Bangladesh Journal of Anatomy January 2013, Vol. 11 No. 1 pp 44-47

Case Report

Multi System Involvement due to Acute Methanol Toxicity in a Young Male

Syed Fazlul Islam[1], AH Hamid Ahmed[2], Bokhtiare Mohammad Shoeb Nomani[3], Syed Mahbub Morshed[4], Syed Mahtab -Ul -Islam[5]

Abstract:

A young male who had history of ingestion of methanol developed severe anorexia, nausea, and profuse vomiting after a short period. After evaluation he was found to develop severe renal failure, metabolic acidosis & dyselectrolemia. He was given haemodialysis for several sessions.

Few days later he developed weakness and blurred vision. Neurological evaluation showed toxic neuropathy. In spite of giving haemodialysis near about three months his renal function did not improved. Renal biopsy showed features suggestive of acute cortical necrosis. He was declared a case of End Stage Renal Disease (ESRD) & an arterio-venus fistula was created in his left forearm for maintenance of haemodialysis.

Key words: *Methanol, ESRD, neuropathy, cortical necrosis.*

Introduction:

Methanol may cause acute toxicity, following inhalation, oral or percutaneous exposure.

Acute toxicity from methanol manifests as CNS depression, followed by a latent period of varying duration from 8-36 hrs and occasionally up to 48 hrs. Subsequently, metabolic acidosis develop, superimposed with headache, nausea and features of ocular toxicity. Ocular toxicity may range from photophobia, blurred vision to markedly reduced visual acuity and complete blindness; ingestion of as little as 4-10 ml methanol in adults may cause permanent damage[1].

Coma and death may occur after substantial exposures. The minimal lethal dose following ingestion is considered to be in the range of 300-1000 mg kg-1[2]. Severe intoxication, if survived, may cause permanent damage to the CNS, manifest as a parkinsonian-like condition and permanent blindness[2]. In humans and primates, toxicity of methanol is mediated via metabolites and not the parent molecule. The liver is the primary site of metabolism for methanol. Through a series of oxidative steps methanol is oxidised to methanol (HCHO, formaldehyde), methanoic acid (H•COOH, formic acid) and finally detoxified to carbon dioxide (CO2). The main enzyme groups involved in each steps are alcohol dehydrogenase, aldehyde dehydrogenase and folate dependent mechanisms respectively. Methanoate (formate) or methanoic acid (formic acid) may be formed, dependent on pH[3]. The term "formic acid" and not methanoic acid persists in the literature and will therefore be used in this text for compatibility. Formic acid is considered to be the key toxicant; and in animal species with a poor ability to metabolise this product (primates and humans) fatal toxicity may occur from metabolic acidosis and neuronal toxicity. Un-dissociated formic acid readily crosses the blood brain barrier leading to CNS toxicity, aggressive alkaline therapy is required to maintain formic acid in the dissociated form.

The patho physiology of acute renal injury is multifactorial and far more complex than shock related tubular necrosis. The kidney is usually not considered as a target organ in methanol poisoning acute renal

1. Department of Nephrology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka
2. Associate Professor, Department of Nephrology, BSMMU, Dhaka.
3. Medical Officer, Department of Medicine, Chittagong Medical College Hospital, Chittagong
4. Assistant Professor, Shaheed Suhrawardy Medical College, Dhaka
5. Assistant Professor, Department of Medicine, East-West Medical College, Dhaka

Correspondence: Dr. Syed Fazlul Islam

failure but has been described in few case reports.The relative affinity of alcohol dehydrogenase for ethanol is much greater than for methanol (20:1) [2]. This difference has been exploited therapeutically in cases of poisoning, where alcohol is administered under medical supervision to reduce the formation of formic acid. At high concentrations, methanol elimination is saturated and is zero order with a rate of approximately 85 mg L-1, about half the elimination rate of ethanol. Maximum excretion of formic acid may be as late as the second or third day following ingestion. Small quantities of methanol are excreted unchanged in the lung and the kidneys (2% of a dose of 50 mg kg-1). Concentration of methanol in the urine may be 20-30% higher than in the blood ingestion of methanol can cause severe acute toxicity, as described in the general toxicity section. There is significant variability within humans on the reported oral toxicity and lethality of methanol. The minimal lethal dose following ingestion is considered to be in the range of 300-1000 mg kg-1[4]. In one review, the minimum lethal dose following ingestion has been reported at 15 mL of a 40% v/v methanol solution [5].

Rationality:

Multi system involvement due to acute methanol poisoning was observed in different literature but acute kidney injury that leads to end stage renal disease is a rare presentation.

Case history:

A 23 years old male working in a pharmacy shop. He was non diabetic, normotensive got himself admitted in a private hospital with the complaints of nausea and vomiting, cessation of urine following ingestion of 250 ml of methanol in a marriage ceremony to have some fun. Almost immediately he took another glass of mustard oil mistaking it to be water. He also complained of pain upper abdomen about 4 days later, cramping in character, of moderate severity, no radiation, has no definite aggravating or relieving factor. After about a week later he became increasingly confused and restless. On examination he was found to have severe renal failure, metabolic acidosis and dyselectrolemia. There he was treated accordingly including haemodialysis via femoral catheter and ICU support for 6 days. Since the patient did not show significant improvement of renal function after 12 days with 6 sessions of haemodialysis, he was referred to Nephrology Dept. BSMMU for further evaluation and management. Here he was further evaluated and continued with haemodialysis every alternate day. After one week since admission he complained of blurring of vision and weakness, more prominent in lower limbs making him unable to walk unaided. Accordingly he was referred to an ophthalmologist, and neurologist for their expert opinion and advice.

Opthalmologist found the patient to have bilateral papilloedema (Fig.-1), haemorrage and macular oedema and neurologist opined that the patient is suffering from toxic neuropathy involving all four limbs with involvement of left 7th cranial nerve. He advised NCS and added tab pregabalin 75mg twice daily, and folic acid antagonist (leucovorine) and to continue other treatment. On examination patient was anxious, ill-looking, have facial asymmetry with angle of the mouth pulled on the left side. Neurological examination revealed higher psychic function intact. Among the cranial nerves- UMN lesion of left 7th nerve was found. Motor function showed mild wasting of thigh and leg muscles, tonemuscle decreased in lower limbs, normal in upper limbs, muscle power 2/5 in all muscle groups of lower limbs bilaterally, 4/5 in upper limbs, knee jerks-absent bilaterally, ankle jerk present on left, absent on right, planter bilaterally flexor, biceps jerks diminished bilaterally, triceps absent bilaterally, supinator jerks normal bilaterally, Coordination normal in upper limbs but could not be tested in lower limbs gait- abnormal(stooped and cautious. Fundoscopy: bilateral papilloedema, and hemorrhage. Liver and spleen were not palpable, kidneys were not ballotable. Other systemic examination revealed nothing abnormality. Bed side urine- protein absent. Urine RME: prot: trace Sugar: nilPC: plenty/HPF RBC: 10-15/HPF Cast: not found C/S no growth CBC: TC- 10500/cmm DC- N40% L38% M07% E15%, ESR-50 Hb-10,5gm/dl serum electrolytes: Na -115 mmol/L, K-4.7, Cl-96,TCo2-21,Total bil-1.1mg/dl, SGPT-304 U/L(< 40) SGOT-180 U/L, Alk. phosphatase-48 U/L- USG of KUB RK 89 mm, LK 103mm Cortical echo-increased, CMD- poor, PVCS- not dilated, UB- normal, prostate-normal. Serum creatine kinase - 101U/L HBsAg – negative, Anti- HCV- negative. LDH level was high, urine showed myoglobline. Renal biopsy showed features suggestive of acute cortical necrosis (Fig.-2). Inspit of getting haemodialysis near about three months his renal function did not improve. An arteriovenus fistula was created in his left forearm for maintenance dialysis.

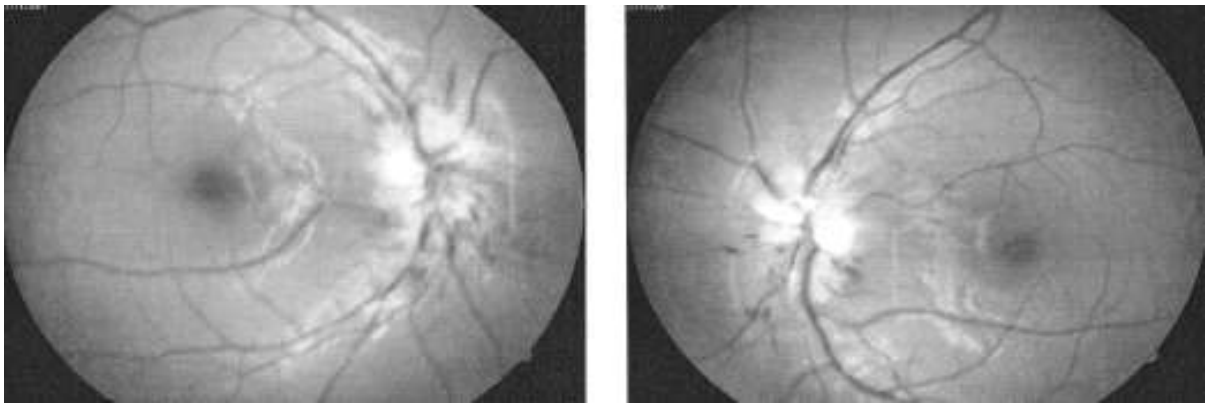

Fig.-1: *Fundoscopic photograph- bilateral gross papilloedema.*

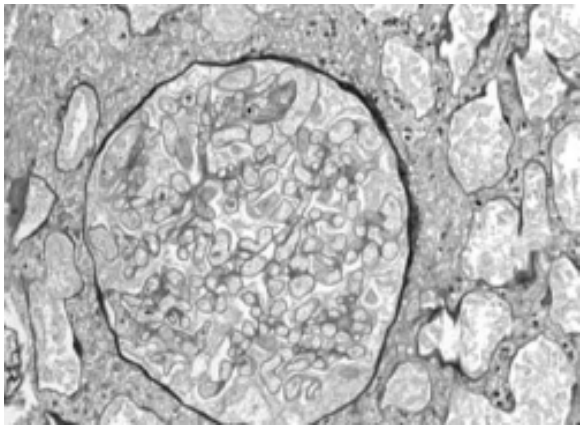

Fig.-2: *Renal biopsy showed acute cortical necrosis.*

Discussion:

In this case report we have observed, multi system involvement of acute methanol toxicity including CNS, eye and kidney. Literature in different study showed- loss of coordination (ataxia), shock, convulsions, seizures, coma, and hyperactivity of the deep tendon reflexes can result from methanol poisoning[6]. The last stage of acute methanol poisoning may cause permanent effects (i.e., damage to central, motor, and optic nerves), even from a single exposure[8]. The most common permanent consequences following severe poisoning are optic neuropathy, blindness, parkinsonism, toxic encephalopathy, and polyneuropathy. Permanent parkinsonian-like syndrome, which usually does not appear until several months to two years after methanol exposure, has been described[7] in this case report our patient developed, blurred vision generalized muscle weakness and tremor and bilateral facial nerve palsy . Fundoscopy revealed bilateral gross pappilloedema. Nerve conduction study showed both sensory and motor neuropathy.

Symptoms of acute methanol poisoning may include cessation of urine excretion (anuria), acute renal failure, and blood in urine (haematuria) [7]

This patient showed a metabolic acidosis, dyselectrolamia. Renal histology showed features suggestive of acute cortical necrosis from which he did not recovered. And he became dialysis dependent. If methanol is splashed into the eyes, it may cause rapid eye movements (nystagmus) and dilated pupils (mydriasis) [8]. Visual disturbances generally develop between 12-48 hours after ingestion, and range from mild photophobia and blurred vision to complete blindness. Toxic effect of methanol is compromised by hemo dialysis and folic acid antagonist leucovorine. Patient received several episodes of hemo dialysis and folic acid antagonist but unfortunately vital organs are not protected. Though there were mild improvement of muscle power , his renal function did not improve. The patient's presentation was delayed and toxic injury was so lethal that it lead to acute tubular as well as acute cortical necrosis, later on he became dialysis dependent.

Proper interpretation of toxicity due to methanol ingestion requires consideration of both methanol and formic acid concentration. Theoretically, toxicity due to methanol itself would include depression of the central nervous system. However, because of accumulation of formic acid subsequent to methanol

metabolism has the predominant toxic effects, acute central nervous system depression due to methanol ingestion unlikely. Rather, the accumulation of and exposure to formic acid result s in metabolic acidosis, potentially causing irreversible optical neuropathy and organ damage.

Most of the methanol poisoned patients exhibit severe metabolic acidosis as a consequence of both formic acid accumulation and, to less extent, lactic acid production. We observed a significant correlation between formic levels and development of acute renal injury. Formic acid is an inhibitor of mitochondrial cytochrome oxidase [8].

The inhibition increases with decreasing P^H, suggesting that the acute inhibitor is the undisassociated acid. This results in tissue hypoxia and cellular injury.

Formic acid the metabolites of methanol is toxic to various tissues. In spite of giving fatal antagonist leucovorin , removal of toxic product formic acid by hemodialysis, damage to the eye, kidney and nervous tissue was observed possibly toxic result was so severe and presentation was delayed. In this case severe metabolic acidosis was found but formic acid level was not done due to limited facilities.

Though histology showed feature of acute tubular necrosis, reversibility of renal function after short period was expected. Unfortunately there was no improvement of renal function was expected and patient become dialysis depended. This can be explained that renal involvement may be multifactorial.

Blood formic acid concentrations above 50 mg/dL have been associated with toxicity due to methanol ingestion, permanent tissue damage, or fatality[9]. The rare exception to this rule appears to be in cases of aggressive, timely hospital intervention[10].

References:

1. Shelby M, Portier C, Goldman L, Moore J, Iannucci A, Jahnke G, et al. NTP-CERHR expert panel report on the reproductive and developmental toxicity of methanol. Reprod Toxicol 2004; 18: 303-90.
2. Nelson BK, Brightwell WS, MacKenzie DR, Khan A, Burg JR, Weigel WW et al. Teratological assessment of methanol and ethanol at high inhalation levels in rats. Fundam Appl Toxicol 1985; 5: 727-36.
3. Darwish A, Roth CE, Duclos P, Ohn SA, Nassar A, Mahoney F, et al. Investigation into a cluster of infant deaths following 2002.
4. Fujita M, Tsuruta R, Wakatsuki J, Takeuchi H, Oda Y, Kawamura Y et al. Methanol intoxication: differential diagnosis from anion gap-increased acidosis. Intern Med 2004: 43.
5. Tephly TR, Wakatsuki, Maekawa T. The toxicity of methanol. Life Sci 1991; 48: 1031-41.
6. Reprotext, 2003: Reprotext® Document. Methanol. In: Hurlburt, KM (Ed.): TOMES System. Micromedex. Greenwood Village, CO 2003: 432-35.
7. Meditext 2003. Meditext® Medical Management (2003). Methanol. In: Hurlburt, KM (Ed.): TOMES? System. Micromedex. Greenwood Village, Co. 2003: 322-26.
8. Liesivori J, Savolinen H. Methanol and Formic Acid toxicity.biochemical mechanisms, pharmacol.Toxicol 1991; 69:157-63
9. Hovda KE, Urdal P, Jacobsen D. Increase serum formate in the diagnosis of methanol poisoning. J. Anal. Toxicol. 2005; 29: 586-88.
10. Hantson P, Haufroid V, Mahieu P. Survival with extremely high blood methanol concentration. Eur. J. Emerg. Med. 2000; 7: 237-40.