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Case Report

Malignant Hyperthermia in Endosulfan Poisoning

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ABSTRACT

We are reporting a case of endosulfan poisoning, admitted in a state of altered consciousness, vomiting, and seizure. The diagnosis was based on history, physical examination and positive reports from toxicological screening. After 8 hrs of admission, a sudden rise in $EtCO_2$, respiratory rate, heart rate, blood pressure, and body temperature was noted. Masseter spasm was there and patient's elbow/knees could not be bent upon manipulation. Caffeine halothane contraction test later confirmed it to be malignant hyperthermia (MH). We suggest that if there is a sudden rise in body temperature, stiffness in limbs or massater spasm in a case of endosulfan poisoning, the diagnosis of MH should be considered as one possibility when etiology is not certain.

Key words: Endosulfan, malignant hyperthermia, poisoning, seizure

INTRODUCTION

Endosulfan is a chlorinated hydrocarbon, used as an insecticide. We are reporting an episode of malignant hyperthermia (MH), in a case of endosulfan poisoning.

CASE REPORT

A 28-year old male with no significant medical/family history was brought to the emergency department, in a state of altered consciousness, vomiting, and after two episodes of seizure. An empty bottle labeled: Akodan (Endosulfan 35%) was collected by the police at the site of incident. On examination, he was afebrile, tachypnoeic and had a blood pressure (BP) of 82/44 mm Hg, heart rate (HR) of 142/min and Glasgow coma score of 8. There was no neck rigidity and reflexes were normal. Chest skiagram and electrocardiogram were unremarkable.

He was rehydrated with isotonic saline (1 liters IV) over 20 minutes and with continued rehydration his BP returned to 110/76 mm Hg within 30 minutes. Invasive positive pressure ventilation was started (continuous positive airway pressure/pressure support mode), gastric lavage was done and 30 g of charcoal slurry was inserted through nasogastric tube. Gastric content had a sulfur odor and sent for toxicological screening. Midazolam (0.05 mg/kg/hr) and sufentanil (0.5 μg/kg/hr) infusion was started. Initial laboratory results revealed elevated creatine kinase (CK), and liver enzymes [Table 1]. After 8 hrs, a sudden rise in end-tidal CO_2 ($EtCO_2$) to 64 mm Hg, respiratory rate (RR) to 42 breath/min, BP to 160/100 mm Hg, nasopharyngeal temperature to 104° F, and SpO_2 to 80% was noted. Drugs administered until this point were midazolam, sufentanil and thiopentone. Breath sounds were vesicular and no arrhythmia was detected. Masseter spasm was there and limb joints could not be bent upon manipulation. He was immediately shifted to synchronized intermittent mandatory ventilation (100% FiO_2, RR~20/min). Dantrolene infusion was started (2.5 mg/kg over 10 min) and repeated after 15 min. Ice packing, cold isotonic saline

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Table 1: Laboratory values

Test (units)	Range	On admission	1 day later	4th day
Hemoglobin (mg/dl)	11.5-17.4	12.0	-	-
Hematocrit	41-53	37%	-	-
Total leukocyte count (cells/dl)	4,000-11,000	13600	11200	8400
Blood urea nitrogen (mg/dl)	7-20	28	62	25
Creatinine (mg/dl)	0.6-1.2	0.6	1.8	0.6
Random blood sugar (mg/dl)		110	112	98
Sodium (meq/L)	135-148	137	136	140
Potassium (meq/L)	3.5-4.5	3.7	5.2	4.2
Calcium ionic (mmol/L)	1.12-1.32	1.0	0.9	1.2
Platelet count (lakh/cu.mm)		2.52	2.46	-
Serological test		Normal	-	-
CK (U/L) *	60-400	489	1667	302
CK-MB (ng/ml)	0-7	7	10	5
Troponin I (ng/ml)	0-0.4	0.03	0.1	0.08
AST (U/L) †	0-35	152	185	36
ALT (U/L)	0-35	186	212	40
LDH (U/L) §	115-221	240	435	206
Myoglobinuria	-	++	++	-
Serum total bilirubin (mg/dl)	0.3-1	0.8	1.2	0.8

*CK=creatine kinase, †AST= alanine aminotransferase, ‡ALT= aspartate aminotransferase, §LDH=lactate dehydrogenase.

infusion (0.9% IV), cold gastric lavage was done and arterial line was placed. Blood gas analysis revealed P_H of 7.13, PaO_2 of 105 mm Hg, $PaCO_2$ of 68 mm Hg, HCO_3 of 22 meq/L, Base excess of −11.3, Na^+ was 142 meq/L, K^+ was 5.8 meq/L, and Ca2+ was 0.9 mmol/L. Other laboratory results include elevated CK, liver enzymes and myoglobinuria. [Table 1] Dextrose/insulin infusion was started and furosemide (10 mg IV) was given. Following initial resuscitation, a rapid drop in temperature to 99.5°F and $EtCO_2$ to 40-50 mm Hg was noted and vitals continued to improve: SpO_2 at 99%, BP at 122/87 mm Hg, HR at 96/min over next half hr. Further lab evaluation revealed normal thyroid profile. In the next 3 days, serum enzymes returned to normal subsequently. [Table 1] He was extubated on the 4th day after admission with no other complication. He subsequently reported that he tried to commit suicide by taking 1 spoonful of Akodan. His EEG after 4 days showed bilateral synchronized intermittent delta activity; however, CT scan was normal. He was advised to take Sodium valproate (2 wks) and shifted to psychiatry clinic. The diagnosis of endosulfan poisoning was confirmed by history, physical examination and positive reports from toxicological screening. 4 weeks later, caffeine halothane contraction test confirmed it to be MH.

DISCUSSION

The pathophysiology of MH is still not fully understood. Patients have higher than normal resting sarcoplasmic Ca2+ concentrations and exposure to agents like volatile anesthetics and neuropsychiatric drugs may trigger uncontrolled intracellular Ca2+ release, leading to excessive muscle contraction, rhabdomyolysis and MH. Midazolam, thiopentone and sufentanil administered to this patient before the onset of MH, are not known to be associated with MH or rhabdomyolysis.[1] So in this case, intracellular accumulation of Ca2+ might have occurred in a state of uncontrolled catecholamine excitation, due to the inhibition of gamma-amino butyric acid receptors by endosulfan.[2] During a normal contractile response, shortly after releasing Ca2+, sarcoplasmic reticulum (SR) begins to re-accumulate it by Ca2+ and Mg2+ ATP ase pump.[3] Thus intracellular accumulation of Ca2+ could also occur by inhibition of Ca2+ and Mg2+ ATP ase, leading to failure of Ca2+ sequestration into SR and also its reduced efflux from the cell.[3] Endosulfan is known to manifests its toxicity by the same mechanism.[2] It could therefore lead to intracellular accumulation of Ca2+ leading to excessive muscle contraction, and rhabdomyolysis. Endosulfan augments lipid peroxidation, increase production of superoxide and significantly alters glutathione redox cycle in neural and hepatic tissues of rats, leading to cell necrosis.[4] Our patient also presented with elevated liver enzymes, myoglobinuria and hypocalcemia. There was no previous history of any thyroid disease/cocaine overdose/pheochromocytoma or any predisposing drugs. Thus in absence of any other predisposing factors, MH in this case could be attributed to endosulfan poisoning.

Endosulfan is well known to cause gastrointestinal symptoms, convulsions, cardiac arrhythmias, renal and pulmonary insufficiency. Our patient also presented with nausea, vomiting and seizures. Further episodes of seizure might have been prevented by the prophylactic use of midazolam. Bilateral synchronized intermittent

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delta activity in his EEG, is a usual feature of endosulfan poisoning.[5]

We suggest that if there is a sudden rise in body temperature, joint stiffness or masseter spasm in a case of endosulfan poisoning, the diagnosis of MH should be considered as one possibility when etiology is uncertain.

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