

The Eye in Neurology: Evaluation of Sudden Visual Loss and Diplopia—Diagnostic Pointers and Pitfalls

S C LOONG,**FAMS, MBBS, FRACP*

Abstract

The evaluation of sudden visual loss should begin with the differentiation between monocular loss and binocular loss. The importance of this is reflected in the differences between the main causes of monocular and binocular losses. In cases of transient monocular visual loss, an ocular cause has to be kept in mind so as to avoid unnecessary and costly cerebrovascular investigations. In cases of persistent monocular visual loss, a compressive lesion of the optic nerve or chiasma may simulate optic neuritis. In the evaluation of diplopia, the main differential diagnoses are nerve lesions and myasthenia. The main causes of nerve lesions responsible for diplopia and their workup are summarised. The usefulness of eye signs in the diagnosis of myasthenia is highlighted. The possibility of compressive lesions co-existing with or masquerading as myasthenia is emphasised.

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An Approach to Sudden Visual Loss

The first step in the evaluation of sudden visual loss is to determine if the visual loss is monocular or binocular. The first diagnostic pitfall to avoid is the assumption that what is one-sided is one-eyed. A patient who complains of visual loss “on one side” may actually have a loss in one hemifield of each eye rather than a loss in one eye. Patients have notorious difficulty in differentiating between visual loss in one eye and in one hemifield. Those who develop a homonymous hemianopia are usually only aware of the loss in the temporal field. This is mainly because of overlapping of the nasal fields which compensates for any visual loss there.

To determine whether an episode of transient visual loss was monocular or binocular, enquiry should include

- i) whether alternate eye cover was attempted;
- ii) whether visual loss was altitudinal—as an altitudinal loss is almost invariably monocular;
- iii) if there was a positive scotoma—a positive scotoma is suggestive of a retinal lesion and hence is likely to be associated with sudden monocular rather than sudden binocular visual loss; and
- iv) if there were associated symptoms—for example, a

transient one-sided visual loss accompanied by vertigo is almost certainly due to a homonymous hemianopia from a vertebro-basilar transient ischaemic attack.

The importance of differentiating monocular visual loss from binocular loss becomes obvious when one looks at the main possible causes of sudden TRANSIENT visual loss (Table I). In the monocular cases, the most important cause in patients after the age of 40 years is ocular transient ischaemic attack from carotid artery disease. In binocular cases, the most important cause is probably raised intracranial pressure. Another important practical point is that if the visual loss is monocular, an ocular cause, in particular intermittent angle closure glaucoma, has to be kept in mind. On the other hand, ocular lesions are very unlikely to present with sudden, simultaneous, bilateral transient visual loss.

Amaurosis fugax due to carotid artery disease usually occurs spontaneously. However, it may be precipitated by light or heavy meal. The reason for light-induced loss is probably increased retinal oxygen demand on exposure to light in an eye with ocular ischaemia. Postprandial loss probably occurs because of the hypoperfusion of the retinal and choroidal circulations secondary to postprandial mesenteric steal.

* Neurologist, Private Practice

Adjunct Associate Professor, Division of Medicine, National University of Singapore

Visiting Consultant, National Neuroscience Institute and Singapore National Eye Centre

Address for Reprints: Dr S C Loong, Loong Clinic, 1 Orchard Boulevard, #07-02 Camden Medical Centre, Singapore 248649.

Intermittent angle closure glaucoma should be considered as a differential diagnosis for amaurosis fugax to avoid unnecessary and costly cerebrovascular investigations. The diagnostic pointers for this condition (Table II) include the “eclipse” sign. This is readily elicited with a pen light directed tangentially on the iris. A normal iris is completely illuminated whereas a shadow will fall on the medial aspect of an iris in an eye with angle closure glaucoma.

The importance of differentiating monocular from binocular visual loss is again evident when one considers the main causes of sudden PERSISTENT visual loss (Table III). In the monocular cases, the two most important causes are anterior ischaemic optic neuropathy (AION) and optic neuritis; while in the binocular cases, the causes are quite different.

The immediate concern in AION is whether it is arteritic or non-arteritic. The pointers for arteritic AION (Table IV) are fairly well recognised¹ and so is the fact that temporal artery biopsy is the only means of confirming the diagnosis. Perhaps not so well recognised is the diagnostic value of colour Duplex ultrasonography of the temporal arteries,² especially in patients who refuse biopsy. It has been shown that the characteristic finding in temporal arteritis is a dark halo around the arterial lumen; this is probably due to oedema of the arterial wall and disappears after steroid therapy.

TABLE I: CAUSES OF SUDDEN VISUAL LOSS—TRANSIENT

| Monocular | Binocular |
|------------------------------------|--|
| Carotid transient ischaemic attack | Raised intracranial pressure Migraine Epilepsy V-B transient ischaemic attack |
| Ocular lesion (glaucoma) | |

TABLE II: INTERMITTENT ANGLE CLOSURE GLAUCOMA—DIAGNOSTIC POINTERS

- Visual loss with poor lighting conditions
- Ocular pain
- Haloes around lights
- Poorly reactive semidilated pupil
- Injection of globe
- Corneal oedema + shallow ant chamber (slit lamp)
- “Eclipse” sign

TABLE III: CAUSES OF SUDDEN VISUAL LOSS—PERSISTENT

| Monocular | Binocular |
|-------------------------------------|----------------------|
| Anterior ischaemic optic neuropathy | Occipital infarct |
| Optic neuritis | Toxic neuropathy |
| Tumour | Pituitary apoplexy |
| Aneurysm | Complicated migraine |
| Infection (ethmoid-sphenoid) | Seizure |

While AION is the commonest neurological cause of sudden monocular persistent visual loss in the older age group, optic neuritis is the commonest cause of sudden monocular persistent visual loss in the young. “Optic neuritis” is a clinical term which refers to an optic neuropathy which is acute in onset, self-limiting and presumably due to inflammation accompanying a plaque of demyelination. The term covers (i) “papillitis”, in which the plaque of demyelination is anterior and causes visible changes in the optic nerve head, and (ii) “retrobulbar neuritis”, in which the plaque of demyelination is posteriorly situated and does not cause any visible change in the optic nerve head (a situation which may be described as “the patient seeing nothing and the doctor seeing nothing”).

Because the diagnosis of optic neuritis is essentially clinical, there are many conditions which can simulate it (Table V). The two most important causes of pseudo optic neuritis are AION and compressive lesions of the optic nerve or chiasma. It is not surprising that AION can simulate optic neuritis as both conditions are acute in onset and self-limiting. What may be surprising is that compressive nerve lesions may also be a culprit. Attention should be drawn to a survey carried out by Cogan³ several years ago. He wrote to 37 clinicians with a practice weighted towards neuro-ophthalmology and asked them to state the three most frequently missed or overlooked diagnoses that they encountered. Topping the list of overlooked lesions affecting the sensory visual system was compressive lesions of the optic nerve or chiasma; the most common compressive lesion was a subfrontal or suprasellar meningioma and the most common wrong label given to these compressive lesions was “optic neuritis”! Possible reasons for

TABLE IV: ANTERIOR ISCHAEMIC OPTIC NEUROPATHY (ARTERITIC)—DIAGNOSTIC POINTERS

- Systemic symptoms
- Preceding amaurosis fugax
- High erythrocyte sedimentation rate
- High C-reactive protein
- Massive visual loss
- Chalky white optic disc oedema
- Cilioretinal artery occlusion
- Fluorescein angiography—absence of choroidal filling

TABLE V: CAUSES OF PSEUDO OPTIC NEURITIS

- Anterior ischaemic optic neuropathy
- Compressive lesions
- Leber’s
- Syphilis
- Collagen vascular disease
- Sarcoidosis
- Cytomegalovirus (HIV)

compressive lesions simulating optic neuritis include:

- i) apparently sudden onset due to sudden discovery of visual loss;
- ii) genuinely sudden onset because of sudden decompensation due to oedema or haemorrhage;
- iii) visual field defects remaining relatively static for long periods; and
- iv) absence of other symptoms apart from visual loss.

The following pointers for pseudo optic neuritis should be kept in mind (Table VI):

- i) onset after 50 years of age—since optic neuritis is a disease of the young, any onset after 50 should raise suspicion;
- ii) inappropriate clinical course, especially if there is no recovery at all 1 month after onset;
- iii) the presence of optic atrophy despite a short history—this means sudden recent discovery rather than sudden recent onset of visual loss;
- iv) atypical visual field defects, especially an upper temporal visual field defect in the asymptomatic fellow eye (junctional scotoma); and
- v) dramatic response to or dependency on steroid—this should raise the possibility of sarcoidosis or collagen vascular disease instead of a demyelinating lesion. Another diagnostic pitfall to avoid is overemphasising the significance of temporal pallor. While it is characteristic, it is not diagnostic of optic atrophy secondary to optic neuritis.

An Approach to Diplopia

As for sudden visual loss, the first step is to determine whether the symptom is monocular or binocular (Fig. 1). For diplopia, the matter is easily settled by covering one eye. On covering one eye, a monocular diplopia will persist whereas a binocular diplopia will resolve. A monocular diplopia is almost always due to optical aberration within the refracting media and is not neurological. Neurological diplopia is binocular and is usually secondary to nerve, neuromuscular junction or muscle lesions.

Apart from thyroid eye disease which causes restrictive rather than paralytic ophthalmoplegia, muscle lesions causing diplopia are quite uncommon. Therefore, most diplopia is due to a nerve lesion or myasthenia. To determine which of the three nerves for ocular movement is responsible

TABLE VI: PSEUDO OPTIC NEURITIS—DIAGNOSTIC POINTERS

- Age >50 years
- Inappropriate course
- Optic atrophy (short history)
- Atypical field loss (junctional scotoma)
- Dramatic response to/dependency on steroids

for a diplopia, the following rules are usually adequate (Fig. 2):

- i) If the lateral rectus is visibly weak or if the diplopia is horizontal and maximum on looking outwards with the false image disappearing on covering the adducting eye, it is a sixth nerve lesion.
- ii) If the superior oblique is visibly weak or if the diplopia is maximum on looking inwards and downwards with disappearance of the false image on covering the adducting eye, it is a fourth nerve lesion.
- iii) Weakness of any of the remaining muscles suggests a third nerve lesion and there is usually a ptosis or dilated pupil to provide an additional clue.

The main causes of sixth nerve palsy and its workup are shown in Table VII. In adults above 50 years, the commonest cause is ischaemia related to diabetes, hypertension or

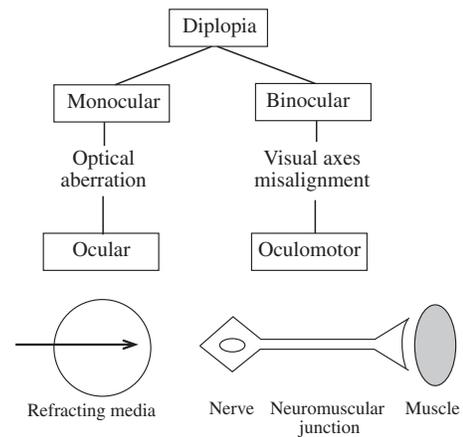


Fig. 1. Causes of monocular and binocular diplopia.

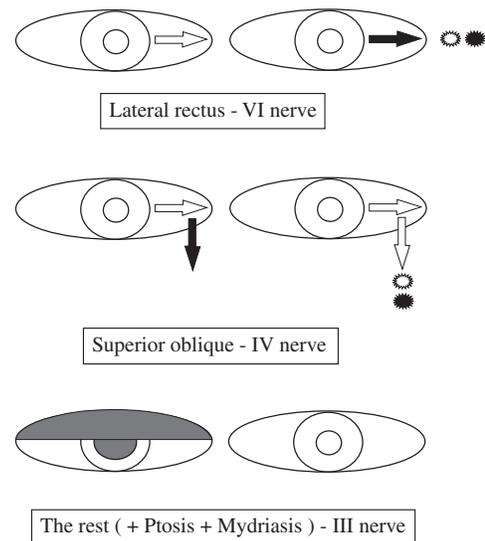


Fig. 2. Extraocular muscle weakness and diplopia in the sixth, fourth and third nerve lesions.

TABLE VII: SIXTH NERVE PALSY

| Causes | Workup |
|------------------------------|---|
| Adult | |
| Ischaemia | Glucose tolerance test Erythrocyte sedimentation test |
| Nasopharyngeal carcinoma | Nasopharyngeal endoscopy Computed axial tomography Magnetic resonance imaging |
| Children | |
| Neoplasm (brainstem) | Magnetic resonance imaging |
| Benign (postviral) | Observation |
| Any age | |
| Raised intracranial pressure | Funduscopy |

TABLE VIII: FOURTH NERVE PALSY

| Causes | Workup |
|-------------------------|---------------------------------------|
| Traumatic | History |
| Ischaemic | Glucose tolerance test, lipid profile |
| Idiopathic (congenital) | Family album tomographic scan |
| Neoplasm | Magnetic resonance imaging |

atherosclerosis; the most worrying cause is neoplasm, in particular nasopharyngeal carcinoma. In children, brainstem glioma is the main worry and an magnetic resonance imaging (MRI) is indicated. However, a history of preceding viral infection would suggest the possibility of a benign postviral sixth nerve lesion which is likely to recover within 10 weeks. At any age, the possibility of raised intracranial pressure must be excluded.

The main causes of fourth nerve palsy and its workup are shown in Table VIII. The commonest cause of a fourth nerve lesion is trauma. Ischaemia is an important cause, just as for a sixth nerve lesion. In the idiopathic group, a decompensated congenital fourth nerve palsy is a common cause and should be considered in all patients between late childhood and late forties with a superior oblique palsy without a history of trauma. The preferred investigation here is not a computed axial tomographic (CAT) scan but family album tomographic (FAT) scan to look for a compensatory head tilt in childhood photos.

For a third nerve palsy, the first and immediate step is to decide whether it is a “medical” or “surgical” third, and the answer lies with the pupil. The pupil is affected in 90% or more third nerve palsies due to aneurysms but spared in about 80% of third nerve palsies due to ischaemia. Therefore, if the pupil is affected, we are dealing with a surgical third until proven otherwise; and since the most important surgical cause is a posterior communicating artery aneurysm, angiography is indicated.

Pupil sparing by itself does not exclude an aneurysm or other compressive lesions as a cause of third nerve palsy.

TABLE IX: ISCHAEMIC THIRD NERVE PALSY—DIAGNOSTIC POINTERS

- Isolated third
- Pupil sparing complete
- External ophthalmoplegia complete
- Recovery within 3 months
- No aberrant regeneration

TABLE X: EYE SIGNS IN MYASTHENIA

- Ptosis
- Asymmetrical
 - Variable
 - Shifting
 - Fatigable: Enhancement-light/contralateral lid elevation
 - Improvement with ice pack
 - Cogan’s lid twitch
 - Lid hopping/fluttering (lateral gaze)
- Ophthalmoplegia
- Pupils normal
 - Not consistent with 3/4/6 (may mimic 3/4/6/internuclear ophthalmoplegia)
 - Isolated med rectus/inferior rectus/superior oblique
- Orbicularis oculi weakness
- Eyelash sign
 - “Peek” sign

For a medical third nerve palsy to be truly medical, the following criteria (Table IX) must be satisfied:

- i) it must be an isolated third nerve palsy;
- ii) the pupil must be completely spared;
- iii) a vascular risk factor must be present;
- iv) the external ophthalmoplegia must be complete;
- v) recovery must occur within 12 to 16 weeks; and
- vi) recovery should not be accompanied by aberrant regeneration.

Whenever analysis of a diplopia shows a pattern of muscle involvement which is not consistent with a third, fourth or sixth nerve lesion, the possibility of myasthenia must be considered. In fact, any ophthalmoplegia with a normal pupil should raise the possibility of myasthenia.

Some ophthalmological diagnostic pointers for myasthenia are shown in Table X. Apart from an ophthalmoplegia which does not fit into a nerve lesion, most of the ophthalmological diagnostic pointers are in the eyelids. There are at least 16 eyelid signs in myasthenia.⁴ The most common eyelid sign is ptosis. A ptosis which varies or fluctuates is suggestive and a ptosis which shifts from side to side is almost pathognomonic of ocular myasthenia. Other lid signs include Cogan’s lid twitch sign and lid hopping sign. Excessive fatigability, which is the hallmark of myasthenia, is usually demonstrable in the levator palpebrae on sustained upgaze. However, the standard procedure of asking the patient to maintain upgaze by

looking at a finger can be a prolonged and frustrating exercise. In fact, it is painful to watch a poor examination candidate trying to demonstrate lid fatigability and finding the arm getting increasingly tired and the examiner getting increasingly impatient while the lid refuses to oblige. Mercifully, the agony for both parties may be shortened by replacing the finger with a pencil light (the glare from the light enhances fatigability) or by passively elevating the contralateral lid. Another very useful eyelid sign to look for is weakness of orbicularis oculi with inability to bury the eyelashes (eyelash sign) or to sustain eye closure (peek sign).

As for diagnostic pitfalls in ocular myasthenia, it is worth bearing in mind that time-honoured signs such as fatigability, Cogan's lid twitch and the Tensilon test can be falsely positive. This is because dysfunction of the neuromuscular junction can occur secondary to a nerve lesion. A timely reminder of this came from Moorthy et al⁵ who reported 8 patients with tumours which affected the third and/or sixth nerves and co-existed with or masqueraded as ocular myasthenia. They were overlooked mainly because the pupils were normal and the ptosis showed fatigability, responded to Tensilon or was intermittent.

One striking fact about tumours causing pseudo myasthenia is that they are almost all in the cavernous sinus or at the sphenoidal ridge. This is not surprising for two reasons: (i) the three nerves responsible for ocular movement come together in these locations; (ii) at these sites, the third nerve has divided or is beginning to divide into a superior and an inferior division and the fascicles for the superior division which not carry the pupillary fibres may be selectively affected.

An analysis of reports of tumours co-existing with or masquerading as ocular myasthenia shows that it is prudent to consider excluding a tumour (Table XI) if:

- i) the muscle involvement is confined to one eye;
- ii) the muscle involvement is consistent with a pupil-sparing partial third and/or sixth nerve lesion;

TABLE XI: DIAGNOSTIC POINTERS FOR POSSIBLE PSEUDOMYASTHENIA

-
- Ophthalmoplegia strictly unilateral
 - Ophthalmoplegia suggestive of pupil-sharing third and/or sixth
 - Absence of orbicularis weakness
 - Pain
 - Impairment of corneal sensation
-

- iii) there is no orbicularis oculi weakness;
- iv) there is pain; and
- v) corneal sensation is impaired.

The usefulness of checking the corneal reflex is due to the close proximity of ophthalmic division of the trigeminal nerve to the third, fourth and sixth nerves in the cavernous sinus and superior orbital fissure. Using a wisp of cotton wool for the corneal reflex costs next to nothing and may save a great deal of headache and money in legal fees later!

In conclusion, the following warning seems appropriate: None is so blind as those who cannot tell if it is one or both eyes; and none is so cross-eyed as those who cannot tell if it is nerve or myasthenia.

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