

Methanol intoxication complicated with intracranial hemorrhage

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Abstract

Methanol is a clear, colorless, highly toxic alcohol which is widely used in paint, varnish removers, automotive radiators and washer fluid. Methanol intoxication can occur after accidental, suicidal, or adulterated wine ingestion. Methanol itself is not toxic, but is metabolized to highly toxic formaldehyde and formic acid. Methanol ingestion leads to high anion-gap acidosis, and neurological complications like drowsiness to coma and devastating intracranial hemorrhages. Serious toxicities can occur with ingestion of 0.25 ml/kg of 100% methanol. Blood level of methanol more than 25 mg/dl are considered toxic. Peak plasma levels are reached within one hour. The treatment involves hemodialysis, antidote therapy and correction of acidosis. Herein, we report a case of young male who ingested methanol and developed intracranial hemorrhage at rare sites.

Keywords

methanol intoxication; intracranial Hemorrhage.

Introduction

Methanol is converted to formaldehyde and then to formic acid by alcohol dehydrogenase and acetaldehyde dehydrogenase, with peak levels attained 30 to 90 minutes after ingestion. It is these two metabolites that are highly toxic and produce severe high anion-gap acidosis, ocular, and neurological symptoms. Most incidents of toxicity occur after oral ingestion, but methanol is rapidly absorbed through lungs or skin. The serum half-life after mild toxicity is 14 to 20 hours, which can increase to 24 to 30 hours in severe toxicity. Methanol (90 to 95%) is eliminated by liver, while renal excretion accounts for 3 to 5 percent; pulmonary excretion is minimal [1]. Since its metabolism is very slow it can be found in the body for up to 7 days after ingestion. Brain injury associated with methanol toxicity can be ischemic, necrotic or hemorrhagic in nature. Putamen necrosis bilaterally, with or without hemorrhage and subcortical white matter lesions are the frequent findings. Possible hypotheses include a direct toxic effect of methanol or its metabolites, injury secondary to anoxia and acidosis. Secondary to anaerobic glycolysis and lactic acidosis, superoxide anions and hydroxyl radicals are generated, leading to cell membrane damage. Following this, there is an influx of calcium into the cell, causing mitochondrial dysfunction, cellular death and cerebral vasospasm [2].

Case Presentation

A 31-year-old male with history of psychiatric illness and alcohol abuse presented to the emergency department (ED) with unconsciousness. His respiratory rate was 30 breaths/min, non-invasive blood pressure 82/41 mm Hg, Heart rate 91 beats/min and temperature 36.8°C. The physical exam showed cardiovascular: S1, S2 normal, ECG- normal with corrected QT interval 470msec. Respiratory: air entry bilaterally equal. Neurological: glasgow coma scale-3/15, pupils bilaterally dilated and non-reactive, reflexes were absent at all joints. Patient was put on mechanical ventilation.

The laboratory investigations (**Table 1**) on admission are as follows: plasma creatinine: 1.9 mg/dl, blood urea nitrogen: 22 mg/dl; arterial blood gases - pH: 6.89, PaCO₂: 52 mm Hg, bicarbonate: 9.2 mmol/l, Base deficit 17.9, potassium: 4.4 mmol/l, sodium: 152 mmol/l and chloride of 118 mmol/l. The anion gap was 25 mmol/l with calculated osmolality: 320 mOsm/kg. Blood lactate levels were not available in the hospital. White blood count was 25000/mm³, hemoglobin 13.7 g/dl, platelets 308 lacs/mm³, random blood sugar 141 mg/dl, aspartate aminotransferase 31 IU/l, alanine aminotransferase 37 IU/l. Drug Toxicology report showed methanol level 131mg/dl. The patient underwent CT scan of brain that was unremarkable (**Figure 1a,1b**). The patient underwent conventional free heparin hemodialysis and was admitted to intensive care unit (ICU) for severe metabolic acidosis. Post hemodialysis methanol level became 28mg/dl. Patient was treated with intravenous normal saline, infusion sodium bicarbonate. Due to non-availability the patient didn't received neither ethanol nor fomepizole. Second day in ICU patient developed sodium-166 mmol/l and passed high volume, diluted urine. Diagnosis of diabetes insipidus was made clinically and CT brain was repeated which showed pontine hemorrhage extending into 4th ventricle, sub-arachnoid hemorrhage and diffuse brain edema (**Figure 2a,2b**). Third day patient developed loss of brain stem reflexes and sodium increased to 190 mmol/l. Electroencephalography (EEG) revealed brain death. No hemodialysis was further considered in view of brain stem death. The patient continued brain death for 7 days and developed cardiorespiratory arrest and died.

Discussion

Methanol is a clear, colorless solvent used in anti-freeze solutions, paint, varnishes, and fuel. Methanol poisoning may occur due to accidental or suicidal ingestion or due to consumption of adulterated alcoholic beverages. Acute methanol poisoning should be suspected in all patients with metabolic acidosis with an elevated anion gap, high osmolal gap and normal delta gap, neurological deterioration or vision disturbances. Since metabolism of methanol is very slow, the symptoms may develop within 40 minute to 72 hours and average incubation period is between 12-24 hours. The lethal dose of methanol is around 50-100ml [3]. Methanol undergoes oxidation in liver to formaldehyde via alcohol dehydrogenase and then to formic acid, which is six times more toxic and leads to weakness, nausea, vomiting, headache, abdominal pain, metabolic acidosis, blindness, seizures, coma and death [4]. The half-life of formaldehyde is 1-2 minutes. Formic acid is further oxidized to carbon dioxide and water in the presence of tetrahydrofolate. The metabolism of formic acid is very slow and thus results in metabolic acidosis [5]. Serum methanol levels of more than 20mg/dl identifies ocular injury. Brain injury can occur in form of ischemic necrosis or hemorrhage involving putamen bilaterally, sub-cortical white matter and pontine tegmentum [6]. Putaminal hemorrhage is also seen in cases of carbon monoxide and |

ethylene glycol poisoning [7]. High concentration of methanol metabolites in basal ganglia and ischemia due to high metabolic demand of basal ganglia and optic nerves causes direct toxicity. Diffuse brain edema, intracerebral and intraventricular hemorrhage with optic nerve necrosis have been identified in methanol intoxication [8]. The treatment involves Conventional Hemodialysis, antidote therapy in the form of fomepizole, ethanol and correction of acidosis with sodium bicarbonate. Bicarbonate therapy may reverse visual deficits and decrease the amount of formic acid. Use of heparin during conventional hemodialysis may lead to the hemorrhage seen in the necrotic areas of the brain and it's better to avoid heparin [9]. The American Academy of Toxicology recommends treatment with fomepizole rather than ethanol. Fomepizole is not commonly available. All alcohols are minimally protein bound, have a low molecular weight and distribution volume and hence efficiently removed by HD [10].

Criteria for therapy initiation in patients with known or suspected methanol poisoning: 1) Plasma methanol > 20 mg/dl. 2) Recent history of methanol ingestion in toxic amounts and an osmolar gap > 10 mOsm/l. 3) Suspected methanol ingestion with at least 2 of the following: arterial pH <7.3, serum bicarbonate <20 mmol/l and osmolar gap > 10 mOsm/l.

Conclusion

1) Possibility of methanol intoxication must be kept in mind in patient presenting with altered level of consciousness, visual disturbances, high-anion gap metabolic acidosis and brain lesions. Early treatment can save the life of patient. 2) Development of diabetes insipidus can give a clue to the development of intracranial hemorrhage. 3) Heparin free hemodialysis must be initiated and if hemodynamically unstable continuous veno-venous hemodiafiltration (CVVHDF) mode on continuous renal replacement therapy (CRRT) is the treatment of choice. Hemodialysis must be continued till the methanol level become below toxic range and correction of metabolic acidosis.

Figures

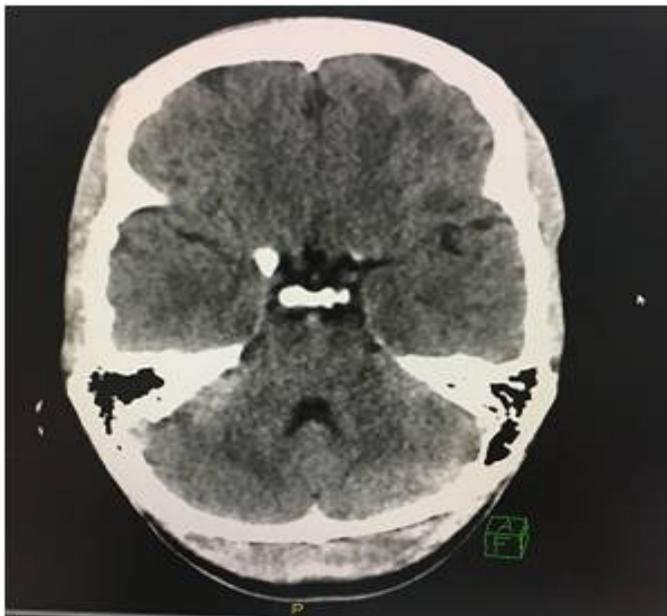


Figure 1a: (Normal CT brain scan without any hemorrhage).

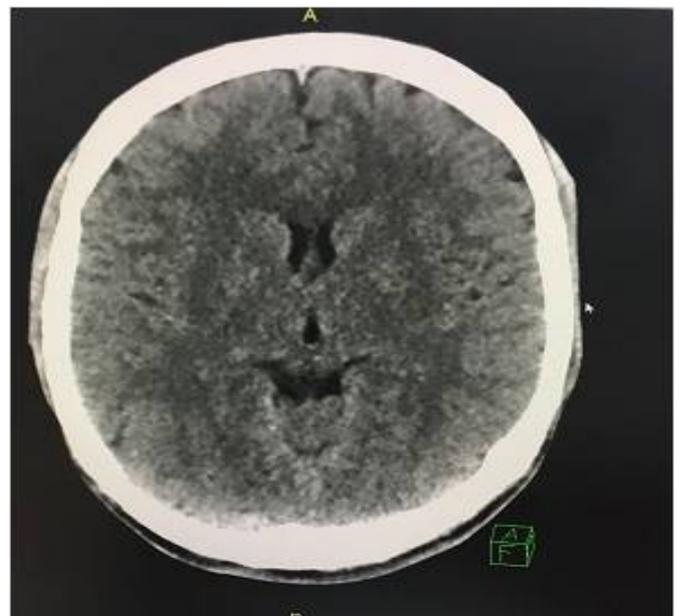


Figure 1b: (Normal CT brain scan without any brain edema).

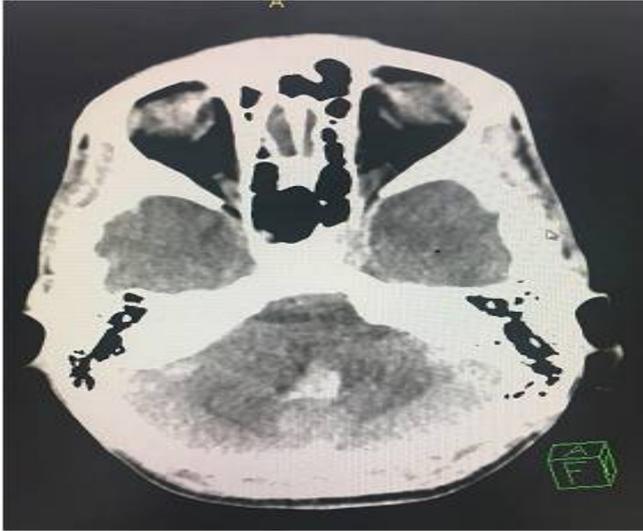


Figure 2a: (CT brain scan showing Pontine hemorrhage).

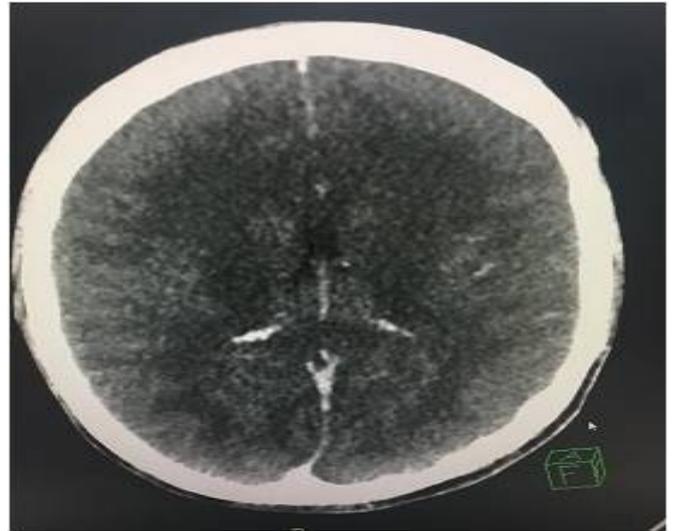


Figure 2b: (CT brain showing subarachnoid hemorrhage with diffuse brain edema).

Table

Table 1: The Laboratory data are as follows.

Blood Tests	Day 1	Day 2	Day 3
Blood gas			
pH	6.89	7.32	7.514
Co ₂ (mmHg)	52	19	34
HCO ₃ (mmol/l)	9.2	13.6	28.7
Base deficit (mmol/l)	-17.9	-15.7	+4.1
Anion Gap (mEq/l)	25	25.4	18.3
Chemistry			
Random sugar (mg/dl)	158	270	164
BUN (mg/dl)	22	13	14
Creatinine (mg/dl)	1.9	1.45	1.33
Calculated Osmolality (mOsm/kg)	320	351	394
Potassium (mEq/l)	4.4	3.6	2.3
Sodium (mEq/l)	152	166	190
Chloride (mEq/l)	118	127	143

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