LEARNING OBJECTIVES

1. The attendee should understand the typology of traumatic optic neuropathy.
2. The attendee should know the evidence behind the various treatment choices for traumatic optic neuropathy.
3. The attendee should know the basis for future treatments in traumatic optic neuropathy.

CME QUESTIONS

1. Treatment of indirect traumatic optic neuropathy with megadose corticosteroids in a patient with significant head injury is:
   a) Recommended.
   b) Not recommended because of lack of evidence.
   c) Not recommended because of increased risk of death.

2. Non-penetrating blunt head trauma with involvement of the optic nerve canal is likely to result in which of these fundus findings acutely?
   a) Disk edema
   b) Central retinal vein occlusion
   c) Central retinal artery occlusion
   d) Any of the above
   e) None of the above

3. The absence of a canal bone fragment or sphenoid sinus fluid essentially rules out:
   a) Significant optic nerve injury
   b) Any optic nerve injury
   c) It does not rule out either.

KEYWORDS

1. Trauma
2. Optic neuropathy
3. Corticosteroids
4. Optic canal decompression
5. Neuroprotection

INTRODUCTION

(Some of this syllabus is taken from Levin LA. Traumatic Optic Neuropathy. In Roy And Fraunfelder’s Current Ocular Therapy, 6th edition. Eds: Roy FH, Fraunfelder F. Saunders, Philadelphia, 2007, which in turn was adapted from the chapter of the same name by Neil Miller in the 5th edition.)

ANTERIOR VS. POSTERIOR TRAUMATIC OPTIC NEUROPATHY

Traumatic optic neuropathy is the name given to the syndrome of an optic neuropathy after head or ocular trauma in the absence of other causes. Like any other optic neuropathy, there are variable degrees of visual acuity and visual field loss, and an afferent pupillary defect if unilateral or significantly asymmetric.

Traumatic optic neuropathy is either anterior or posterior, and within each category, can either be direct or indirect. Trauma to the anterior optic nerve usually injures the central retinal artery and vein, which enter or exit the nerve approximately 10 mm posterior to the globe. This vascular injury often results in retinal infarct, hemorrhages, and/or disk edema, manifestations of central retinal or branch artery occlusion, central retinal vein occlusion, or anterior ischemic optic neuropathy.

Trauma posterior to the entrance and exit of the central retinal artery and vein from the optic nerve does not cause retinal vascular changes unless those vessels are simultaneously involved within the orbit. Axonal injury in the posterior optic nerve does not cause any acute effects on the disk, nerve fiber layer, or retinal ganglion cell layers. Axonal transport abnormalities posteriorly do not affect the more anterior nerve fibers, so disc edema is not seen in posterior traumatic optic neuropathy. For these reasons, isolated posterior traumatic optic neuropathy is associated with a normal fundus examination at presentation, and can be misdiagnosed, for example as factitious visual loss. Only after a few weeks are the structural signs of optic neuropathy evident, namely disk pallor and thinning of the retinal nerve fiber layer.

A particular type of posterior traumatic optic neuropathy is when there is injury to the chiasm, in which case there may be unilateral or bilateral temporal visual field defects respecting the vertical meridian. Chiasmal injury can be seen with posterior avulsion of the optic nerve, e.g. traumatic enucleation, or penetration from a foreign body.)
DIRECT TRAUMATIC OPTIC NEUROPATHY

Direct traumatic optic neuropathy is defined when there is penetration of the optic nerve by a foreign body or projectile. Anterior direct optic nerve injuries result from penetrating ocular or orbital trauma that damages the anterior optic nerve, e.g. a knife transecting the optic nerve just posterior to the globe. Posterior direct optic nerve injuries result from penetrating orbital or head trauma more posteriorly, e.g. a bullet that passes just anterior to the chiasm.

Direct injuries tend to produce severe and immediate visual loss, with little likelihood of recovery. The reason for this presumably is that a major element in these injuries is transection injury to retinal ganglion cell axons, which causes instantaneous loss of axonal conduction and an inability to regenerate axons later.

INDIRECT TRAUMATIC OPTIC NEUROPATHY

Indirect traumatic optic neuropathy is diagnosed when there is traumatic optic neuropathy but no foreign body. Indirect injuries are caused by forces transmitted at a distance from the optic nerve, e.g. blunt head trauma without penetration. The least common are anterior indirect injuries, which often usually associated with sudden rotation of the globe from blunt trauma. Examples include a digit to the globe or falling and hitting the eye on the corner of a table. Anterior indirect traumatic optic neuropathy can cause partial or total avulsion of the optic nerve, with associated hemorrhage and occlusion of the central retinal artery and vein.

Posterior indirect injury is the most common cause of traumatic optic neuropathy. Posterior indirect traumatic optic neuropathy results from blunt head trauma that transmits a concussive force to the optic nerve, resulting in contusion or sometimes transection. There may be little or no evidence of significant head trauma; a fall from a bicycle may suffice. In other cases there is multisystem trauma or significant brain injury. Loss of consciousness occurs in 40% to 72% of patients with traumatic optic neuropathy. Motor vehicle and bicycle accidents are the most frequent causes of traumatic optic neuropathy, accounting for 17% to 63% of cases. Traumatic optic neuropathy may be iatrogenic, especially after maxillofacial or endoscopic surgery as a result of inadvertent direct injury to the optic nerve or transmitted force fracturing the optic canal.

The most common site of posterior indirect optic nerve injury is the optic canal; the intracranial optic nerve is the next most common site of injury. There may or may not be bone fractures. Despite being most common, posterior indirect traumatic optic neuropathies fortunately occasionally have the most favorable prognosis, with spontaneous visual recovery sometimes occurring at variable times after injury. Presumably, the injury causes concussion and focal blockade of axonal conduction without loss of its structural integrity. Once there is healing of the edema or other molecular events blocking conduction, axonal function can return.

The severity of initial visual loss in patients with traumatic optic neuropathy varies from no light perception to better than 20/20, with sometimes only a visual field defect as functional evidence of disease. Patients with very poor vision (e.g. light perception only or no light perception) are less likely to improve, regardless of therapy, than are patients with vision better than light perception. The reason is likely that severe injury causes either axonal transection, membrane disruption, or cytoskeletal disorganization, any of which can lead to axonal dissolution and irreversible loss of conduction of visual information.

In some cases the visual loss only begins several hours to days after the injury. If this happens, the possibility of an intrasheath hemorrhage should be entertained, and neuroimaging repeated.

NEUROIMAGING

Neuroimaging is important in the evaluation of a patient with traumatic optic neuropathy not only for demonstrating correlative signs of injury, but also detection of pre-existing structural lesions and coincident intracranial effects of trauma, e.g. hematomas or carotid-cavernous fistulas. CT scanning is superior to magnetic resonance imaging (MRI) in delineating fractures of bone. It is critical that CT be performed with very thin sections, and reconstructions performed, particularly in the coronal plane. From 20% to 50% of patients with posterior traumatic optic neuropathy have evidence of an optic canal fracture by neuroimaging, and sometimes the clue is a small loss of contour of bone. Although the displacement on neuroimaging may be small, it is possible that at the time of injury, there was a much larger displacement of the bone into the canal. Even in the absence of a fracture, blood in the sphenoid sinus should raise suspicion for optic nerve injury.

MRI is better for imaging soft tissue, particularly the intracranial optic nerve and chiasm, and may be useful for delineating intrasheath hemorrhage or optic nerve transection within intact meninges. It is critical that MRI only be performed after a metallic intracranial, intraorbital, or intraocular foreign body has been ruled out by CT scanning or conventional radiography. If CT is used for screening, care should be taken to use thin slices and no interslice skip.

TREATMENT OF TRAUMATIC OPTIC NEUROPATHY

Anterior and Direct Traumatic Optic Neuropathy

There is no evidence that treatment of anterior optic injuries or direct optic nerve injuries is efficacious. In the former, the concurrent vascular injuries cause direct ischemia and infarction to the neural retina and/or optic nerve head, and the time until irreversible neuronal death
is measured in minutes to hours. In the latter, there is often sufficient direct axonal trauma to disrupt the integrity of the axon, up to and including its transection, and in the central nervous system of mammals, this is a point of no return for neuronal function.

An exception is anterior traumatic optic neuropathy associated with neuroimaging evidence of an enlarged optic nerve sheath. In these cases, an optic nerve sheath fenestration should be performed in the hopes of evacuating an intrasheath hematoma.¹

Posterior Indirect Traumatic Optic Neuropathy

With respect to posterior indirect traumatic optic neuropathy, the three commonly used approaches that have been used are very high doses ("megadoses") of corticosteroids, decompression of the optic canal, and observation alone.

Unfortunately, there is insufficient evidence from good quality randomized trials to guide decision-making on how to treat traumatic optic neuropathy. Because visual function often spontaneously improves in this disease, clinical trials are particularly necessary for physicians to select therapies based on evidence. Some of the critical issues are discussed below.

Megadose Corticosteroids

Experimental models of white matter trauma in animals showed that doses of fifteen to thirty milligrams per kilogram of intravenous methylprednisolone is protective for injured neurons². The NASCIS 2 and 3 studies found that patients treated within 8 hours of spinal cord injury with a loading dose of 30 milligrams per kilogram of intravenous methylprednisolone load followed by 5.4 ml/kg/hr continuous infusion for 48 hours had a better outcome than control patients³, ⁴. Extrapolating these results to traumatic optic nerve injury, it was thought reasonable to believe that similar doses should be used for injury to this comparable central nervous system white matter structure. However, over the years there has been controversy about interpretation of the NASCIS data⁵, ⁶, and its application to the treatment of spinal cord injury is not uniform⁷, ⁸. Furthermore, animal and cell culture data suggest that high doses of methylprednisolone may actually be toxic for the retinal ganglion cell and/or its axon⁹-¹¹. Finally, the Corticosteroid Randomisation After Significant Head Injury (CRASH) trial demonstrated that 48 hours of megadose methylprednisolone significantly increased the risk of death after head injury¹², with a hazard ratio at 6 months of 1.15 (95% CI 1.07-1.24)¹³. The authors concluded:

"...these final results still provide clear evidence that treatment with corticosteroids following head injury affords no material benefit. The absence of evidence of any neurological benefit from corticosteroid treatment after head injury might also have implications for the use of corticosteroids in spinal cord injury, which should remain an area for debate."¹³⁺

Optic Canal Decompression

Decompression of the optic canal is usually achieved through the transethmoidal route, most commonly via an external ethmoidectomy or endonasally.¹⁵, ¹⁶ The canal is then decompressed inferomedially from the superior lateral wall of the sphenoid sinus, with care taken to avoid the carotid artery. Although the canal can also be decompressed through an intracranial approach, the former is less invasive. However, if surgery is being performed for other reasons necessitating unroofing of the canal, then an argument can be made that decompression of the canal should be done through this approach.

However, there is also no evidence that optic canal decompression is efficacious. A recent Cochrane review concluded that:

"There is no conclusive evidence that any particular form of surgical decompression improves the visual outcome in TON. The decision to proceed with surgery in TON remains controversial and each case needs to be assessed on its own merits. The final decision will inevitably reflect a combination of clinical judgement, the availability of local surgical expertise and the patient’s perception of the possible risks and benefits."¹⁷

If surgery is to be considered, it should only be performed in centers with experience with the procedure. Because of the possibility that the carotid may be iatrogenically injured, there should be informed consent regarding the risk of death or stroke. Surgery should not be performed on an unconscious patient because of the difficulty in assessing visual function. A possible exception is when the pupil in the affected eye is amaurotic, i.e. nonreactive to light but reactive to light in the contralateral eye. The presence of a relative afferent pupillary defect indicates only that an optic neuropathy is present; it does not indicate the severity. A patient with a relative afferent pupillary defect may have 20/20 visual acuity.

Observation

Traumatic optic neuropathy may improve without any treatment¹⁸. There are no convincing randomized control trials to show a treatment benefit in traumatic optic neuropathy, and a nonrandomized concurrent comparative study did not demonstrate clear differences between treatments and observation¹⁹. Therefore when a patient cannot give informed consent for corticosteroid or surgical therapy, some neuro-ophthalmologists may simply observe the patient. This is especially reasonable when it is difficult to assess the status of the afferent visual system, e.g. in an unconscious or pediatric patient, unless one eye is completely blind, as manifested by an amaurotic pupil (one that does not react directly to light but does react consensually).
FUTURE TREATMENTS

Neuroprotection has been a popular subject of research for optic nerve disease, as a way of preventing the death of retinal ganglion cells. Most studies of neuroprotection in animals use as an outcome measure the number of surviving retinal ganglion cells. However, treatments that maintain retinal ganglion cell viability without taking into account their ability to function are unlikely to be useful clinically when translated to human use. For patients, visual function is the critical endpoint, and the value of neuroprotection directed at retinal ganglion cell soma survival alone is questionable.

The questionable utility of somal neuroprotection is especially true for traumatic optic neuropathy, which occurs as a result of axonal damage. A treatment which maintains the viability of the ganglion cell body but leaves the axon injured is unlikely to be effective at maintaining function. On the other hand, treatments that not only keep the retinal ganglion cell from dying, but also maintain its metabolic and biochemical functions, might still be helpful because the “invigorated” cell body could better maintain an injured axon. This would explain why treatments which work at the cell body (e.g. NMDA antagonists) help preserve visual function despite axonal degeneration is delayed in these mice, death of the cell soma by classic apoptosis occurs at the same rate as wild type mice. Therefore, axonal degeneration and somal apoptosis occur by different and autonomous molecular mechanisms22,23, and it is likely that therapeutic approaches aimed at the former may be of value for traumatic optic neuropathy.

Another approach is based on the studies of the Wallerian degeneration slow (Wld) strain of mice. Wld mice have a mutation which results in delayed Wallerian degeneration in both the peripheral and central nervous systems. Axonal degeneration takes place in weeks instead of days after injury or axonal disease. Although axonal degeneration is delayed in these mice, death of the cell soma by classic apoptosis occurs at the same rate as wild type mice. Therefore, axonal degeneration and somal apoptosis occur by different and autonomous molecular mechanisms22,23, and it is likely that therapeutic approaches aimed at the former may be of value for traumatic optic neuropathy.

CME ANSWERS

1. c
2. e
3. c

REFERENCES


