Author's response to reviews

Title: Bilateral blindness secondary to optic nerves ischemia from severe amlodipine overdose - A Case Report

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Author’s response to reviews:

Response to reviewers’ comments:

We would like to thank all the reviewers and members of the editorial board who spent the time to read our manuscript and made comments to help us improve the manuscript. Following is an itemized response to the reviewers’ comments. All modification to the manuscript will be in red.

To the comments of Reviewer #1:

While the story of the initial interventions and then subsequent successful attempt to recover the patient to some meaningful function are interesting, it is not necessarily unique to have a patient with pre-existing optic nerve damage develop blindness after severe hypotension from an antihypertensive overdose.

Response:

We agree with the reviewer. However, the pre-existing optic atrophy was not known to us until after patient’s recovery from the severe hypotensive crisis. More importantly, with the multiple organ failure in the ICU such as kidneys, heart and lungs which were all recovered with successful resuscitation, with the exception for the pre-existing optic atrophy which worsened to bilateral blindness even with excellent ICU care. This case warrant reporting to the greater audience that certain pre-existing diseases are at risk of developing severe complications even after full recovery from the insult.

To the comments of Reviewer #2:
The authors should include and discuss the following papers:


Bilateral Anterior Ischaemic Optic Neuropathy in a Child on Continuous Peritoneal Dialysis: Case report and literature review.

Al-Kaabi A1, Haider AS2, Shafeeq MO3, El-Naggari MA4, El-Nour I4, Ganesh A2.

Abstract

Non-arteritic anterior ischaemic optic neuropathy (NAION) is a serious complication of continuous peritoneal dialysis (CPD) which can lead to poor vision and blindness. We report a five-year-old girl who had undergone a bilateral nephrectomy at the age of one year and was on home CPD. She was referred to the Paediatric Ophthalmology Unit of Sultan Qaboos University Hospital, Muscat, Oman, in 2013 with acute bilateral vision loss, preceded by a three-day history of poor oral intake. At presentation, the patient had severe systemic hypotension. An ophthalmological examination revealed severe bilateral visual impairment and NAION. She was treated with intravenous methylprednisolone and normal saline boluses. At a five-month follow-up, the visual acuity of the right eye had improved but vision in the left eye remained the same. Acute bilateral blindness due to NAION while on CPD is a rare condition in childhood. Paediatricians should be aware of this complication in order to ensure prompt management.


Perioperative visual loss following prone spinal surgery: A review.

Epstein NE

Abstract

BACKGROUND:

Postoperative visual loss (POVL) following prone spine surgery occurs in from 0.013% to 1% of cases and is variously attributed to ischemic optic neuropathy (ION: anterior ION or posterior ION [reported in 1.9/10,000 cases: constitutes 89% of all POVL cases], central retinal artery occlusion [CRAO], central retinal vein occlusion [CRVO], cortical blindness [CB], direct compression [horseshoe, prone pillows, and eye protectors Dupaco Opti-Gard]), and acute angle closure glaucoma (AACG).

METHODS:
Risk factors for ION include prolonged operative times, long-segment spinal instrumentation, anemia, intraoperative hypotension, diabetes, obesity, male sex, using the Wilson frame, microvascular pathology, decreased the percent of colloid administration, and extensive intraoperative blood loss. Risk factors for CRAO more typically include improper positioning during the surgery (e.g., cervical rotation), while those for CB included prone positioning and obesity.

RESULTS:

POVL may be avoided by greater utilization of crystalloids versus colloids, administration of α-2 agonists (e.g., decreases intraocular pressure), avoidance of catecholamines (e.g., avoid vasoconstrictors), avoiding intraoperative hypotension, and averting anemia. Patients with glaucoma or glaucoma suspects may undergo preoperative evaluation by ophthalmologists to determine whether they require prophylactic treatment prior to prone spinal surgery and whether and if prophylactic treatment is warranted.

CONCLUSIONS:

The best way to avoid POVL is to recognize its multiple etiologies and limit the various risk factors that contribute to this devastating complication of prone spinal surgery. Furthermore, routinely utilizing a 3-pin head holder will completely avoid ophthalmic compression, while maintaining the neck in a neutral posture, largely avoiding the risk of jugular vein and/or carotid artery compromise and thus avoiding increasing IOP.


Vidal E, Schaefer F.

Adv Perit Dial. 2015;31:54-8

4. Hypotension-induced blindness in haemodialysis patients.

Bansal S, Ansons A, Vishwanath M.


5. Acute bilateral visual loss related to orthostatic hypotension.

Kim JY, Kim KN, Kim WJ, Lee YH.

Response to points 1, 2, 3, 4 and 5:

The recommended papers will be added to the manuscript in the Discussion section:

An important condition to consider is anterior ischemic optic neuropathy (AION), which is characterized by a sudden loss of vision due to optic nerve head ischemia. Infarction of the short posterior ciliary artery supplying the optic nerve head is believed to be the culprit, causing ischemia, edema and compartment syndrome [33]. AION is subdivided into arteritic (10%) and non-arteritic (90%) causes [34]. Non-arteritic AION (NAAION) occurs in the setting of compromised blood flow associated with several comorbidities including hypertension, smoking, hypercholesterolemia, atherosclerosis and diabetes mellitus [33,34]. An anatomically small or “crowded” disc has also been identified as a risk factor [33]. The clinical presentation includes painless visual loss and swelling of the optic disc, followed by pallor. NAAION can present with visual loss upon waking, due to nocturnal hypotension [33]. NAAION typically involves unilateral visual loss, but 14.7% of patients over a 5-year follow-up period in the ischemic optic neuropathy (ION) decompression trial progressed to second eye involvement [35]. In most cases of hypotension-induced NAAION, bilateral visual loss occurs simultaneously or within weeks of the initial unilateral symptoms [33].

NAAION has also been described in patients undergoing chronic renal replacement therapy, but is largely underdiagnosed in this population [33,34,36]. Interestingly, not only patients underdoing intermittent hemodialysis are at risk. In a case report by Al-Kaabi et Al., a five-year-old child undergoing continuous peritoneal dialysis (CPD) for a period of four years developed acute bilateral vision loss upon waking from sleep [34]. In this patient, frequent systemic hypotensive episodes and one instance of PRES had required previous hospitalization. Fundoscopic examination was consistent with NAAION, and anemia, uremia, as well as infiltrative optic neuropathy and other intracranial causes were ruled out. The resulting diagnosis was NAAION caused by hypotension-induced low perfusion and ischemia of the optic nerve [34]. Vidal et Al. reviewed the occurrence of AION in infants, and found it to occur in 1% of children on CPD [36]. Risk factors in this population included very young age, autosomal recessive polycystic kidney disease, and sustained hypotension [36]. While poor visual outcomes have been reported among both children and adults undergoing CPD diagnosed with NAAION, the primary treatment remains reversal of hypotension and optimization of optic nerve perfusion [34]. Steroid therapy has also been shown to provide some therapeutic effect, although it remains controversial [37–39].

NAAION due to hypotensive insult is not isolated to those undergoing chronic renal replacement therapy. Kim et Al. published a case report on a 50-year-old male following a lumbar laminectomy, with subsequent prolonged immobilization for a three-month period [40]. Upon sitting upright for the first time since his operation, he experienced significant orthostatic hypotension. Within several hours, he developed acute visual loss and was ultimately diagnosed with NAAION by means of optic disc filling delay on fluorescein angiography [40]. Interestingly, he was also found to be anemic, a known secondary risk factor for the development of NAAION [33]. Partial recovery of vision was noted in this patient upon 6-month follow-up, although the visual fields remained severely constricted [40].
Perioperative vision loss (POVL) following prone spine surgery has been described in the literature, occurring in 0.013-1% of cases [41]. While AION has been identified in some cases, other causes include posterior ischemic optic neuropathy (PION), central retinal artery occlusion, central retinal vein occlusion, cortical blindness, direct compression, acute angle closure glaucoma, epidural spine injections, and other less common factors [41]. In terms of AION in this setting, identified risk factors include prolonged operative times, long-segment spinal instrumentation, anemia, intraoperative hypotension, diabetes, obesity, male sex, greater estimated blood loss, microvascular pathology and decreased percent colloid administration [41].

Hypotension-induced NAAION can also occur following acute blood loss and in patients prescribed medications such as phosphodiesterase type 5 inhibitors and interferon-α [34,42,43]. In terms of hemorrhagic shock, NAAION can result from both spontaneous and traumatic blood loss [31,40,44–46]. Reported outcomes have ranged from some degree of vision recovery in 50% of patients, while 10-15% of patients experienced complete recovery of vision [40]. Overall, hypotension-induced NAAION could help explain the pathophysiology of bilateral vision loss in our patient, although a definitive diagnosis would have required further diagnostic testing in the setting of chronic optic atrophy.

To the comments of Reviewer #3:

1. Do you believe the case report is authentic?

Response:

We the authors cared for this patient from admission to the ICU and in the ward after recovery. Her complication of bilateral blindness was followed up by ophthalmology.

2. Do you have any ethical concerns? Please consider if local Institutional Review Board approval or ethical approval was obtained (if appropriate) and if the patient (or their parent or guardian in the case of children under 18) gave written, informed consent to publish this case and any accompanying images. A statement to this effect should appear in the manuscript.

Response:

We the authors do not have any ethical concerns. Since this case report is not human or animal research the local institutional review board was not required. However, the senior author RK obtained written and informed consent from the patient to publish this case and its accompanying images. A statement to this effect is on the manuscript.

3. Does the Introduction explain the relevance of the case to the medical literature?

Response:

The introduction explained the relevance of CCB overdose and its complications and this is the first reported case of bilateral blindness.
4. Does the article report the following information? Where information is missing, please specify.

a. The relevant patient information, including:
   - De-identified demographic information (age, gender, ethnicity)
   - Main symptoms of the patient
   - Medical, family and psychosocial history
   - Relevant past interventions and their outcomes

Response:

The information requested in 4 is reported in the manuscript.

b. The relevant physical examination findings

Response:

The relevant physical examination is reported in the case presentation of the manuscript.

c. Important dates and times in this case (if appropriate, organized as a timeline via a figure or table); if specific dates could lead to patient identification, consider including time relevant to initial presentation, i.e. initial presentation at T = 0, follow up at T = 1 month.

Response:

The important dates and time of major events are reported in the manuscript. Those timeline/dates do not lead to patient identification therefore as timeline suggestion is not required.

d. Diagnostic assessments, including:
   - Diagnostic methods
   - Challenges (e.g., financial, language/cultural)
   - Reasoning and prognostic characteristics (e.g., staging), where applicable

Response:

All diagnostic methods are included in the manuscript. There were no challenges regarding to financial, language and cultural issues. Reasoning and prognostic characteristics are not relevant in this case report.
e. Types and mechanism of intervention

   Response:

   The type and mechanism of intervention is listed in the manuscript.

f. A summary of the clinical course of all follow-up visits

   Response:

   A summary of the clinical course of follow-up visits is listed in the manuscript.

5. Is the interpretation (discussion and conclusion) well balanced and supported by the case presented?

   Response:

   The discussion and conclusion in the manuscript described the pharmacodynamics of CCB and its complications as result of an overdose. The various managements and the possible complications were also described in detail and supported in the case presentation. The conclusion is supported by the discussion in that this is the first reported bilateral blindness from severe CCB overdose.

6. Is the anonymity of the patient protected? Please consider any identifying information in images such as facial features or nametags, whether the patient is named etc. If not, please detail below.

   Response:

   The anonymity if the patient is protected and any identifying information in the image are removed.

7. Is the Abstract representative of the case presented?

   Response:

   The abstract summarized the relevant information of this case report.

8. Does the case represent a useful contribution to the medical literature?

   Response:

   This case presentation will make a useful contribution to the medical literature in that one must be aware of pre-existing diseases which can worsen as resulted of severe hemodynamic instability.
9. Additional comments for the author(s)?

Response:

The authors would like to thank the reviewers for their input and suggestions which will strengthen this manuscript.