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Research Paper

A Case of Accidental Aniline Poisoning In a Glucose-6-Phosphate Dehydrogenase Deficient Technical Staff

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ABSTRACT
Chemical Poisoning is high in this environment, mostly due to farm agents (pesticides and insecticides) commonly used for suicidal attempts in adults. However, accidental poisoning is mostly recorded in children from household agents.

We described a case of accidental chemical poisoning from aniline in a University male laboratory support staff who was rushed to accident and emergency (A/E) of the teaching hospital in coma. He was transferred to the Intensive Care Unit(ICU) after being stabilized and managed as unconscious patient. However, patient could not receive methylene blue as an antidote due to unknown Glucose-6-Phosphate dehydrogenase (G6PD) status. He developed intravascular haemolysis on the 3rd day of admission while awaiting G6PD result which came out deficient. He developed suspected transfusion reaction while on an exchange blood transfusion with features suggestive of intravascular haemolysis and died on day 6post admission.

KEY WORDS: *Aniline, Poisoning, G-6-PD deficiency*

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I. INTRODUCTION

Globally, acute accidental poisoning is responsible for 2-3million of poisoning cases annually in adults[1]. They are mostly due to contamination of food and water, or exposure to fumes from farm agents. In rural to agrarian communities, farm chemicals are mostly responsible for cases of poisoning while in urban centre, drugs (overdose) and industrial chemicals are the causal agents. Accidental poisoning is more common among children than adults while most cases of poisoning in adults are due to suicidal attempts usually among teenagers and young adults.

Cases of poisoning are responsible for 9.4% of admissions in emergency department[2]. Most presentations are due to unconscious or confused states. Agents could easily be identified in most cases from history and examination. Initial management include elimination of agent to reduce further absorption, stabilization of patient following ABCD of resuscitation and administration of appropriate antidote.

We report a rare case of aniline poisoning in a 57year old male University laboratory support staff.

Case Report

57year old male laboratory support staff of a University, who was rushed to the accident and emergency (A and E) of the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC) by colleagues and family members due to 4hour history of loss of consciousness from acute chemical intoxication. He was a level 3 officer with a secondary school certificate who was employed as an office messenger at entry level and had no formal training on laboratory safety before being upgraded to the post of a laboratory support staff.

He had an accidental percutaneous spillage of aniline dye kept in the pocket of his laboratory coat while moving bottled reagents from the chemical store to the laboratory for Students' practical demonstration. He had his right thigh and abdomen affected by the aniline spillage. He removed the Lab coat and immediately irrigated the affected sites of the body copiously with water. However, he became dizzy after 15mins and lapsed into unconsciousness. Examination revealed a middle aged unconscious man with GCS: 7/15 (EO:2, VR:1, MR:4), in respiratory distress evidenced by dyspnea and central cyanosis. There was no pallor, fever, icterus,

dehydration, lymphadenopathy, pedal edema or neck stiffness. Pupils were 3 mm dilated and reactive to light. He had a pulse rate and blood pressure of 106/bpm and 110/60 mmHg respectively. Cardiovascular, respiratory and abdominal examinations revealed no abnormalities.

Patient's medical and social history did not suggest any psychiatric or medical illness. He took alcohol occasionally. He was rushed to the university health center where he was placed on intranasal oxygen and IVFs. Problems identified in the patient were unconsciousness, central cyanosis and hypoxaemia. He was transferred to the ICU to be managed by a multidisciplinary approach as an unconscious patient on mechanical ventilation which improved the oxygen saturation to 96%. He was also placed on infusion midazolam at 0.05mg/Kg/hr (3mls in 1:1/hr) and rabeprazole 40mg 12hrly. He had a suprapubic cystostomy done due to difficulty in catheterization for fluid monitoring. Results of preliminary investigations yielded mild anemia, anisocytosis with normal WBC and platelet counts on peripheral blood film and hemoglobinuria on urinalysis. He was however, awaiting results of G6PD assay before commencing methylene blue in a dose of 1-2mg/Kg, as antidote to aniline poisoning.

On Day 2 post-exposure, patient was febrile, tachycardic and hypoxic with hypertension. Urgent blood film for malaria parasite was positive and he was commenced on parenteral antimalaria and antihypertensive (IV labetalol slowly over 15 minutes and tabs amlodipine daily via NG tube), while IVF was changed to 5% D/S to alternate with ringers lactate 1L 6hrly. On day 3, result of G6PD assay revealed deficient status and methylene blue was suspended for risk of hemolysis. As an alternative to methylene blue, he was commenced on exchange blood transfusion (EBT) with 20mg Lasix cover. However, patient became febrile with rigors and restlessness which necessitated a stop of procedure. Urgent urinalysis showed haemoglobinuria, urobilinuria and hematuria suggesting intravascular hemolysis. He was given IM pcm (600mg stat), IM hydrocort (100mg stat), IM promethazine (25mg stat), IVF 0.9 % N/S 1 L fast, recommence midazolam infusion at 3mg/hr. Post EBT results of investigations showed anemia, direct Coombs test was negative, re-grouping and cross-matching for both donor and recipient was A^+.

On Day 4, patient was conscious but sedated, pale and febrile. Urine Input/output in the preceding 24hrs showed a negative balance of 903ml with an episode of watery, foul-smelling (about 700mls) stool since admission. Vital signs revealed low oxygen saturation, elevated BP, tachycardia and tachypnoea. Lab results showed severe anemia, leukocytosis with neutrophilia and normal platelet count. Assessment of sepsis with anaemia was made and patient had 1 unit of blood transfused, IV ceftriazone was commenced. On day 5, he became restless despite sedation with midazolam, hypoxemic with elevated BP, tachypneic, febrile and oliguric. On Day 6, Patient also had 4 episodes of foul smelling loose mucoid stools. Available EUCR result suggestive of renal insufficiency and assessment of acute kidney injury secondary to sepsis with possible GIT as focus of infection in a patient with aniline poisoning was made. Antibiotics was changed from ceftriazone to meropenem and he was prepared for haemodialysis. IV lasix 100mg stat then 100mg into alternate pint of IVF. After 1hour, patient vital signs declined, hypotensive, pulse inpalpable, hypoglycaemic (urgent RBS: 1.7mmol/L) necessitating urgent IV 50% D/W 25mls 1:1 dilution slowly over 5 mins.CPR, IV adrenaline 1:1000mg 1 mg stat. Repeat vital signs following resuscitation showed elevated BP, PR 96bpm, RPG of 6.7mmol/L.The plan was to monitor vital signs every 15 minutes for an hour then every 30 minutes for 2 hours followed an hour monitoring. Repeat plasma glucose every 4 hour, if < 2.5 mmol/L, to give IV 50% D/W 25mls 1:1 dilution over 5 minutess and continue other line of management. After about 30 minutes, he suffered another cardiac arrest, CPR was repeated and IV adrenaline 1 mg was administered.There was a response,however, he suffered a 3rd episode of cardiac arrest about 20 minutes later.Both CPR and a shot of adrenaline were repeated twice within 10 minutes.There was no response.He was certified clinically dead at 6:35 pm on 6th day post-aniline poisoning exposure.

Table 1: Summary of Clinical Examination

	Baseline	4hours	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6
T^OC	36.4	37.2	38.2	39.5	36.6	38.2	39.4
R.R(cpm)	10	20	20	15	30	20	24
P.R(bpm)	106	114	102	110	108	102	94
SBP(mmHg)	110	110	160	150	120	160	110
DBP(mmHg)	60	70	90	70	80	90	60
SPO_2 (%)	77	88	98	78	97	98	78

R.R respiratory rate; P.R pulse rate; B.P blood pressure; SPO_2 oxygen saturation

Table 2: Summary of Treatment Plan

	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6
Midazolam	0.05mg/kg	0.05	0.05	0.05	0.05	-
Rabeprazole(mg)	40	40	40	40	40	40
IM EMAL (mg)	-	150	150	150	-	-
IV Labetalol(mg)	-	5	5	5	5	5
IV Ceftriaxone(g)	-	1	1	1	1	-
IV Meropenem(mg)	-	-	-	-	-	500
Amlodipine(mg)	-	5	5	5	5	5
Fluid (mL)	3000	3200	3800	4000	3700	-
Output (mL)	535	2220	2897	1590	395	-

Table 3: Summary of Laboratory Results

	Day 1	Day 2	Day 3	Day 4
PCV (%)	35	32	31	19
WBC (/mm^3)	-	-	-	18,000
Neutrophils (%)	-	-	-	86
Lymphocytes (%)	-	-	-	14
Platelets (/mm^3)	-	-	-	356,000
Blood film	-	1+ malaria parasite	-	-
Na^+	-	140	-	139
K^+	-	5.3	3.6	3.3
Cl^-	-	NA	NA	NA
HCO_3	-	-	-	26
Urea	-	4.6	-	9.5
Creatinine	-	79	82	168
Urinalysis	Haemoglobin	-	Haemoglobin urobilin	-

NA not available

II. DISCUSSION

Aniline is a weak base commonly used in manufacturing of dyes, antioxidant, rubber, drugs, chemicals and herbicides. It is an oxidizing agent rapidly absorbed through the skin, nasal and gastric mucosa[3,4]. The most reported mechanism of exposure remains inhalational but for this case, it was dermal. Following exposure, aniline binds to hemoglobin Fe^{2+} ferrous oxidizing it to ferric Fe^{3+} resulting in methemoglobinemia with reduced oxygen carrying capacity and ensuing hypoxia. Clinical features of methemoglobinemia are respiratory distress and central cyanosis which were striking signs in this case table 1. Methemoglobin is a common cause of methemoglobinemia[5]. The oxygen saturation for this case was between 77 and 91. It has reported that higher methemoglobin level reduces the O_2 saturation is lower[6-7]. On the other hand, patients with methemoglobinemia may have normal PO_2 despite life threating MHb[6].

Previously reported cases had their MHb concentrations quantified, however, we were not able to quantify the MHb fraction of this patient due to lack of facility in the managing hospital, and financial constraint which hindered sending the patient's sample to an outside laboratory where it could be done (healthcare at the management Centre is by out of pocket mode). This may have resulted in the delay of management with dire consequence.

Management options for aniline poisoning include non-pharmacological and pharmacological approaches using high flow oxygen therapy, methylene blue as an antidote in a dose of 1-2mg per kilogram body weight which can be repeated but not exceeding 7mg/kg in 24hours, exchange blood transfusion and hemodialysis[8] along hydrocortisone and bronchodilators[8-9]. Ascorbic acid has been reported to directly reduce metHb irrespective of the G6PD status by shifting the oxyhemoglobin dissociation curve to the right[10] thereby improving the O_2 delivery to tissues. The guideline recommends methylene blue be given 4hours post exposure which was delayed in this case due to his unknown G6PD status. This is because in individuals with G6PD

deficiency, there's lack of NADPH which could render methylene blue ineffective[9]. Also, G6PD deficient individuals are prone to hemolytic anemia from oxidative stress like infections, sulfonomide containing drugs like dapsone or and chemicals like aniline. Methylene blue as an antidote for aniline poisoning could not be commenced for this patient due to the G6PD result which came out deficient. It is advised to withhold methylene blue as an antidote to aniline poisoning in G6PD deficient patients and institute other supportive management[10]. This informed our decision to perform exchange blood transfusion (EBT) in this case. However, patient developed hemolysis during the procedure. The development of hemolytic anemia in this patient was probably worsened by his G6PD status. Previously reported cases found their subjects developing hemolytic anemia following doses of met-blue with no recorded mortality although the G6PD status of those cases were not ascertained[8]. Reasons being that hemolytic anemia could result from both MHb and methylene-blue administration due to oxidative stress leading to red cell destruction[9]. Therefore, the hemolytic anemia observed in this case may be due to the oxidative stress caused by methemogblobinemia resulting in red cells destruction despite withholding methylene blue. Some studies have suggested that patients with G6PD deficiency are more prone to developing hemolytic anemia[11], whether with methylene blue administration or not remains unknown. However, there are suggestions to be cautious in administering methylene blue to patients with renal insufficiency and G6PD deficiency[12-14]. It therefore implies that patients with aniline poisoning with G6PD deficiency may still benefit from methylene blue antidote if cautiously administered since it can potentiate MHb to causing hemolysis. This present case did not receive hydrocortisone as part of early supportive management until the day 3 post-exposure, this would have probably delayed the hemolytic anaemia precipitated by aniline poisoning. Also, ascorbic acid was not given probably due to its less importance as supportive management. Previous studies reported that glutathione and ascorbic acid reduce metHb directly but are quantitatively of minor importance[15]. This index patient was noticed to develop acute kidney injury which could be a direct effect of the haemoglobinuria, and indirect effect of anemia induced renal hypo-perfusion. He however, died on day six post exposure before results of re-grouping and cross-matching came out and he could not benefit from hemodialysis which is another approach to managing aniline poisoning.

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