin of the optic disc
   (C) Optic cup
   (D) Internal limiting membrane

10. OCT scanners are being developed that can adjust for tilt because the fovea is typically _______ to the horizontal center of the optic nerve.
    (A) 7° inferior
    (B) 2° inferior
    (C) 2° superior
    (D) 7° superior