Author's response to reviews

Title: Reversal of isolated unilateral optic nerve edema with concomitant visual impairment following blunt trauma: a case report

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Author's response to reviews: see over
Dear Editor,
Dear Referees,

first of all, please allow me to apologize for the delay in revising and resubmitting the above referenced manuscript due to the tragic loss of a close family member. Thank you for your understanding and for the extension of the deadline for resubmission.

To the manuscript:

Thank you very much for considering my above referenced manuscript for publication in the “Journal of Medical Case Reports” as well as for your valuable comments and suggestions with regard to further improvement of the manuscript. I was happy to note that it contains some interesting informational value to the readers of the “Journal of Medical Case Reports”. In the following, please find my detailed comments to each of the reviewer´s points of criticism, point by point. The corresponding changes and modifications within the manuscript are highlighted in bold.

Reviewer #1: Michael Lee
The major issue is that the CRASH trial published in the Lancet in 2002 showed that patients with head injury should not be treated with high dose corticosteroids because it increases the risk of mortality. This needs to be addressed since the author is advocating an intervention that is not standard of care. The International Traumatic Optic neuropathy Study found no difference between observation, steroids, and surgery. In fact more than 50% of patients in the observation group improved. The author needs to comment on that this patient may have improved without any therapy whatsoever.

The author agrees with this reviewer´s comment and suggestion. The author is aware of the results of the CRASH trial as well as of the results of the International Traumatic Optic Neuropathy Study. The results from both trials are now considered as the author has considerably rewritten the “Discussion”-section of the revised manuscript. The sub-section on potential therapeutical options in traumatic optic neuropathy within the revised “Discussion”-section of the manuscript now reads as follows:

Currently, there is no validated approach to the management of traumatic optic neuropathy. The International Optic Nerve Trauma Study [12] was initiated to compare the visual outcomes of patients observed without treatment with those of patients treated with corticosteroids and of patients treated with optic canal decompression surgery. This multicenter, comparative, interventional but non-randomized trial comprised 133 patients with traumatic optic neuropathy
from 16 countries. Treatment decisions were according to the investigators' customary practice and no specific protocols for corticosteroid treatment or surgical technique were followed. The results showed that visual acuity improved in 32% of patients treated with surgery, in 52% of patients treated with corticosteroids, and in 57% of untreated patients. Thus, there was no clear benefit observed for either corticosteroid therapy or optic canal decompression. The results further showed that neither the dosage or timing of corticosteroid treatment nor the timing of optic canal decompression were associated with an increased probability of improved visual acuity. The authors concluded that neither corticosteroid therapy nor optic canal decompression should be considered the standard of care for patients with traumatic optic neuropathy and that therapeutical decisions should be made on an individual patient basis. In the present case, the patients' symptoms quickly responded to corticosteroid therapy but considering the results from the International Optic Nerve Trauma Study, this patient may have improved without any specific therapy whatsoever as well.

The rational for intravenous corticosteroids for the treatment of traumatic optic neuropathy was derived from the results of the National Acute Spinal Cord Injury Study 2 (NASCIS 2). The NASCIS 2 was a multicenter clinical trial that evaluated patients with acute spinal cord injury treated with placebo, methylprednisolone, or naloxone. Pharmacologically, corticosteroids are considered to reduce microvascular spasm and soft tissue edema via stabilization of the microvascular circulation and calcium homeostasis, thereby enhancing blood flow and reducing cell death. The study showed that methylprednisolone started within 8 hours of injury was associated with a significant improvement in both motor and sensory function compared to patients treated with a placebo. Although widely accepted, the question whether corticosteroids are of similar effect in the treatment of traumatic optic neuropathy is unproven. The majority of case reports and series with corticosteroids in traumatic optic neuropathy are retrospective, non-consecutive, non-randomized, and uncontrolled. Meanwhile, several non-clinical studies questioned the therapeutical benefit associated with corticosteroids in acute traumatic optic neuropathy [13,14]. The results from the CRASH-trial indicated even a higher risk of mortality in patients with head injury treated with high-dose corticosteroids. One may speculate that the pure white matter optic nerve is not pharmacologically affected in the same manner as the mixed white and gray matter spinal cord.

Surgical optic nerve decompression has similarly been advocated to improve visual prognosis in traumatic optic neuropathy. Recently, Yu Wai Man and Griffiths [15] assessed the effects and safety of surgical interventions in the management of traumatic optic neuropathy. Based upon only small and retrospective case series and the wide range of surgical interventions they encountered considerable difficulties in comparing the body of evidence available. Given the relatively high rate of spontaneous visual recovery they concluded that there is no evidence that surgical decompression of the optic nerve provides any additional benefit [15]. However, in selected cases in which orbital bone fragments or foreign bodies impinge on, but do not transect, the optic nerve, surgical intervention may be indicated. In any case, one should be aware of the fact, that surgical intervention carries a definite risk of complications such as i.) collateral damage to structures of the orbital apex as well as other intracranial structures, ii.) iatrogenic direct and indirect optic nerve damage, the latter via disruption of the pia, and iii.) postoperative cerebrospinal fluid leaks and meningitis. Similar to corticosteroids, the approach with surgery in traumatic optic neuropathy remains controversial and each case needs to be individually assessed.
In the discussion the author states that visual acuity and pupillary (NOT PAPILLARY) reaction, and visual field needs to be assessed. The report does not give us this information. Tell us what the pre and post treatment acuity and the pupil exam showed. Please send the pre and post visual fields or were these simply confrontation fields. If the pupil exam did not show an afferent pupillary defect then this very well may not have been traumatic optic neuropathy. Retinal edema can be traumatic and can cause a transient loss of vision or visual field. Retinal injury would not likely show an afferent pupillary defect.

The author agrees with all comments and suggestions made by this reviewer and has thus revised the manuscript accordingly. Visual fields have only been investigated via confrontation fields. Please find all requested changes highlighted in bold in the revised version of the manuscript now submitted where it now reads as follows:

[...] On day 2 after trauma the patient complained about blurred vision. Ophthalmology was called and revealed a visual field loss to the right lower quadrant upon confrontation field testing. Clinical eye examination further revealed a visual acuity for the right eye of 0.5 decimal (LogMAR 0.30, Snellen ratio 20/40) and for the left eye of 0.8 decimal (LogMAR 0.1, Snellen ratio 20/25); pupil testing indicated an afferent defect to the right eye. There was no history of eye disease prior to the accident upon questioning. Imaging studies including magnetic resonance imaging (MRI) of the orbit showed an isolated unilateral distension of the right optic nerve with an edematous soaking of the adjacent retroorbital fat (Figure 1). No fracture of the skull and of the optic canal and no intracranial pathology was noted. High-dose corticosteroids were administered for three consecutive days and then reduced. The patient’s symptoms responded quickly to this approach. Repeated eye examination after one week showed normal testing results for pupillary function and confrontation fields, visual acuities returned to 1.0 decimal on both eyes (LogMAR 0.00, Snellen ratio 20/20).

*It is not clear that the right optic nerve is swollen on the MRI. Did it show any abnormal signal? Did it enhance with gadolinium? The fat on the bottom part of the figure may just be poor fat suppression.*

The author agrees with this reviewer’s points of criticism and has thus rewritten the sub-section on his MRI-findings. Re-consultation with the local neuroradiologists once again re-confirmed the picture of an unilateral distension of the right optic nerve with an edematous soaking of the adjacent retroorbital fat. Within the revised version of the manuscript it now reads as follows:

Imaging studies including magnetic resonance imaging (MRI) of the orbit showed an isolated unilateral distension of the right optic nerve with an edematous soaking of the adjacent retroorbital fat (Figure 1).

Contrast enhancement, for example with gadolinium, was not performed. As the fat on the bottom part of the original figure may have been just poor fat suppression the lower panel of the figure, e.g. panel c, was removed.

*Minor changes to English dictions.*

The entire manuscript has been revised by the author as well as by a native speaker with special reference to English dictions.
MRI is magnetic resonance imaging.

The author agrees with this suggestion and the entire manuscript has been revised accordingly.

**Reviewer #2: Patrick Yu Wai Man**

[...] revealed a visual field loss in the right lower quadrant with absent organ pathology [...] What were the actual visual acuities (Snellen or LogMAR)? What does the author mean by absent organ pathology? Does it mean that there was no disc swelling or retinal changes on fundoscopy?

[...] The patient’s symptoms responded quickly to this approach and decompression was not indicated [...] The actual visual improvement needs to be clearly stated.

This reviewer requests more detailed information on the clinical presentation and course of the patient reported here. The author agrees that some relevant information was missing in the first version of the manuscript that was submitted for publication. The sub-section of the manuscript in which the author presents the patient’s history and clinical course has been revised according to this reviewer’s suggestions and requested clinical information and data is now presented. In the revised version of the manuscript it now reads as follows:

[...] On day 2 after trauma the patient complained about blurred vision. Ophthalmology was called and revealed a visual field loss to the right lower quadrant upon confrontation field testing. Clinical eye examination further revealed a visual acuity for the right eye of 0,5 decimal (LogMAR 0,30, Snellen ratio 20/40) and for the left eye of 0,8 decimal (LogMAR 0,1, Snellen ratio 20/25); pupil testing indicated an afferent defect to the right eye. There was no history of eye disease prior to the accident upon questioning. Imaging studies including magnetic resonance imaging (MRI) of the orbit showed an isolated unilateral distension of the right optic nerve with an edematous soaking of the adjacent retroorbital fat (Figure 1). No fracture of the skull and of the optic canal and no intracranial pathology was noted. High-dose corticosteroids were administered for three consecutive days and then reduced. The patient’s symptoms responded quickly to this approach. Repeated eye examination after one week showed normal testing results for pupillary function and confrontation fields, visual aquities returned to 1,0 decimal on both eyes (LogMAR 0,00, Snellen ratio 20/20).

[...] The further sequelae of the patient was uneventful [...] I think this sentence should be rephrased for clarity.

This entire phrase has been removed from the manuscript.

[...] Computed tomography, that was negative in our case, has come to play a major role in the orbital examination of acute trauma patients and defines fractures, bony fragments or hematoma directly impinging on the optic nerve [...] The indication for neuroimaging remains a controversial issue and practice varies worldwide. Some clinicians request CT or magnetic resonance imaging (MRI) or both for all cases, whereas others limit them to those patients with progressive visual deterioration or when therapeutic interventions are being considered. The clinical usefulness of neuroimaging in TON remains debatable since there is no consistent correlation between the finding of an optic canal fracture, severity of visual loss and prognosis for visual recovery.
The author has reconsidered current clinical practice and literature and agrees with this reviewer’s criticism. The corresponding section within the original manuscript has been revised according to the reviewer’s suggestion. It now reads as follows:

[...] Altenmüller et al. [3] reported good correlation of initial VEPs with visual acuity and visual fields examined after patients had regained consciousness. The role of neuroimaging remains controversial and practice varies between institutions. While some colleagues request computed tomography (CT) and/or magnetic resonance imaging (MRI) for diagnosis, others limit these to patients with progressive visual deterioration or if therapeutic interventions are being considered. The clinical value of neuroimaging in traumatic optic neuropathy is further debatable since there is no consistent correlation between the finding of an optic canal fracture, the severity of visual loss and the prognosis for visual recovery. Recently, ultrasonography [...] 

[...] The early use of steroids in the course of treatment is widely accepted although the lack of prospective clinical trials has perpetuated controversy as to the optimum treatment of patients with traumatic optic neuropathy [...] A different word to “perpetuated” should be used.

The entire paragraph on potential therapeutical options in patients with traumatic optic neuropathy has been revised (see below) and the word “perpetuated” does not occur any more within the revised version of the manuscript.

We have recently conducted a systematic review of steroids and surgery in traumatic optic neuropathy (TON).
1. Yu Wai Man P, Griffiths PG. Steroids for traumatic optic neuropathy. Cochrane Database of Systematic Reviews. 2007 [In Press]
The author also fails to mention the findings of the largest prospective trial of TON published to date and its findings in their discussion.
There is a relatively high rate of spontaneous visual recovery in TON and no robust data that steroids provide any additional benefit over conservative management. Based on the current evidence, TON cases presenting more than 8 hours after the initial injury should not be treated with steroids. The decision to initiate treatment for patients seen within the 8-hour window remains controversial and the supporting evidence is weak. The patient presented in this case report received steroids > 2 days after the initial trauma. Similarly, there is no evidence that surgical decompression of the optic nerve has any role to play in the management of TON. On the other hand, surgery carries a definite risk of complications such as postoperative cerebrospinal fluid leak and meningitis.

Conclusion
TON is a well recognised complication following road traffic accidents and as such this case report does not describe anything new. There is an extensive literature around the controversy surrounding the use of steroids and surgical decompression in the management of TON which the author fails to discuss and put in context. Steroids and surgery cannot be considered the standard of care in TON based on the current evidence available.
The author agrees with all points of criticism by this reviewer and has thus considerably revised the section on potential therapeutical options in patients with traumatic optic neuropathy. The author further apologizes for not having cited the literature suggested by this reviewer. The author revisited the literature and incorporated those suggested by this reviewer into the revised version of the manuscript. Similarly, the conclusion of the present case report has been modified. Within the revised version of the manuscript it now reads as follows:

Currently, there is no validated approach to the management of traumatic optic neuropathy. The International Optic Nerve Trauma Study [12] was initiated to compare the visual outcomes of patients observed without treatment with those of patients treated with corticosteroids and of patients treated with optic canal decompression surgery. This multicenter, comparative, interventional but non-randomized trial comprised 133 patients with traumatic optic neuropathy from 16 countries. Treatment decisions were according to the investigators' customary practice and no specific protocols for corticosteroid treatment or surgical technique were followed. The results showed that visual acuity improved in 32% of patients treated with surgery, in 52% of patients treated with corticosteroids, and in 57% of untreated patients. Thus, there was no clear benefit observed for either corticosteroid therapy or optic canal decompression. The results further showed that neither the dosage or timing of corticosteroid treatment nor the timing of optic canal decompression were associated with an increased probability of improved visual acuity. The authors concluded that neither corticosteroid therapy nor optic canal decompression should be considered the standard of care for patients with traumatic optic neuropathy and that therapeutical decisions should be made on an individual patient basis. In the present case, the patient’s symptoms quickly responded to corticosteroid therapy but considering the results from the International Optic Nerve Trauma Study, this patient may have improved without any specific therapy whatsoever as well.

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encountered considerable difficulties in comparing the body of evidence available. Given the relatively high rate of spontaneous visual recovery they concluded that there is no evidence that surgical decompression of the optic nerve provides any additional benefit [15]. However, in selected cases in which orbital bone fragments or foreign bodies impinge on, but do not transect, the optic nerve, surgical intervention may be indicated. In any case, one should be aware of the fact, that surgical intervention carries a definite risk of complications such as i.) collateral damage to structures of the orbital apex as well as other intracranial structures, ii.) iatrogenic direct and indirect optic nerve damage, the latter via disruption of the pia, and iii.) postoperative cerebrospinal fluid leaks and meningitis. Similar to corticosteroids, the approach with surgery in traumatic optic neuropathy remains controversial and each case needs to be individually assessed.

Conclusion
The coincidence with the traumatic event, the absence of any eye pathology prior to the traumatic event and the exclusion of any alternative cause for an optic nerve swelling, for example confounding anterior segment pathologies, optic nerve neuritis, ocular ischemia/vascular occlusion, hemorrhage, vascular dissection, tumor, osteopetrosis and intracranial hypertension, prompted the diagnosis of a post-traumatic unilateral optic nerve contusion with corresponding visual deficit quickly responsive to steroid therapy. This approach was successful in the case reported here but the current body of evidence still lacks a validated approach to the management of traumatic optic neuropathy and each case needs to be individually assessed. There is a need for a large, prospective, randomized controlled trial to assess the different therapeutical approaches in traumatic optic neuropathy but such a trial may be challenging given the low frequency of the disease and the difficulties inherent in randomizing patients.

The author thanks both reviewers for their valuable comments and suggestions with regard to further improvement of the submitted manuscript. The author hopes to have met and satisfactory responded to each of the reviewers’ points of criticism. He now asks the Editorial Board to reconsider his manuscript for publication in the “Journal of Medical Case Reports”.

With best wishes and warm regards

Marc Maegele, M.D.