METHANOL TOXIC OPTIC NEUROPATHY: A CAUSE OF BILATERAL BLINDNESS

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ABSTRACT

Background: Methanol poisoning and toxic optic neuropathy is still seen in many parts of the developing countries. Methanol intoxication causes irreversible neurologic sequelae if unrecognized and untreated. It induces acute optic neuropathy with possible long-term visual damage. The benefit of high dose corticosteroids intravenous in methanol intoxication has been proposed due to anti-inflammatory and immunosuppressant effect of steroids.

Case Presentation: A 25-year old male came with complaint of sudden visual loss on both eyes, one week before admission, with history of consuming mixed alcohol presumed to contain methanol. Ophthalmology examination showed visual acuity no light perception on both eyes with nonreactive pupil. The fundus showed optic nerve head swelling on both eyes and patient was managed with high-dose intravenous steroids and coenzyme q10 orally. This patient also revealed a positive value without any symptoms of COVID-19 at first and the symptoms appeared in second day of inpatient care. The COVID-19 was a co-incidence in this case. After three days inpatient care visual acuity was not improved, but in two weeks later, the visual acuity improved to hand movement on both eyes and therapy continued with oral methylprednisolone.

Conclusion: High dose intravenous corticosteroids is drug of choice for methanol toxic optic neuropathy to improve visual acuity, but most methanol toxicity cases give unsatisfied result as studies show various factor influenced the result.

Keywords: methanol, optic neuropathy, steroid intravenous

BACKGROUND

Methanol is one of the most widely applied toxic alcohols in industry, agriculture and households. It is used as an organic solvent, biofuel, antifreeze fluid component, for car chemistry, and in the production of other chemical substances and compounds. Poisoning may occur after ingestion, dermal application, or inhalation. Although uncommon in the United States, methanol toxicity poses a significant public health problem in developing countries, and in Southeast Asia, where the most common source of poisoning is via adulterated liquor in local drinks. Methanol intoxication is a present with mild symptoms such as headache, altered mentation, blurring of vision, abdominal pain, and vomiting.1-3

Methanol intoxication is associated with a severe and irreversible optic neuropathy and neurologic deficits. Toxic optic neuropathy refers to visual impairment due to optic nerve damage caused by a toxin characterized by bilateral, usually symmetric vision loss, papillomacular bundle damage, central or cecocentral scotoma, and reduced color vision. Vision loss is brought about by the affinity of the toxic metabolite of methanol, formic acid, to the optic pathway.3-5

Management of methanol induced toxic optic neuropathy is challenging and the outcome is often unsatisfying. The administration of intravenous high dose steroids showed an improvement of visual status especially in patients with short interval between methanol consumption.
and treatment initiation. Very few reports in effectivity of methanol toxic optic neuropathy therapy in late phase are found. The improvement of visual function might vary, from very minimal improvement to good improvement.\textsuperscript{5,7,16} Therefore, the purpose of this report is to report clinical presentation, management, and outcomes of methanol toxic optic neuropathy that treated with high dose intravenous methylprednisolone one week after first onset of complaint.

**CASE PRESENTATION**

A 25-year-old man came to Cicendo Eye Hospital with a chief complaint of sudden visual loss on both eyes one week before admission. There were no symptoms of red eye, pain, double vision, floaters or photopsia. The chief complaint was not accompanied by headache, nausea, vomiting, or limb weakness. There was no history of trauma, fever, flu-like syndrome. He had history of mixed alcohol consumption one day before vision loss complaint. He consumed approximately 1.5 litres of mixed alcohol, presumably methanol. There was no history of systemic disease. Physical examination revealed Glasgow Coma Scale (GCS) 15, blood pressure 110/80 mmHg, pulse 78x/minute, respiratory rate 15x/minute and temperature 36.3°C.

Ophthalmology examination showed visual acuity of both eyes are No Light Perception (NLP) and intraocular pressure with Non-Contact Tonometry (NCT) were within normal limit on both eyes. The movement for both eyes was full to all direction and not accompanied with pain. The anterior segment of both eyes within normal limit but the pupils were dilated and there was no light reflex on both eyes. The posterior segment showed swelling of optic nerve head and there were myelinated retinal nerve fiber layer on both eyes. Ishihara examination, Amsler’s grid examination, and contrast sensitivity examination were not applicable on both eyes. Optical Coherence Tomography (OCT) examination was done and showed swelling on both optic nerve head.

![Figure 1. Optic Nerve Head OCT before intravenous methylprednisolone admission showed retinal nerve fiber layer thickness increased on both eyes.](image)

Patient was diagnosed with Methanol Toxic Optic Neuropathy ODS and underwent rapid antigen COVID-19 test as the requirements for inpatient care administration. Rapid antigen COVID-19 showed a positive value and then this patient underwent PCR COVID-19 test. The PCR COVID-19 test revealed a positive value and the patient was diagnosed with Methanol Toxic Optic Neuropathy ODS + COVID-19 (PCR confirmed). This patient was managed with methylprednisolone injection 1000mg intravenously divided in 4 doses, coenzyme Q10 tablet 3x30mg orally, and vitamin D3 tablet 2x400IU orally for 3 days. On the second day of inpatient care, the patient had a fever presumed as COVID-19 symptoms. He was treated with COVID-19 therapy such as acetaminophen 3x500mg tablet orally, azithromycin 1x500mg tablet orally, favipiravir 2x600mg tablet orally, vitamin C
2x500mg, and acetylcysteine 3x200mg orally, as the instruction from the internist.

Figure 2. Fundus photography examination before inpatient care showed optic disc swelling and myelinated nerve fiber layer on both eyes (B) Fundus photography examination after inpatient care showed optic disc pallor on both eyes.

After 3 days of inpatient care in COVID-19 room, visual acuity was still NLP on both eyes. The anterior segment of both eyes within normal limit and still no light reflex on both eyes. The posterior segment showed swelling of optic nerve head on both eyes. Ishihara examination, Amsler’s grid, and contrast sensitivity are not applicable on both eyes. Patient was allowed to continue treatment in outpatient clinic with therapy methylprednisolone 1mg/kg of body weight, coenzyme Q10 tablet 3x30mg orally and vitamin D3 2x400IU orally and followed up 10 days after self-isolation or 3 days free of symptoms of COVID-19.

On the two weeks of follow up, the visual acuity was closed face finger counting (CFFC) on both eyes. The direct and consensual light reflexes can be seen decreased equally on both eyes and fundus examination showed indistinct optic nerve head borders with pallor disc on both eyes as seen as fundus photograph. The previous therapy was continued with tapered dose of oral methylprednisolone 8 mg/week. The patient was followed up every two weeks and was suggested to undergo head Computer Tomography Scan (CT scan) examination with the result within normal limit.

Figure 3. Head and orbita CT scan with contrast within normal limit

DISCUSSION

Methyl alcohol or methanol (CH₃OH) or wood alcohol, is a colorless, volatile and toxic liquid. It is found frequently in high concentration in automotive antifreeze, de-icing solutions, windshield wiper fluid, varnishes, paint thinner and many other industrial products. Although ingestion is the most commonly implicated route of toxicity, methanol can be absorbed by inhalation and dermal exposure and these serve as uncommon routes of acute and chronic intoxication. Formic acid and formaldehyde form are the toxic metabolites of methanol. These metabolites may cause metabolic acidosis, blindness, cardiovascular instability and even death.³,⁸,⁹ This patient had a history of mixed alcohol presumed methanol consumption one day before visual complaint and suffered sudden visual loss. The chief complaint was not accompanied by headache, nausea, vomiting, or limb weakness.

In the body, methanol is metabolized in a sequential fashion, principally in the liver. It is oxidized by the Alcohol
Dehydrogenase (ADH) enzyme to formaldehyde, which does not accumulate to a significant degree, but is rapidly converted within a half-life of 1-2 minutes by the formaldehyde dehydrogenase enzyme into formic acid, which is metabolized more slowly and accumulates, about 20 hours. Formic acid is also cause metabolic acidosis, neurotoxicity and direct damage to the optic nerve, which results in ocular toxicity, visual impairment or blindness.\textsuperscript{2,6,7} This patient did not show the systemic symptoms of methanol toxicity. Visual disturbance appears right after this patient ingested the mixed alcohol. The patient in this case also showed dilated and no light reflex pupils on the examination. In the literature, the blurred vision, dilated, and nonreactive pupils could be happened as the symptoms of methanol toxicity. The optic disc swelling of both eyes were found in fundoscopy examination. Severity of symptoms varies widely from mild progressive and painless decreases in vision to no-light perception vision, dyschromatopsia, scotomata, and photophobia. Pupillary examination may demonstrate dilated, nonreactive pupils. The optic discs may be normal in some patients in the early stages, but disc edema, hyperemia and hemorrhage may occur, especially in acute intoxication. A definitive diagnosis of methanol toxicity requires a confirmed increase in serum methanol level with gas chromatography is about >20 mg/dL. Peak levels are achieved 60–90 minutes after ingestion, but they do not correlate with the toxicity level and thus are not a good indicator of prognosis. Other laboratory results show the presence of metabolic acidosis accompanied by an increase of anion and osmolarity gap.\textsuperscript{8-10}

This patient also had positive COVID-19 test confirmed by PCR with the CT value 19.8. On second day, the patient had fever as the symptom of COVID-19. There was no case reported or evidence base literature that methanol toxication is related in any degree with COVID 19. Therapy of high dose corticosteroid is presumed to cause development of symptoms of COVID-19 because in this patient is initially asymptomatic. There was still on study that steroid may cause delay of viral clearance of COVID-19.\textsuperscript{11,12} In a conclusion, there still need more research about the relationship between COVID-19 and methanol toxic optic neuropathy.

This patient came to Cicendo Eye Hospital one week after the first onset of visual disturbance and came with the full level of consciousness without any sign of metabolic acidosis. In acute condition, treatment of methanol poisoning must be promptly instituted. Supportive therapy is aimed at initiating airway management, correcting electrolyte disturbances and providing adequate hydration. Gastric lavage is only useful if the patient is presented within 2 hours of ingestion. Initial treatment with sodium bicarbonate 1-2 mg/kg via intravenouslybolus is required for patient with pH below 7.3 followed by maintenance infusintill arterial pH is above 7.35. Treatment with ADH inhibitors, fomepizole (4-methylpyrazole) or ethanol is initiated earlier to delay the metabolism of methylalcohol to its toxic metabolite and to prevent its accumulation and toxicity. Hemodialysis may also be required to further correct severe metabolic abnormalities and to enhance methanol and formate elimination.\textsuperscript{6,7,13}

Degree of vision loss also at severe stage that also affect the prognosis. Worse vision loss can predict worse visual acuity after treatment.\textsuperscript{8} Highdose intravenous pulse steroid treatment, using an anti-inflammatory, neuroprotective, and immunosuppressant agent has clinical benefits, is effective for other types of optic neuropathies, including optic neuritis.
and traumatic optic neuropathy. Methanol toxicity in acute cases is mostly caused by inflammation. Bhalsing et al. reported that highdose steroid treatment might reduce edema of the optic nerve sheaths, resulting in good recovery of vision and preventing permanent blindness. Shukla et al., tried intravenous methylprednisolone in 17 cases of methanol toxicity and reported that the time of starting treatment after alcohol consumption which varied from 6 to 45 days, had no effect on the final visual outcome and 3 patients who reported for treatment after more than one month after alcohol intake also had a good visual recovery. Delayed treatment and signs of optic atrophy at the initial clinical presentation may result in bad outcomes. On the other hand, Soumaya et al. reported there was an improvement on visual acuity in patient with delayed consultation after 8 days of onset. Intravenous methylprednisolone for 3 days followed by oral steroids for week were given for this patient. Visual acuity showed a minimal improvement. Patient came one week after onset of complaint which can be predisposes outcome after therapy. On two weeks after inpatient care, the funduscopy of this patient showed an optic disc pallor.

The patient also received coenzyme Q10 as a treatment. Coenzyme Q10 is ubiquinone analogs that is an important component of the mitochondrial electron transport chain and is also a strong antioxidant that has been shown to haveneuroprotective effects on neuropathy resulting from alcohol toxicity and in other neurodegenerative diseases. Kartika et al., conclude that coenzyme Q10 has a promising potency of neuroprotection. This study showed a higher density of retinal ganglion cells of methanol toxic optic neuropathy model rats which were treated with coenzyme Q10 than the control group. Prognosis in this patient were quo ad vitam dubia ad bonam and quo ad functionam dubia ad malam. The visual outcome in this patient can be resulted from several factors. The onset of the treatment and visual symptoms that was over than 24 hours may contribute to the visual outcome.

CONCLUSION

Methanol ingestion is the most widely recognized caused of toxic optic neuropathy. Formic acid is responsible for the majority of the toxicity associated with methanol. High dose corticosteroids intravenous and other therapy such as coenzyme Q10 are considered as study shows improvement, but sometimes give unsatisfied result. There was no evidence that COVID-19 had a direct relationship with methanol toxic optic neuropathy, but in this case, high dose corticosteroid is presumed to cause development of symptoms because in this patient is initially asymptomatic. However, the interval between ingestion, substance concentration and start of therapy was found to be a critical factor.

REFERENCES


