Clinical Evaluation of Blepharoptosis: Distinguishing Age-Related Ptosis from Masquerade Conditions

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Abstract

Aponeurotic ptosis accounts for the majority of acquired ptosis encountered in clinical practice. Other types of ptosis include traumatic, mechanical, neurogenic, and myogenic. In addition to true ptosis, some patients present with pseudoptosis caused by globe dystopia, globe asymmetry, ocular misalignment, or retraction of the contralateral lid. It is particularly important for the clinician to rule out neurologic causes of ptosis such as dysfunction of the third cranial nerve, Horner's syndrome, and myasthenia gravis, as these conditions can be associated with significant systemic morbidity and mortality. A thorough history and physical examination is necessary to evaluate each patient presenting with a complaint of ptosis. Correctly identifying the cause of the patient's complaint allows the ptosis surgeon to plan for appropriate surgical repair when indicated and to defer surgery when observation or additional clinical evaluation is warranted.

Keywords

- ▶ ptosis
- ▶ blepharoptosis
- ▶ neurogenic ptosis

"Ptosis" is derived from the Greek word meaning "to fall." In oculofacial surgery, ptosis most often refers to blepharoptosis or drooping of the upper eyelid below its normal anatomical position that is typically found 1 to 2 mm inferior to the superior corneoscleral limbus.¹

The most common cause of acquired blepharoptosis is age-related stretching of the levator aponeurosis or dehiscence of the levator aponeurosis from its attachment to the tarsal plate of the upper eyelid.² Aponeurotic ptosis can be surgically repaired by resecting or advancing a portion of the levator aponeurosis, or in the case of dehiscence, by reattaching the distal margin of the levator aponeurosis to its normal site of attachment on the anterior surface of the superior tarsus.

Although a majority of patients presenting with a complaint of a drooping eyelid will have age-related aponeu-

rotic ptosis, a significant percentage of patients will have other causes for their complaints (▶ **Table 1**). It is important for the clinician to evaluate each patient with a thorough yet focused history and a physical examination to distinguish patients who require observation or further work-up from those who might benefit from surgical repair without further work-up.

Not All Eyelid Asymmetry Is True Ptosis

Some patients who present to the ptosis surgeon for surgical evaluation will have what is known as *pseudoptosis* or *apparent ptosis* due to globe dystopia, globe asymmetry, ocular misalignment, or retraction of the contralateral lid.

Table 1 Differential diagnosis of blepharoptosis

Neurogenic
Oculomotor / cranial nerve 3 dysfunction
Horner's syndrome / oculosympathetic paresis
Myasthenia gravis / ocular myasthenia subtype
Guillain-Barré syndrome / Fisher's variant
Multiple sclerosis
Cluster headache
Ophthalmoplegic migraine
Marcus Gunn jaw-winking syndrome
Botulism
Myogenic
Congenital ptosis
Congenital fibrosis of the extraocular muscles
Chronic progressive external ophthalmoplegia / Kerns-Sayre syndrome subtype
Muscular dystrophy
Oculopharyngeal muscular dystrophy
Mechanical
Eyelid tumors
Cicatricial processes (ocular cicatricial pemphigoid, Stevens-Johnson syndrome)
Dermatochalasis
Brow ptosis
Floppy eyelid syndrome
Pseudoptosis
Enophthalmos (orbital fracture, scirrhous tumor)
Contralateral lid retraction (thyroid eye disease)
Contralateral proptosis
Hypotropia
Irritative (secondary to conditions affecting the ocular surface)
Giant papillary conjunctivitis second to contact lens wear
Squinting or guarding from ocular surface disease (corneal erosion, abrasion, infiltrate, ulcer)
Iatrogenic
Botulinum toxin injection
Following cataract surgery or trabeculectomy
Traumatic (can be neurogenic, myogenic, or aponeurotic)

Dermatochalasis

Dermatochalasis or redundancy of the upper eyelid skin is common in older adults and can occur with or without true ptosis. Although true ptosis correction requires surgery to elevate the position of the upper eyelid margin, isolated dermatochalasis can be corrected by removal of excessive skin with or without fat debulking or redistribution. When a patient presents with redundant upper eyelid skin, gently lifting the excess eyelid skin allows the clinician to evaluate

the position of the underlying eyelid margin (► **Fig. 1**). Patients with both ptosis and dermatochalasis may benefit from combined ptosis repair and upper lid blepharoplasty. Correcting the ptosis alone may worsen the dermatochalasis as elevating the upper eyelid margin will increase the redundancy of the overlying skin.

Contralateral Eyelid Retraction

Some patients who complain of a drooping eyelid are found to have a normal position of the eyelid in question, but retraction of the contralateral eyelid causing asymmetry. The upper eyelid margin normally rests ~1 to 2 mm inferior to the superior corneoscleral limbus.¹ In patients with retraction of the upper eyelid, the margin may be flush with the superior corneoscleral limbus or several millimeters above it.³ The most common cause of eyelid retraction is thyroid eye disease (TED).^{4–6} Eyelid retraction is the most common finding in TED and is seen in over 90% of patients with thyroid dysfunction at some point in their clinical course.^{7,8} Ocular findings in TED may be seen in patients who are hyperthyroid, hypothyroid, or euthyroid,⁸ and may precede the onset of clinically detectable thyroid dysfunction.^{9,10}

Eyelid retraction can also be seen as a compensatory response in patients with severe ptosis of the contralateral eyelid. This is particularly true if the dominant or better-seeing eye is obstructed by the ptotic lid. As the patient strains to elevate the ptotic lid, increased firing of neurons results in the overelevation of the contralateral lid due to Hering's law of equal innervation.¹¹ Ptosis in this scenario is clinically obvious; however, the clinician may question whether the contralateral retraction is due to increased effort or a separate pathological process. Before assuming two separate processes (ptosis and contralateral eyelid retraction due to TED, for example) lift the ptotic eyelid to see if the contralateral lid returns to its normal anatomical position. If the eyelid does relax to a normal position, the mechanism of retraction is most likely secondary to the contralateral ptosis.

Globe Dystopia

Globe dystopia can result in the appearance of ptosis in the absence of true eyelid pathology. Enophthalmos or posterior displacement of the globe relative to the orbital rim most commonly occurs following orbital fractures, but can also be seen in silent sinus syndrome, in conditions associated with a decrease in the volume of orbital fat, and with fibrotic contracture of orbital contents such as in scirrhous breast cancer metastatic to the orbit.^{4,12} Although silent sinus syndrome often presents with few clinical signs and symptoms,^{13–17} processes that result in fibrotic contracture of orbital contents tend to be associated with restricted extraocular motility.^{18–23}

Hyperglobus and hypoglobus can be associated with an abnormal position of the eyelids relative to the globe and can be confused clinically as ptosis. It is important for the ptosis surgeon to carefully assess the position of the globe to rule out an orbital process masquerading as simple ptosis.

Occasionally, an orbital process will cause both globe dystopia and true ptosis. For example, a superior orbital

Fig. 1 Dermatochalasis masquerading as ptosis. (A,B) Redundant upper eyelid skin gives the appearance of a droopy lid. (C,D) Normal position of the eyelid margin can be seen after blepharoplasty to remove excess skin.

mass such as an orbital lymphoma involving the levator complex can cause both hypoglobus and ptosis. Often, the levator function will be reduced in this scenario, a very important finding that should alert the surgeon to a possible neurogenic, myogenic, or mechanical mechanism of the ptosis as opposed to aponeurotic ptosis, where the levator function should be normal. Assessing for a subtle malposition of the globe allows the ptosis surgeon to avoid surgically correcting the ptosis, while missing a potentially life-threatening diagnosis.

Globe Asymmetry

Asymmetry in the size of the globe can give the appearance of a ptotic lid. In unilateral myopia, the myopic eye is often longer and relatively more prominent, resulting in the appearance of contralateral ptosis. Microphthalmia, phthisis bulbi, and other conditions associated with a decrease in the size or volume of the globe can appear as ipsilateral ptosis. Although globe asymmetry may be clinically subtle in unilateral myopia, requiring additional history to make the diagnosis, microphthalmia and phthisis bulbi are often quite apparent, even to the nonophthalmologist.

Ocular Misalignment

In downgaze, the levator muscle relaxes allowing the upper eyelid margin to descend following the position of the globe. Patients with vertical strabismus may present with a com-

plaint of a droopy eyelid on the side of the hypotropic eye. In the presence of vertical strabismus, it is important to evaluate the eyelid's position with each eye fixating separately. When the hypotropic eye elevates to fixate on a distant target, the ipsilateral eyelid margin should elevate to a normal anatomical position.

Not All Ptosis Is Benign

Although a thorough examination is key in the evaluation of all patients with a complaint of ptosis, the clinical triad of eyelid position, pupillary examination, and extraocular motility is particularly important in the diagnosis of neurogenic ptosis (►Table 2).⁴ If one of the three is abnormal, the remaining two must be evaluated. Many clinicians would argue that the presence or absence of globe dystopia should be included, expanding the diagnostic triad to a tetrad. Failure to evaluate and document these physical examination findings in a patient with ptosis puts the patient at risk for harm and leaves the physician vulnerable to litigation.

In every patient presenting with ptosis, normal pupillary examination and extraocular motility testing must be documented prior to proceeding with ptosis surgery. Exceptions to this general principle include the presence of physiologic anisocoria or a documented history of a long-standing, stable, extraocular motility defect that has been worked-up previously (e.g., following strabismus surgery or in a patient with a

Table 2 The diagnostic triad in neurogenic ptosis

Diagnosis	Eyelids	Extraocular motility	Pupils
Cranial nerve 3 palsy	Unilateral ptosis	Limited adduction, supraduction, and infraduction	Normal to dilated; when present, anisocoria worse in dim illumination
Horner's syndrome	Mild unilateral ptosis "reverse ptosis"	Normal unless concurrent pathology is present. Motility deficit suggests a cavernous sinus process.	Constricted; anisocoria worse in bright illumination
Myasthenia gravis	Variable ptosis, unilateral or bilateral	Variable deficit, any pattern of limitation may be seen	Normal

documented history of a congenital third cranial nerve [CN3] palsy).

Physiologic Anisocoria

Physiologic anisocoria is relatively common, occurring in roughly one in five individuals.^{24,25} It is particularly common in patients who have had prior intraocular surgery such as cataract extraction from mechanical trauma to the iris sphincter.^{26,27} Because both ptosis and physiologic anisocoria have an increased incidence with age, it is not uncommon for the clinician to encounter patients with both ptosis and pupillary asymmetry.

Physiologic anisocoria is defined as 1 mm or less of pupillary asymmetry that does not vary significantly between dim and bright illumination.^{24,25} Anisocoria worse in dim illumination can be indicative of oculosympathetic paresis or Horner's syndrome. Anisocoria that is worse in bright illumination can be indicative of the parasympathetic dysfunction that can accompany a lesion of the CN3. It is essential that the ptosis surgeon feel comfortable in the assessment of pupillary size and light reactivity to determine which patients may safely proceed to surgery and which patients require further evaluation (►Fig. 2).

When pupillary asymmetry is present, evaluating old photos can be helpful to determine whether the asymmetry is long-standing and likely benign. If pupillary asymmetry cannot be confirmed as physiologic, the patient should promptly be referred to a neurologist or neuro-ophthalmologist for further evaluation.

Oculomotor Nerve Dysfunction

Oculomotor or CN3 dysfunction can occur due to the pathology of the brainstem nucleus or an injury of the nerve anywhere along its course from the brainstem, through the

cavernous sinus, into the orbit. There are multiple causes of acquired dysfunction of CN3, including compressive, ischemic, demyelinating, inflammatory, infiltrative, toxic, and traumatic etiologies. The most feared etiology is that of an expanding aneurysm of the posterior communicating artery, which can spontaneously rupture resulting in subarachnoid hemorrhage, brainstem herniation, and death.

CN3 palsy presents as unilateral ptosis with ipsilateral deficits of adduction, supraduction, and infraduction (►Fig. 3B-D). Because of the relatively unopposed function of the lateral rectus muscle innervated by the sixth cranial nerve and the superior oblique muscle innervated by the fourth cranial nerve, the eye is often slightly adducted and depressed, or in other words, in a "down and out" position. Parasympathetic fibers to the pupillary sphincter travel along the periphery of CN3 and receive more collateral innervation than the nerve itself.^{28,29} For this reason, compressive lesions are more likely to cause pupillary dysfunction, whereas ischemic infarcts of CN3 are more likely to be nonpupillary involving.²⁸

Under physiologic conditions, parasympathetic input to the pupillary sphincter muscle causes the pupil to constrict resulting in miosis. When parasympathetic input to the pupillary sphincter is interrupted, as in a compressive aneurysm, the affected pupil will fail to constrict resulting in relative mydriasis or pupillary dilation (►Fig. 3). In dim illumination, the contralateral pupil is also dilated, and the pupillary asymmetry is less pronounced. In bright illumination, the normal pupil constricts resulting in exaggeration of the asymmetry.

In patients presenting with *complete* CN3 palsy as indicated by the presence of complete ptosis and an inability to

Fig. 2 An algorithm for evaluating the patient presenting with ptosis and anisocoria. CN3, third cranial nerve; EOMS, extraocular movements; CT, computed tomography; CTA, computed tomography angiography; MRA, magnetic resonance angiography; MRI, magnetic resonance imaging.

Fig. 3 Pupil involving cranial nerve three palsy. (A) Incomplete ptosis of the right upper lid is noted. (B–D) The right eye is found to have deficits of supraduction (B), infraduction (C), and adduction (E). (E) Abduction of the right eye is normal. (F,G) Anisocoria is greater in bright illumination (G) as the right pupil fails to constrict.

adduct, supraduct, and infraduct the eye, management depends on the pupillary findings. If a dilated, sluggishly reactive pupil is present, emergent imaging with either magnetic resonance imaging/magnetic resonance angiography (MRI/MRA) or computed tomography/computed tomography angiography (CT/CTA) is mandatory to rule out a compressive aneurysm.^{30–32} For the ptosis surgeon evaluating a patient in the office, this clinical scenario warrants calling an ambulance to transport the patient to the nearest emergency room for urgent neuroimaging. A pupil involving complete CN3 palsy is an intracranial aneurysm unless proven otherwise by neuroimaging.

The management of a patient who presents with a non-pupil involving complete CN3 palsy is slightly more nuanced. If the pupil is not involved, and the patient is over 50 years of age with medical risk factors for microvascular disease, many clinicians will ascertain that microvascular ischemic disease is the most likely etiology and the ptosis will likely improve with time.^{32–35} If the patient is under 50 years of age, or lacks vascular risk factors, neuroimaging is required as microvascular disease is unlikely the cause. In practice, many clinicians will image all patients with a complete CN3 palsy regardless of age or pupillary involvement.

In patients with a *partial* CN3 palsy (incomplete ptosis and limited, but not absent extraocular motility) neuroimaging with either MRI/MRA or CT/CTA is indicated regardless of pupillary involvement as the patient may have an expanding aneurysm.^{32,35} For the nonophthalmologist, it is reasonable to refer all patients with suspected acute CN3 palsy for urgent imaging.

Although a complete CN3 palsy is not subtle, the ptosis and extraocular motility defect seen in a partial CN3 palsy can be easily overlooked. A cursory evaluation of extraocular motility can cause the examiner to miss slight limitations of adduction, supraduction, and infraduction at the extremes

of gaze, leading the clinician to miss a potentially life-threatening diagnosis.

Though pupillary findings are variable in patients presenting with CN3 palsy, some degree of extraocular motility deficit is always present. With a careful assessment of extraocular motility, the ptosis surgeon can avoid missing this possibly fatal diagnosis.

Horner's Syndrome/Oculosympathetic Paresis

Similar to other causes of neurogenic ptosis, the clinical findings in Horner's syndrome can be relatively subtle, yet the consequences for missing the diagnosis quite grave. Horner's syndrome or oculosympathetic paresis occurs due to pathology anywhere along the course of the oculosympathetic pathway. The first-order or central neuron in the sympathetic chain originates from the posterolateral hypothalamus and descends through the brainstem and cervical spinal cord to synapse at the ciliospinal center of Budge-Waller located at spinal cord levels C8 through T2. The preganglionic second-order neuron exits the spinal cord at approximately spinal cord level T1 and traverses the lung apex before ascending with the sympathetic chain to synapse at the superior cervical ganglion. The postganglionic third-order neuron travels superiorly along the common and internal carotid artery through the cavernous sinus and into the orbit.^{36,37} Sympathetic fibers innervate the superior and inferior tarsal muscles that act as secondary retractors for the upper and lower lid, respectively. The pupillary dilator muscle also receives sympathetic innervation resulting in pupillary dilation or mydriasis. Ipsilateral miosis or dilation lag are seen with disruption of the oculosympathetic pathway.

Congenital Horner's syndrome most commonly occurs due to birth trauma, although neoplasms and congenital abnormalities of the carotid vasculature can also be causative.^{38,39}

Congenital Horner's syndrome often can be identified by the presence of hypochromia of the ipsilateral iris as sympathetic innervation is thought to be necessary for normal pigmentation of the iris stroma.^{40,41}

The most common cause of acquired Horner's syndrome is iatrogenic disruption of the sympathetic chain due to surgery of the neck, cervical spine, or lung apex.⁴² Due to the close anatomical relationship of the sympathetic chain to the upper lung fields, Horner's syndrome may be seen in tumors affecting the pulmonary apices known as *Pancoast tumors*. The most feared cause of Horner's syndrome is a dissection of the internal carotid artery, which can occur spontaneously or due to trauma and can result in massive hemispheric stroke.⁴³

Clinically, Horner's syndrome presents as mild unilateral ptosis and a miotic pupil that dilates poorly in response to dim illumination. Although the classic triad is "ptosis, miosis, and anhydrosis," anhydrosis is rarely detected on clinical examination.³⁷ Transient ipsilateral ocular hyperemia may occur due to a lack of vascular tone from decreased sympathetic input.³⁷ Like anhydrosis, ocular hyperemia is often either too transient or too subtle to detect.

Eyelid findings in Horner's syndrome are due to the lack of sympathetic innervation to the upper and lower eyelid tarsal muscles. The upper eyelid tarsal muscle, also known as *Muller's muscle*, originates from the undersurface of the levator aponeurosis and inserts on the superior margin of the tarsus. It is thought to contribute to elevation of the upper lid contributing ~2 mm of elevation. Because of the relatively small contribution of Muller's muscle, the ptosis seen in Horner's syndrome is relatively subtle and can easily be missed. The sympathetically innervated inferior tarsal muscle has a similar role in augmenting the pull of the lower lid retractors. A loss of sympathetic tone to the inferior tarsal muscle results in "reverse ptosis" or elevation of the lower eyelid margin relative to its normal position at the inferior edge of the corneoscleral limbus.¹ Reverse ptosis is a relatively subtle clinical finding, but can be useful in making the diagnosis of Horner's syndrome if suspected. The combined effect on the positions of the upper and lower eyelid margins results in a decrease in the vertical component of the palpebral fissure and pseudoenophthalmos.⁴⁴

Pharmacological testing is used to confirm the diagnosis in cases of suspected Horner's syndrome (► **Table 3**).^{37,45–50} With the exception of cases known to be caused by surgical trauma and congenital cases that have previously been imaged, patients with Horner's syndrome should undergo imaging of the skull base, neck, and upper lung fields to determine the etiology of the oculosympathetic paresis. Unless the history provides localizing information, the first imaging study is typically MRI/MRA or CT/CTA of the head and neck to rule out a carotid dissection. If imaging of the skull base and neck are nondiagnostic, imaging of the pulmonary apex with a chest CT or a chest MRI is indicated. If the history or examination is highly suggestive of a pulmonary etiology, then imaging of the pulmonary apex can be the primary study. For a majority of patients, targeted imaging can be performed based on localizing information from the patient's history.⁴²

If ptosis is acute, with onset within 4 weeks of presentation, urgent imaging is indicated. For ptosis present for greater than 4 weeks at the time of initial assessment, nonurgent imaging can be scheduled, as studies have found the risk of stroke from a carotid dissection to significantly decrease after the first 2 weeks of symptoms.^{51,52}

Because the sympathetically innervated Muller's muscle is indicated in the pathophysiology of Horner's syndrome, conjunctivo-mullerectomy is often the surgery of choice for ptosis correction in patients with Horner syndrome.⁵³

Myasthenia Gravis

Myasthenia gravis (MG) is caused by antibodies to postsynaptic nicotinic acetylcholine receptors (AChR) at the neuromuscular junction of striated muscle.⁵⁴ Autoantibodies to the AChR receptor result in a loss of functioning AChR receptors at the postsynaptic motor endplate and reduced capacity of the muscle fiber to generate an action potential.^{54–56}

The orbicularis oculi, levator palpebrae superioris, and extraocular muscles are the most commonly affected muscles in MG with over 85% of patients presenting with periocular symptoms as the first manifestations of disease.⁵⁷ Unlike Horner's syndrome and CN3 palsy, which typically present with unilateral ptosis, ptosis in MG is often bilateral, although unilateral or asymmetric ptosis is not uncommon.

The hallmark feature of ptosis in MG is its variability. Ptosis in MG often varies throughout the course of the day and typically demonstrates fatigability with sustained effort. Variability of ptosis may be seen clinically as worsening of ptosis following sustained upgaze or inconsistent values when measurements of eyelid position and levator function are taken in planning for ptosis surgery. A complaint of ptosis that worsens at the end of the day is not particularly suggestive of MG, as virtually all ptosis worsens at the end of the day as the patient tires of using the frontalis muscle to assist in elevating the ptotic lid.

Due to weakness of the extraocular muscles, diplopia is a common complaint in patients with MG and limitations of extraocular motility are frequently seen on examination. Virtually any motility deficit can be seen. For this reason, MG should be considered in any patient presenting with ptosis, external ophthalmoplegia, or both. Because the causative antibody in MG affects only striated muscles, there is no involvement of the pupillary dilator or sphincter muscles. If a patient presents with ptosis, external ophthalmoplegia and nonphysiologic anisocoria, consider an alternative diagnosis.

Twenty percent of patients with MG have isolated ocular symptoms,⁵⁷ a condition referred to as ocular myasthenia (OM). In 80% of patients who initially present with OM, systemic symptoms will develop with time.⁵⁷ Systemic symptoms such as weakness and fatigue may be overlooked in elderly patients or falsely attributed to other conditions associated with aging.^{58–60} It is important to have a high index of suspicion in this population. Beware of bulbar symptoms such as shortness of breath, dysphagia, or dysarthria as these can indicate an impending myasthenic crisis.⁶¹

There are several ways to test for myasthenia. Ice testing can be done in any office setting and has high specificity and

Table 3 Pharmacological testing for Horner's syndrome

Agent	Response of normal pupil	Response of pupil affected in Horner's syndrome	Clinical finding with positive test	Mechanism	Notes
Cocaine (2%, 4%, 5%, or 10%)	Dilation	Minimal to no dilation	Exaggeration of anisocoria	Blocks reuptake of norepinephrine at the neuromuscular junction. If the sympathetic chain is disrupted anywhere along the 3 neuron chain, norepinephrine is not present in the neuromuscular junction, and cocaine will not cause pupillary dilation.	Controlled substance, difficult to obtain
Hydroxyamphetamine	Dilation	Presynaptic lesion: Dilation Postsynaptic lesion: Minimal to no dilation	Exaggeration of anisocoria	Causes release of norepinephrine from presynaptic terminal. In postganglionic lesions, no norepinephrine is available for release and the pupil will fail to dilate. In preganglionic lesions, the postsynaptic neuron is intact and the pupil will dilate.	Cocaine decreases effect of hydroxyamphetamine. Must be done 72 h or more after cocaine testing. Norepinephrine stores are depleted ~1 wk after onset of insult. Must be done 1 wk or more after symptom onset.
Phenylephrine (1%)	Minimal to no dilation	Presynaptic lesion: Minimal to no dilation Postsynaptic lesion: Dilation	Reversal of anisocoria	Denervation sensitivity of the iris sphincter occurs following loss of sympathetic innervation from a postsynaptic lesion resulting in pupillary dilation in response to dilute phenylephrine. Normal pupil fails to dilate in response to dilute phenylephrine.	Only useful after denervation hypersensitivity has developed (takes between 4–10 d), not useful in the diagnosis of acute Horner's syndrome. Requires dilution of 2.5% or 10% phenylephrine. False-negative results can be seen with excessive dilution. False-positive results can be seen with inadequate dilution.
Apraclonidine (0.5% or 1%)	Slight constriction	Dilation ^a	Reversal of anisocoria	α 2 adrenergic agonist with weak α 1 agonist activity. In the presence of chronic denervation, α 1 receptors are upregulated and the α 1 effect results in pupillary dilation.	Only useful after denervation hypersensitivity has developed (takes several weeks), not useful in the diagnosis of acute Horner's syndrome. Risk of CNS depression with use in children

Note: CNS, central nervous system.

^aThe pupil is larger than the other eye.

reasonably high sensitivity for MG.⁶² Ptosis measurements are made before and after an ice pack is applied to the upper eyelids and left in place for 2 to 3 minutes. Resolution or improvement of ptosis following application of the icepack is considered a positive ice test and suggests a diagnosis of myasthenia. A majority of myasthenic patients demonstrate an improvement of 2 mm or more in the position of the ptotic lid.⁶² Photographs taken before and after the icepack is applied can be useful for documenting the change in eyelid position. It is important to note that myasthenic patients with complete ptosis are less likely to respond to ice testing.⁶² When patients with complete ptosis are excluded, ice testing has both very high specificity and sensitivity for myasthenia.⁶²

The diagnosis of MG often can be confirmed by serologic testing assessing for antibodies to AChR, although 10 to 20% of patients with MG will be seronegative.^{63,64} Patients with OM are more likely than those with generalized MG to be seronegative, perhaps due to insufficient sensitivity of the test to detect low circulating antibody levels.^{63,64} Of the patients with generalized MG who test negative for the presence of AChR antibodies, 40 to 70% will demonstrate antibodies to muscle-specific tyrosine kinase (MuSK).^{65–67} MuSK antibody positivity is not seen in patients with isolated OM, but can be seen in patients with generalized MG and periocular symptoms.⁶⁷

If serologic testing is negative and clinical suspicion high, single-fiber electromyography (SFEMG) of the orbicularis oculi or frontal muscle can be done to confirm the diagnosis.⁶⁸ Edrophonium (Tensilon) testing can be done, although it is less commonly used due to the risk of cardiovascular side effects.

Although no urgent imaging is required in cases of suspected MG, patients should ultimately undergo a chest CT to evaluate for the presence of thyroid nodules or thymoma.⁶⁹ All patients with MG should be referred to a neurologist for further evaluation and treatment.

History and Physical Examination: Keys to Determining the Etiology of Ptosis

All patients presenting with a complaint of ptosis should undergo a thorough history and examination to determine the specific etiology of the droopy lid. Because many serious neurologic conditions can present as simple ptosis, it is important to utilize the history and examination to ensure that neurologic causes of ptosis are not missed.

History

Patient history should include duration of symptom onset (acute, subacute, or chronic), clinical course (improving, worsening, or unchanged), and any associated changes in vision such as blurry vision, diplopia, or loss of peripheral vision. Reviewing old photographs such as a driver's license photograph may help to determine whether the ptosis is acute or chronic. In some instances, patients will present with a complaint of recent-onset ptosis and a review of old photographs will reveal the ptosis to be mild, long-standing

congenital ptosis that has only recently been noticed or become bothersome to the patient.

Ocular history should include history of contact lens wear, strabismus, prior ocular trauma, and prior intraocular or eyelid surgery, including office-based cosmetic procedures such as injections of botulinum toxin or fillers. The medical history should include a history of obstructive sleep apnea and prior malignancy.

A review of systems should probe for complaints common in neurogenic ptosis such as headache, diplopia, or generalized weakness (►Table 4). Additionally, the surgeon should assess for bleeding tendencies and a history of adverse reactions to anesthesia.

Examination

At a minimum, a focused ptosis evaluation must cover the following clinical tetrad: eyelids, pupils, extraocular motility, and globe position. It is advisable to check pupils, extraocular motility, and globe position first, prior to in-depth assessment of eyelid position, as these exam findings are more likely to be forgotten if not done routinely at the start of the exam.

Pupils

A completely normal pupillary examination is often written "PERRLA" for Pupils Equal, Round, Reactive to Light and Accommodation. Key aspects of the pupillary exam that are missed by the PERRLA acronym are a response to dim illumination as well as the presence or absence of a relative afferent pupillary defect (rAPD). The four main questions the ptosis surgeon must answer with the pupillary exam are as follows: (1) Are the pupils symmetric in bright illumination? (2) Are the pupils symmetric in dim illumination? (3) Does the amount of asymmetry vary between bright and dim illumination? (4) Is there an afferent pupillary defect? An additional finding that should be noted is asymmetry in the speed of reactivity. For example, a pupil that is symmetric to its fellow pupil in light and dim illumination, but slower to dilate or constrict could indicate Horner's syndrome or CN3 palsy, respectively.

A pupil that is irregularly shaped may suggest an intraocular rather than neurologic cause for pupillary asymmetry. For example, an eye that has had cataract surgery or other intraocular surgery may have experienced iatrogenic injury to the iris sphincter muscle resulting in a pupil that is slightly larger than the contralateral pupil and that constricts poorly. Similarly, a patient with a history of prior intraocular inflammation may have a small pupil that is minimally reactive to light and dilates poorly due to the presence of adhesions between the iris and lens. If asymmetry is present, it is important to document the size of each pupil under both illumination settings.

One millimeter or less of pupillary asymmetry that is present unchanged in both bright and dim illumination may represent benign physiologic anisocoria. If anisocoria is thought to be physiologic, it is essential to specifically document that the amount of asymmetry is the same in both bright and dim illumination. For patients with light irides, evaluating old photographs often can confirm that the

Table 4 Neurogenic ptosis review of systems

CN3 dysfunction	Headache, diplopia, vasculopathic risk factors (hypertension, diabetes, hyperlipidemia), symptoms of giant cell arteritis
Horner's syndrome	Headache, neck or facial pain; recent head or neck trauma; prior neck, spine or chest surgery; history of tobacco use, shortness of breath, shoulder or arm pain
Myasthenia gravis	Muscle weakness, diplopia, shortness of breath, dysphagia, dysarthria

anisocoria is long-standing rather than acute. If there is any question as to whether anisocoria is physiologic, the patient should be referred urgently for neurologic or neuro-ophthalmic evaluation.

Extraocular Motility

Extraocular motility should be assessed in every patient presenting with ptosis as ocular motility deficits and ptosis tend to co-occur in neurologic and myopathic processes.

Many clinicians will assess supraduction and infraduction by instructing the patient to follow the examiner's finger as he or she makes an imaginary plus sign. Others will make an imaginary "H," which has the advantage of distinguishing the action of the vertical rectus muscles that maximally elevate and depress the globe in abduction from the inferior and superior oblique muscles that maximally elevate and depress the globe in adduction. Regardless of the approach, comparison with the fellow eye is useful, looking for symmetry in the capacity to supraduct and infraduct each eye. It is important to note that a mild symmetric supraduction deficit is not uncommon in the elderly.

When assessing adduction, look for the patient's ability to "bury" a portion of the nasal cornea into the medial canthal region. With maximal abduction, the temporal corneoscleral limbus should reach the lateral canthus and the temporal sclera should be entirely concealed. Comparison between the eyes is useful to detect subtle defects.

Bell's phenomenon or supraduction of the eye on voluntary lid closure is a corneal protective mechanism that should be assessed prior to ptosis surgery. Intact Bell's phenomenon indicates an ability to protect the cornea from exposure in the presence of mild lagophthalmos, which may be present transiently in the postoperative period. Patients with poor Bell's phenomenon have an increased risk of exposure keratopathy following ptosis surgery, particularly if overcorrected.

Globe Position

In each patient presenting with ptosis, it is important to assess globe position, noting any asymmetry between the eyes or globe dystopia. As discussed previously, enophthalmos and ocular misalignment can cause pseudoptosis in which the abnormal finding is related to the position of the globe rather than a primary lid issue. Proptosis or nonaxial dystopia may indicate a space-occupying lesion of the orbit.

Hertel exophthalmometry is useful as a quantitative measure of axial dystopia. In the absence of a Hertel exophthalmometer, laying the patient supine or in a reclined position and looking from above the top of the patient's head can be useful for a qualitative measure of relative globe position.

Brow and Forehead

Patients with ptosis often rely on the frontalis muscle, an elevator of the brow, to assist in lifting a ptotic lid. Deep horizontal creases in the midforehead and elevation of the brow are suggestive of frontalis recruitment. It is important to neutralize the action of the frontalis muscle prior to assessing the position of the upper eyelid. When taking measurements, gently apply digital pressure immediately above the ipsilateral brow to fixate the brow and neutralize the effect of the frontalis muscle on eyelid position.

Eyelid

The margin reflex distance-1 (MRD1) is the distance between the upper eyelid margin and the corneal light reflex with the eye in primary gaze. This measurement can be used to determine the presence or absence of ptosis and its severity. A normal value for MRD1 is 3.5 to 5.0 mm.^{70,71} It is important to ensure frontalis function is neutralized prior to measuring eyelid position. If the contralateral lid is ptotic, manually elevate the contralateral lid to eliminate the effect of Hering's law on the lid being measured.

Margin reflex distance-2 (MRD2) is the distance between the lower eyelid margin and the corneal light reflex with the eye in primary gaze. A normal value for MRD2 is between 4.0 and 5.0 mm. An abnormally low value for MRD2 characterizes what is known as "reverse ptosis" or "inverse ptosis," a finding that may be seen in Horner's syndrome due to a lack of sympathetic innervation to the inferior tarsal muscle. Other than its role in identifying the presence of "reverse ptosis," MRD2 is of relatively low diagnostic value and is not routinely measured by most ptosis surgeons.

The most important measurement when planning for ptosis surgery is the levator function as this measurement has implications for surgical technique. Levator function (LF) is measured as the total excursion of the upper eyelid margin from maximum downgaze to maximum upgaze. A normal value for levator function is between 13 and 16 mm.⁷² It is important to ensure the frontalis muscle is neutralized to obtain accurate measurements. In the presence of good levator function and mild ptosis, a conjunctivo-mullerectomy may be appropriate.^{73,74} If levator function is good but the ptosis is relatively severe (> 4 mm), a levator advancement procedure may be indicated. In the presence of poor levator function (5 mm or less), frontalis suspension often is required.⁷²

An additional measurement that can be of diagnostic value is the palpebral fissure or primary fissure, the distance between the upper and lower eyelid margins in primary gaze. A normal value for the height of the palpebral fissure is between 10 and 12 mm.¹ Measurements of the palpebral fissure in downgaze are

often increased in congenital ptosis due to fibrosis of the levator muscle and decreased in aponeurotic ptosis due to disinsertion of the levator aponeurosis from the tarsal plate.

There are several qualitative measures useful in ptosis evaluation. It is important to note whether significant dermatochalasis is present, and if so, to gently elevate the excess skin to assess the position of the underlying lid margin. In the presence of significant dermatochalasis, blepharoplasty should be considered in conjunction with ptosis repair.

When assessing the eyelids, the examiner should note the presence or absence of a lid crease and its distance from the eyelid margin. A normal lid crease is usually 8 to 10 mm superior to the upper eyelid margin centrally.¹ This distance is often increased in aponeurotic ptosis due to disinsertion of the aponeurosis from the superior tarsal plate.

Weakness of the orbicularis oculi muscle may be seen in MG and other myopathic etiologies for ptosis. The examiner can assess the strength of the orbicularis muscle by asking the patient to close his or her eyes tightly and resist the examiner's efforts to manually open them.

Examination of the lids should include an assessment of horizontal lid laxity. Horizontal lid laxity can be assessed by noting the extent to which the upper eyelid can be distracted horizontally, pulled up and away from the globe, or easily everted. Horizontal lid laxity can result in peaking of the lid margin following ptosis surgery if left uncorrected.

The presence or absence of lagophthalmos should be noted, and if present, the amount of exposure should be measured. The presence of lagophthalmos, orbicularis weakness, and absent or poor Bell's phenomenon are all predictive of exposure keratopathy following ptosis surgery.

In the presence of mild-to-moderate ptosis and good levator function, many clinicians will assess the response of the upper eyelid to administration of 10% phenylephrine; 2.5% phenylephrine may be used as an alternative to decrease the risk of systemic sympathomimetic toxicity. If the upper eyelid elevates to a normal or near normal position with the administration of topical phenylephrine, many clinicians will proceed with a conjunctivo-mullectomy.^{73,74} The exact amount of Muller's muscle resected is often determined by the amount of lid elevation achieved with topical phenylephrine administration.^{73,75}

Appropriate Management of Ptosis Depends on Accurate Diagnosis

It is essential to determine the cause of a ptotic lid as management will differ based on etiology. Traumatic ptosis and ptosis associated with vasculopathic CN3 palsy often improve or resolve spontaneously over a period of several months. For either condition, it is advisable to observe the patient for a minimum of 6 months prior to proceeding with ptosis surgery.

Ptosis associated with MG often improves with systemic therapy. Systemic treatment should be tried first, prior to proceeding with surgery. If ptosis persists despite appropriate treatment, surgical repair may be required, but is often challenging due to the inability to obtain consistent preoperative measurements.

Even among causes of ptosis correctable by surgery, the specific clinical diagnosis may guide the surgical plan. In Horner's syndrome and other cases of mild ptosis with good levator function and a positive response to topical phenylephrine, conjunctivo-mullectomy may be the procedure of choice.

When patient history or old photographs suggest longstanding, congenital ptosis, measurements of levator function often determine which surgical option is most appropriate. Patients with good levator function may benefit from resection of Muller's muscle or levator, depending on the severity of ptosis.^{76,77} Those with poor levator function often require frontalis suspension.^{72,78}

In a patient with CN3 palsy or other cause of poor supraduction with limited or absent Bell's phenomenon, the clinician may plan to lift the ptotic lid just high enough to clear the visual axis, preventing the risk of exposure keratopathy following surgery. This may also be a consideration in patients with orbicularis weakness and poor or incomplete blink.

Horizontal lid shortening is almost always required in patients with ptosis and floppy eyelid syndrome due to marked horizontal lid laxity.^{79,80} For the patient with ptosis found to have horizontal laxity of the upper eyelid on exam, a horizontal lid shortening procedure may be done alone or concurrent with levator advancement. In cases of mild ptosis, correction of horizontal laxity alone may result in adequate elevation of the eyelid margin.⁸¹

Conclusion

Each patient presenting with a chief complaint of ptosis should be evaluated with a thorough history and physical examination. Particular attention should be paid to pupils, extraocular motility, and globe position, as abnormalities may suggest neurogenic or myogenic processes. It is essential to rule out neurologic causes of ptosis such as dysfunction of the CN3, Horner's syndrome, and MG, as the consequences of missing these diagnoses can be quite grave. Correctly identifying the etiology of a ptotic lid allows the ptosis surgeon to plan for appropriate surgical repair when indicated and to defer surgery when observation or additional clinical evaluation is warranted.

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