Spectrum of MRI findings in 58 patients with methanol intoxication: Long-term visual and neurological correlation

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Abstract  Purpose: To describe MRI and DWI spectrum of brain and optic pathway changes in cases who survived acute methanol poisoning and explore whether there is correlation between imaging features and long-term visual and neurological sequelae.

Materials and methods: We retrospectively reviewed the conventional MRI and DWI of 58 consecutive patients with methanol poisoning. All patients were examined in the chronic phase.

Results: Optic nerve enhancement and atrophy were detected in 33 cases (56.9%). Degree of optic nerve atrophy correlated well with cupping and time lag since initial exposure to methanol. Bilateral putamen necrosis was present in 45 cases (77.6%), 19 showed asymmetrical involvement, and caudate was involved in 6 cases. Asymmetrical necrosis and caudate involvement were correlated with higher grade of neurological deficit. Twenty-one cases (36.2%) showed combination of bilateral putamen necrosis and optic nerve enhancement. Subcortical white matter high SI was detected in 25 patients (43.1%). DWI clearly depicted putamen necrosis with non-restricted pattern.

Conclusion: Spectrum of residual MRI Findings in patients who survived methanol poisoning included bilateral optic nerve atrophy and enhancement, bilateral putamen and caudate necrosis as well as subcortical white matter high SI at T2WI. Diffusion WI did not have additional value in chronic stage.

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1. Introduction

Methanol intoxication appears after accidental, suicidal oral ingestion of industrial solvents, and cleaning of antifreeze liquids, or occasionally is due to fraudulent adulteration of wine or other alcoholic beverages (1).

Methanol is a highly toxic substance and acute methanol poisoning produces severe metabolic acidosis and serious neurological symptoms, including severe visual impairment, extrapyramidal signs and coma (2). Optic neuropathy and putaminal necrosis are the two main complications of methanol poisoning, generally occurring in combination after severe intoxication. Surviving patients usually show permanent sequelae (residual visual) and consist of bilateral blindness and motor dysfunction including rigidity, hypokinesia, and other Parkinsonian-like signs (3).

There are few reported specific findings for methanol intoxication on magnetic resonance imaging (MRI) of the brain and optic pathway, fewer on DWI.

The aim of this study was to describe MRI and DWI spectrum of brain and optic pathway changes in cases that survived acute methanol poisoning and explore whether there is correlation between imaging features and long-term visual and neurological sequelae.

2. Patients and methods

This is a retrospective case series of 58 consecutive patients seen at the King Khaled Eye Specialist Hospital and the King Saud University hospitals from September 2010 to November 2015. Informed consent was waived for this Health Insurance Portability and Accountability Act (HIPAA)-compliant institutional review board-approved retrospective study.

2.1. Case selection

Inclusion criteria included patients who presented with different degree of visual or neurological deterioration with past history of methanol intoxication (oral intake) at least 4 weeks prior to examination and performed MRI examination of the brain and orbit including post contrast study and DWI. Exclusion criteria included cases that did not perform complete MRI examination or lack visual field examination, cases with other medical diseases that could affect visual acuity or motor function such as glaucoma, diabetes or Parkinsonism, cases who had no clear history of methanol ingestion or there is denial from the patient or their family, and cases who have contraindications to do MRI (cardiac pacemaker, metallic FB in the eye, claustrophobic, etc.) were also excluded. None of the patients were examined during the acute phase of intoxication.

2.2. Clinical assessment

All patient charts were reviewed including gender, age, date of methanol ingestion, any persistent or newly developed signs or symptoms since date of methanol ingestion and any other concurrent medical disease. The following tests were performed: optical coherence tomography or OCT with evaluation of the retinal nerve fibers layer (RNFL), visual evoked potentials (VEP), complete ocular examination (visual acuity/field, color vision, contrast sensitivity, and fundus), neurological examinations, and biochemical tests.

Assessment motor function is evaluated by board certified neurologist (TB) with further grading of residual motor effect into grade I (rigidity) and grade II (rigidity + tremors).

Visual acuity, visual fields, pupillary reaction, and fundus features were assessed by board certified senior neuroophthalmologist (AG and TB) and ratio of optic disk cupping was recorded.

2.3. Imaging

MR imaging studies were performed at 3-T scanner (Magnetom Allegra 3 T; Siemens, Erlangen, Germany) with the use of a dedicated head coil. The gradient strength was 40 mT/m and the slew rate was 400 T/m/s. First, sagittal spin-echo T1-weighted MR images were obtained with TR/TE of 350–7500/9–13 ms. Transverse T2-weighted MR images were obtained with TR/TE of 2400–2800/19–96 ms, FOV of 20 × 22 cm, section thickness of 4 mm, interslice gap of 1–2 mm, and matrix of 320 × 180. Coronal T2-weighted MR images with fat suppression were obtained with TR/TE of 2400–2800/19–87 ms, FOV of 20 × 22 cm, section thickness of 4 mm, inter-slice gap of 1–2 mm, and matrix of 320 × 216.

The diffusion gradients were applied along the three orthogonal directions (x, y, and z) with the same strength. Diffusion-weighted MR images were acquired with a diffusion-weighted factor b of 0, 500, and 1000 s/mm², and ADC maps were generated for all images using a multi-slice spin echo planar imaging sequence. Imaging parameters were TR/TE of 3200/81 ms, FOV of 20 × 22 cm, section thickness of 4 mm, inter-slice gap of 1–2 mm, number of excitations of 6, matrix of 128 × 128, EPI factor of 128, and RF pulse and width of 1200. The data acquisition time for the diffusion weighted images was 1.33 min.

After intravenous injection of 0.1 mmol/kg gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany), axial, coronal, and sagittal T1-weighted MR images (TR/TE = 400–575/13–15 ms) with fat suppression was applied. Fat suppression was accomplished with a frequency selective pre-saturation pulse.

2.4. Image interpretation

Senior neuroradiologist (SE) who was blinded to the clinical diagnosis and the degree of visual field affection re-reviewed the MRI images of all patients. Any abnormal high SI in the basal ganglia or subcortical white matter was assessed in both conventional images, diffusion weighted images (DWI) and ADC map (to detect areas of restricted or non restricted diffusion). The caliber and enhancement of the Optic nerves (ON) were assessed visually by the senior neuroradiologist (SE) with further grading into either normal or mild, moderate and severe atrophied in coronal T2 image which provided the best cross sectional view of the ON. The slice was selected then the retrolubar area was zoomed to 300 ×, and then ON diameter was measured 3 mm behind the globe using an electronic caliper. The ON diameter obtained from both sides was correlated in collaboration with the vision acuity and fundus examination as there are a lot of normal variations in the size of the optic nerve.
2.5. Statistical analysis

Statistical analysis was performed using Statistical Package for Social Sciences version 18 (SPSS Inc., Chicago, IL, USA).

3. Results

Fifty-eight patients were included in this study. All were young to middle aged males (mean age 38.1 years; range 17–64 years). All eventually admitted to drinking unbranded alcohol. Some admitted to drinking alcohol, cologne, or perfume only when family members were not present. Thirty patients were able to provide medical records from their initial evaluation, and 15 had fundus photographs from that time. Time lag between methanol intake and imaging ranged from 12 week to 40 months.

Patients presented with different symptoms including headache, malaise, rigidity, tremors and decreased visual acuity as shown in Table 1. Residual extrapyramidal motor deficits including rigidity, hypokinesia and tremors were detected in 45 patients. Residual visual deficits were found in 33 cases, and all were suffering from severe visual loss (hand movement up to complete blindness). Cupping greater than 0.8 cup to disk ratio (c/d) was present in at least one eye of 22 patients (43/116 eyes).

Optic nerve enhancement was detected in 33 cases (56.9%), and all of them showed bilateral affection (as shown in Fig. 1). None of them showed restricted diffusion. All cases that showed optic nerve enhancement were associated with variable degree of optic nerve atrophy. No significant correlation was found between optic nerve atrophy and patients’ age. On the other hand optic nerve atrophy was significantly correlated with optic disk cupping (Pearson correlation = 0.624) and with time lag since first exposure to methanol (Pearson correlation = 0.674).

MRI brain demonstrated bilateral putamen necrosis in 45 cases, 19 of them showed asymmetrical involvement (as shown in Figs. 2–4). Additional lesions in caudate nuclei were noted in 6 cases (as shown in Fig. 4). None of these cases showed diffusion restriction denoting chronic stage. All were suffering from motor symptoms, but asymmetrical putaminal necrosis and associated caudate necrosis were significantly correlated with higher degree of motor disturbance (Pearson correlation = 0.683). No significant correlation was found between patients’ age and severity of motor symptoms.

Subcortical white matter high SI in T2WI was detected in 25 patients (as shown in Fig. 4), and low SI in T1WI was detected in 9 of these patients. No significant correlation was detected between the presence of subcortical white matter SI and severity of motor symptoms or visual disturbance. Putaminal necrosis did not correlate with degree of visual acuity or visual field loss.

Different MRI findings are illustrated in Table 2.

Twenty-one cases (36.2%) showed combination of bilateral putamen necrosis and optic nerve enhancement.

4. Discussion

This study evaluated the spectrum of MRI findings in 58 patients who survived acute methanol intoxication. All were males, most of them were young to middle aged. They presented with several symptoms and signs ranging from mild headache to severe visual disturbance and even blindness.

Methanol is a potent toxic substance for the optic nerves, and even small amounts of ingested methanol can cause acute permanent neurological dysfunction and irreversible blindness up to death (4). Visual disturbances generally develop between 18 and 48 h after methanol ingestion and range from mild photophobia and misty or blurred vision to markedly reduced visual acuity and complete blindness (5–7). In the early period, there is disk edema and congestion from accumulation of axonal material. Two months after exposure, optic nerve atrophy may appear (8). The minimum lethal dose of methanol is generally considered to be 30 ml of 40% methanol, but as little as 10 ml of methanol may cause blindness (9).

Optic nerve atrophy suggests loss of ganglionic cells, which is a secondary change caused by the degenerative demyelination of the retrolubar optic nerve rather than direct damage to axonal cells of the optic nerve. Although the actual incidence is unknown, optic nerve atrophy from methanol poisoning is relatively common, but cases with disk cupping are rare. The mechanism of disk cupping in methanol poisoning is not yet clear (10). Although optic nerve appears to be the main target of methanol poisoning, studies in both humans and animals have demonstrated retinal toxicity as well (11,12). Peripapillary retinal edema is commonly observed after acute methanol intoxication (12).

This study included 33 cases suffering from severe visual loss (hand movement up to complete blindness) after methanol ingestion. All showed bilateral enhancement of optic nerves with variable degree of optic nerve atrophy. Optic nerve atrophy correlated well with time lag since methanol ingestion which suggests that the process of cell degeneration is progressive; however, the pattern of enhancement could not predict optic nerve atrophy relation and/or the outcome or degree of visual acuity. Other studies reported bilateral optic nerve atrophy (4,13) while Chung et al. (14) reported optic nerve enhancement in patients suffering from methanol toxicity. Mechanism of methanol toxicity to central nervous system could be explained by the fact that after absorption it is oxidized in the liver to formaldehyde and formic acid (15). Formic acid is toxic to central nervous system and controls cytochrome oxidase and interferes with adenosine triphosphate (ATP) production from mitochondria. Therefore, it causes histologic hypoxia which induces axonal cell death (16).
Brain pathology has been documented in earlier studies showing the specific involvement of the basal ganglia, especially the putamen as bilateral putaminal hemorrhage, and necrosis (1,13,17–20) in acute stage of methanol toxicity. Pelletier et al. (3) reported bilateral putaminal edema and cavities 3 weeks after initial exposure to methanol that persisted after 2 months on a repeat MRI examination. Recent studies reported that DWI images enabled detection of acute ischemic areas in frontal and occipital lobes which were not depicted in other sequences (21).

In the current study all cases were examined in the chronic stage and none of which showed restricted diffusion. Forty-five cases showed bilateral putamen chronic ischemic changes and gliosis in the form of curvilinear areas of CSF SI on all pulse sequences, more evident in T2WI and relative decrease of size of putamen nucleus. All these cases suffered from extrapyramidal signs and symptoms that included rigidity and tremors. Nineteen cases showed asymmetrical involvement which correlated with higher grade of motor disturbance. Six cases showed additional involvement of caudate, which was also correlated with higher grade of motor disturbance, yet no correlation to the degree of optic nerve atrophy or visual acuity.

Several theories tried to explain the mechanism of injury in methanol intoxication. Although MRI findings are similar to and compatible with ischemic necrotic lesions but the primary site of predilection in our study was putamen with minor involvement of caudate, whereas, in usual deep MCA infarcts, the caudate nucleus is generally involved (taking into consideration that the arterial supply of the putamen is provided by the lateral lenticulostriate arteries, originating from the proximal middle cerebral artery). Orthner (22) proposed that putaminal necrosis resulted from decreased venous outflow through the veins of Rosenthal. Another suggestion was that formic acid may achieve higher concentrations within the putamen.

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Fig. 1  (A and B) Axial T2WI at the level of optic nerve shows bilateral moderate optic nerve atrophy in 2 different patients. (C) Axial fat suppressed post contrast images (another different patient) show bilateral atrophic enhanced optic nerves.
than in other brain structures (23,24), contributory blood flow patterns in the basal ganglia, increased metabolic sensitivity of striatal neurons to methanol metabolites, or increased vulnerability to apoptosis (24). Sharpe et al. (25) proposed that methanol could provoke a specific histotoxic anoxia with myelinoclastic effect. However, white matter damage is not the rule in most cases of methanol intoxication (3).

Bilateral putaminal lesions with optic neuropathy were described in methanol intoxication, hydrogen sulfide toxicity, Leigh’s disease and other mitochondrial diseases (26), while the differential diagnosis of bilateral putamen necrosis included more conditions such as Wilson’s disease, hypoxic-ischemic insults, encephalitis, Kearns-Sayre syndrome, striatal degeneration associated with Leber’s optic atrophy, certain types of metabolic disorders, carbon monoxide inhalation and hypoxic-anoxic injuries such as near-drowning (27). The main clue to proper diagnosis is history of recent consumption of adulterated or non-standard alcohol. Predilection to putamen not caudate helps to differentiate methanol poisoning from other ischemic conditions (CO poisoning) that tends to involve mainly the caudate nucleus. Also the combination of optic nerve atrophy eliminates other differentials. However this combination was only found in 23 cases (36.2%) in this study.

**Fig. 2** Axial T2WI and FLAIR images (A and B) show bilateral symmetrical putamen necrosis in 2 different patients 12 and 15 weeks after methanol intoxication. Note the abnormal high SI in the subcortical white matter in image (A).

**Fig. 3** Axial FLAIR and T2WI (A and B) shows bilateral asymmetric putamen necrosis. The core lesion is centered on the putamen.
Other studies described subcortical white matter edema in cases of acute methanol intoxication (1). Although abnormal high SI in the subcortical white matter was detected in 25 cases (43.1%) included in the current study, we could not describe this finding as specific for methanol toxicity. It did not show any correlation with severity of residual motor or visual symptoms. Abnormal subcortical white matter SI is described in a wide range of diseases especially in the elderly (28). We recommend that it should be taken in consideration only if it is associated with other more specific findings such as optic nerve atrophy and bilateral putamen necrosis, or when it is detected in young patient.

There are several limitations to this study. All patients included in this study were examined in the chronic state and were not followed from the initial exposure to methanol, so we were not able to assess the progress of MRI findings. No MRI films were available before exposure to methanol to exclude the possibility of pre-existing abnormal SI or optic nerve changes; however, we excluded patients with co-morbidities that may produce similar neurologic/visual effects. Unfortunately we could not exclude patients older than 50 years who may have subcortical white matter high SI as part of chronic microvascular ischemic changes.

5. Conclusion

Spectrum of residual MRI Findings in patients who survived methanol poisoning included bilateral optic nerve enhancement, bilateral putamen and caudate necrosis as well as subcortical white matter high SI at T2WI. Diffusion WI did not have additional value in chronic stage.

Conflict of interest

The authors declare that there are no conflict of interests.

References


