

MARGOSA OIL POISONING AS A CAUSE OF TOXIC ENCEPHALOPATHY

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ABSTRACT

Margosa Oil is an extract of the seed of the Neem tree and is widely used as a traditional medicine by Indians in India, Sri Lanka, Burma, Thailand, Malaysia and Indonesia. Used mainly for external applications, it is often administered orally to neonates and infants regularly in small amounts.

Margosa Oil causes toxic encephalopathy particularly in infants and young children. The usual features are vomiting, drowsiness, tachypnea and recurrent generalised seizures. Leucocytosis and metabolic acidosis are significant laboratory findings. Management is aimed primarily towards the control of convulsions although supportive management is equally important. Prognosis is usually good but fatalities and neurological deficits have been reported.

We report here two infants with Margosa Oil poisoning presenting with encephalopathy.

Keywords: Margosa Oil, Poisoning, Toxic Encephalopathy.

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INTRODUCTION

Margosa Oil (MO), also known as Neem Oil, is a deep yellow oil with an unpleasant taste and smell. It is an extract of the seed of the Neem tree (*Azadirachta indica* A. Juss) a native tree of India but now widely distributed throughout Indo-Malaya⁽¹⁾. The oil contains volatile sulphur compounds and fatty acids which give it a strong odour and bitters (nimbin, nimbinin, nimbidin and nimbidol) which are responsible for its toxicity⁽²⁾. The oil is marketed locally in bottles under different brand names (Fig 1 & 2).

MO is known to cause toxic encephalopathy especially in infants and young children. We report here two cases of encephalopathy caused by MO poisoning.

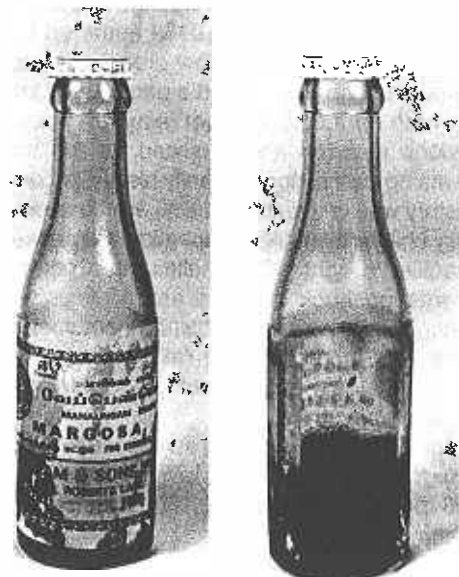
Case 1

AA, a 5-month old Indian male, was admitted to the Department of Paediatrics, Tan Tock Seng Hospital on 13 Feb 1987 at 1739 hours with a history of cough and running nose for one week before admission. He also had fever and diarrhoea but these symptoms had

subsided. At 1520 hours on 13 Feb 1987, AA was given 5 ml of Margosa Oil by the caregiver, followed by a milk feed. The child vomited half an hour later and soon after, there were generalised convulsions with loss of consciousness which lasted until admission. There was no past history or family history of convulsions. Birth and perinatal history had been normal.

Clinical examination revealed an afebrile child who was cyanosed, comatose and having generalised tonic-clonic seizures. Pupils were sluggishly reactive to light. There was no localising sign. Fundoscopy was normal. Tone and reflexes were diminished (postictally). The liver was palpable 2 cm below the right costal margin. The spleen was not palpable. No other clinical abnormality was noted. The seizures were aborted in the ward with intramuscular paraldehyde, intravenous valium and phenobarbitone.

Fig 1 and 2. Margosa Oil, available in small bottles as shown.



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The following investigations were done on admission:
Hb 11.5g%, Tw 35,800 P65 L33 M1 E1,
Platelets 265,000 ,
Urea 21 mg/dl, Na 134 mmol/L, K⁺ 4.8 mmol/L,
Cl 100 mmol/l Creatinine 0.8 mg/dl
Glucose 429 mg% (on admission), 354 mg % (Day 2),
79 mg% (Day 3)

Blood Gases: pH 6.903
pCO₂ 25.2 mm Hg
pO₂ 204.4mm Hg
HCO₃ 4.3 mmol/L
Base Excess -26.1
Saturation 97.8%

Urine Salicylates : Not detected

Blood Salicylates : < 1 mg%

Liver Function Tests : Total Protein 6.5 g/dl
Albumin 4.2 g/dl
Bilirubin 0.4 mg/dl
SAP 459 U/L
SGPT 355 U/L
SGOT 913 U/L

Prothrombin Time: 15 sec (15 sec)

Partial Thromboplastin Time (PTT): 36 sec (<38 sec)

Blood Culture: No growth.

AA had no further convulsions. His metabolic acidosis was corrected with intravenous sodium bicarbonate and a repeat blood gas study done five hours later showed the following: pH 7.334; pCO₂ 32.5 mm Hg; pO₂ 110 mm Hg; Bicarbonate 16.9 mmol/L; Base Excess -7.0; Saturation 96.8%. A lumbar puncture performed a day after admission was normal: CSF clear; cells – nil; Glucose 72 mg %; Cl 702 mg %; Total Protein 30 mg/dl; globulin negative; CSF culture grew no organism and CSF for Neurotropic viruses (Herpes Simplex, Measles, Mumps, Jap. B Encephalitis) were negative by Complement Fixation Tests.

He recovered without any complications and was discharged after one week. Electro-encephalographic studies (EEG) done two months after discharge was normal for his age. The child did not show any neurological deficit when seen three months after the illness. Unfortunately he defaulted further follow up.

Case 2

PT, a 3-month old Indian female, was admitted to us on 9 Sep 1987 with cough and running nose of four days duration but without fever. At 0900 hours on the day of admission, she was given 'a few drops' of Margosa Oil. Three hours later, the child had a generalised convulsion lasting half an hour. On her way to hospital, the convulsions recurred and persisted for the next hour. There was no past history or family history of convulsions. Birth history was uneventful. Clinical examination revealed a drowsy child with shallow respiration. Pupils were equal and reactive to light. Fontanelles were normotensive. There was no neck stiffness and Kernigs' sign was negative. Liver was 3 cm below the right costal margin. Her tone was increased and reflexes were brisk with ankle clonus. However there was no localising sign and funduscopy was normal.

On admission, the following investigations were done:
Hb 10.0 g%, TW 26,800 P22 L75 M2 E1
Urea 36 mg/dl, Na 135 mmol/L, K 4.9 mmol/L
Cl 110mmol/L
Glucose 94 mg%
Urine and Blood salicylates were not detected.

Blood Gases : pH 6.688
pCO₂ 58.4 mmHg
pO₂ 135.9 mmHg
HCO₃ 6.3 mmol/L
BE -31.6
Saturation 90.5%

Liver Function Tests: Total Protein 6.1 g/dl
Albumin 3.9g/dl
Bilirubin 0.6 mg/dl
SAP 239 U/L
SGPT 50 U/L
SGOT 157 U/L

Prothrombin Time (PT) 13 sec (13 sec)

Partial Thromboplastin Time (PTT) 26 sec (38 sec)

Blood culture was negative.

The convulsions were aborted with intramuscular paraldehyde, intravenous diazepam, phenobarbitone and phenytoin. Intravenous sodium bicarbonate was given to correct the metabolic acidosis and blood gas studies repeated 1 1/2 hours later showed : pH 7.311, pCO₂ 20.8 mmHg, pO₂ 176.5 mmHg, HCO₃ - 10.3 mmol/L, BE - 14.7, Saturation 99.2%. There was no recurrence of convulsions.

Lumbar puncture done the day after admission showed the following : CSF clear, cells 0, Glucose 63 mg%, Cl 708 mg%. Total protein 30 mg/dl, globulin negative. CSF culture no organism. CSF for Neurotropic Viruses was negative for Herpes Simplex, Measles, Mumps, JE by Complement Fixation tests (Titres were < 8).

The child was discharged well on the fourth day of admission. Electroencephalographic studies (EEG) done 2 1/2 months later was normal. The child had gone through normal development two years after his illness.

DISCUSSION

MO is widely used as a traditional medicinal remedy by Indians in India, Sri Lanka, Burma, Thailand, Malaysia and Indonesia. It is mainly used for external applications but is often given to neonates and infants regularly in small amounts for 'good health'. The toxins present in MO cause symptoms in the young but not in older children and adults.

Sinniah et al⁽³⁻⁵⁾ have reported a Reye-like syndrome in thirteen infants and children, all of whom were of Indian origin, with MO poisoning. The usual features are vomiting, which occurs within minutes to hours following ingestion of the oil, drowsiness, tachypnea with acidotic respiration followed by recurrent generalised seizures. The seizures are usually associated with loss of consciousness and coma and may last from a few minutes to several hours until relieved by treatment. All the above features were seen in both patients, who were also of Indian origin.

Investigations showed a significant leucocytosis in both cases but whereas Sinniah reported a polymorphonuclear leucocytosis in almost all his cases, we found a predominantly lymphocytic count in Case 2 (PT). This was probably due to a viral upper respiratory tract infection. Both patients had a marked metabolic acidosis which was easily correctable with intravenous sodium bicarbonate. Blood glucose estimation was high in Case 1 but the estimate had followed an infusion of dextrose saline given at the emergency department. Both cases also had raised transaminases which returned to normal on follow up.

Management of the patients was aimed towards controlling the convulsions, correcting metabolic acidosis and supporting with intravenous fluids and oxygen, where necessary. The seizures were controlled with valium, paraldehyde, phenobarbitone and in our second patient, phenytoin had to be added because of persistent convulsions. Intravenous sodium bicarbonate readily corrected the metabolic acidosis present in both patients. In animal studies, metabolic acidosis was found to be a main feature of MO poisoning and early treatment of acidosis could prevent the convulsions that are associated with this condition (3). Hence, treatment of metabolic acidosis is an important aspect of management of MO poisoning.

Prognosis is generally good with most showing no long term neurological sequelae as in both our patients. However, neurological deficits such as delayed

milestones, recurrent seizures and abnormal EEG have been observed. Death arising from MO poisoning has also been reported. Autopsy findings revealed changes resembling those observed in Reye's syndrome viz. fatty infiltrations of the liver and proximal renal tubules, with mitochondrial damage and cerebral oedema⁽⁶⁾.

CONCLUSION

Despite its extensive use as traditional medicine, MO ingestion is not without danger. MO poisoning is not commonly seen locally. Cases of poisoning could be missed or misdiagnosed as other disease conditions such as Reye's syndrome, encephalitis and febrile fits. Hence it is important to be aware of this condition and educate the public regarding the use of Margosa Oil.

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