Compartment Syndrome of the Lower Limbs in Association with Paraphenylinediamine Poisoning: Case Report and Literature Review

Kaballo B G[1], Mahgoub M A[2] , Elnazir EM[2] , Omer OH[2], Ibrahem A H[2], Gadour MO [3]

A 36-year old Sudanese military officer presented to the medical casualty at a rural hospital in western Sudan, with facial and neck swelling, enlargement of the tongue, difficulty in breathing and hoarseness of voice. Symptoms developed immediately after having a cup of tea in the morning. He also had burning sensation in the mouth and throat, severe epigastric pain and nausea but no vomiting. The patient felt generalized body aches, severe calve muscles pain associated with paraesthesia and tingling sensations in upper and lower limbs. He also complained of severe intractable burning feet. The patient had no history of psychiatric illness or any chronic disease and was not on long term medications.

He was not known to be sensitive to drugs or allergens. He is married and has sons and daughters. The patient was diagnosed to have angioneurotic oedema and was managed accordingly. Tracheostomy was immediately performed along with intravenous hydrocortisone, antihistamine injections and oxygen therapy. Three days later he noticed that his stool was loose yellowish, turned dark and his urine was reduced in amount. Foley's catheter was introduced and moderate amount of dark brown urine passed immediately. After another three days he became anuric. The patient was then referred to renal centre at Omdurman Military Hospital with a diagnosis of acute renal failure (ARF) following hair dye poisoning.

On Physical examination, he was ill, not pale, jaundiced or cyanosed. His pulse was 100/min., peripheral pulses in lower limbs were impalpable. BP was 170/90 R.R 24/min. JVP was raised .Apex in the 5th I.C.S. normal S_1, S_2 no evidence of pulmonary oedema. Abdomen was normal. Neurological examination revealed no abnormality. Lower limbs were swollen, very tense and tender particulary in calve muscles, Investigations showed urinanalysis: Colour brownish (fig 1), Albumin three (+).

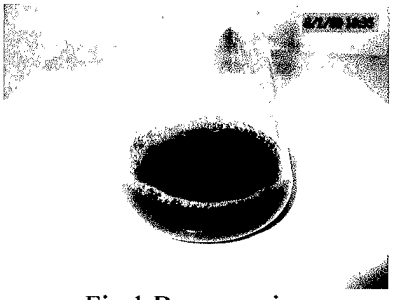

Fig.1 Brown urine

Pus cells: uncountable. RBCs: uncountable, granular cast four (+) (fig 2&3).

Blood picture, HB 12.0 gm/dl, WBCs 22300 cu/ml, ESR 50mm. Blood urea 195 mg/dl, S. creatinine 12 mg/dl, S. Ca^+ 7.3 mg/dl (R.V 9 – 10.4 mg/dl), S. uric acid 9.5 mg/dl, Na^+ 116 mmol/L K^+ : 4.2 mmol/L, Phosp. : 9.1 mg/dl (R.V 2.5 – 5.0 mg/dl), CPK : 50130 U/L (R.V 24 – 190), S. Alb. : 3.5 g/dl, S. Globulin : 2.9 g/dl, T. Bilirubin : 0.7 mg/dl, S. GPT115 U/L, SGOT : 150 U/L, Abdominal ultrasound: Normal size both kidneys, with bilateral loss of cortico-medullary differentiation and prominent pyramids (suggestive of ARF), no calculi or obstructive changes, normal liver, gallbladder, spleen, urinary bladder with small residue and no ascites. Chest X-ray: normal. HCV, HIV and HBS Ag were negative.

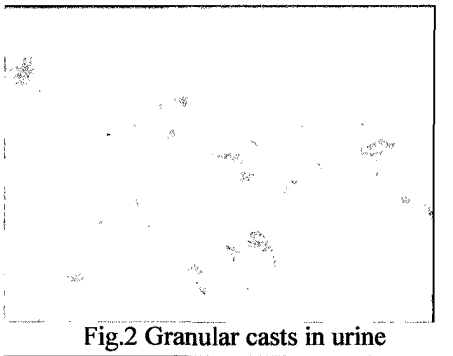

Fig.2 Granular casts in urine

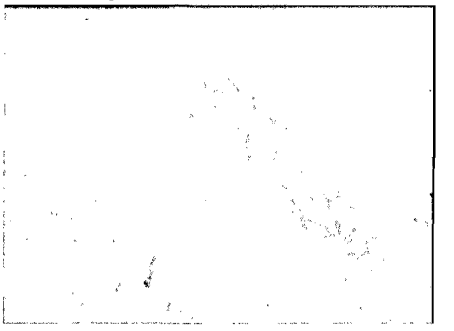

Fig 3. Granular casts in urine

1. Nephrology Unit, Military Hospital Omdurman, Sudan
2. Pathology department, Military Hospital Omdurman, Sudan
3. Department of Medicine, Omdurman Islamic University, Sudan

Corresponding author: Nephrology Unit, Military Hospital Omdurman, Sudan. Fax: 00249 15 529584
E-mail: B.Kaballo@hotmai.com

Paraphenylene diamine (PPD) was detected in the sample of urine collected two days before admission by Thin Layer Chromatography method (TLC) confirming the diagnosis of Acute Hair dye poisoning. Gastroscopy showed acute gastric erosions. Renal biopsy report: Thirty three glomeruli were seen with unremarkable changes but few showed mesangial expansion, wide spread tubular necrosis with intra-luminal casts composed of tubular proteinecous eosinophlic material, detached tubular cells, debris and inflammatory cells. The interstitium was infiltrated by neutrophils and eosinophils. The interstitial blood vessels were normal. These features are consistent with acute tubular necrosis (ATN). (fig 4 and 5).

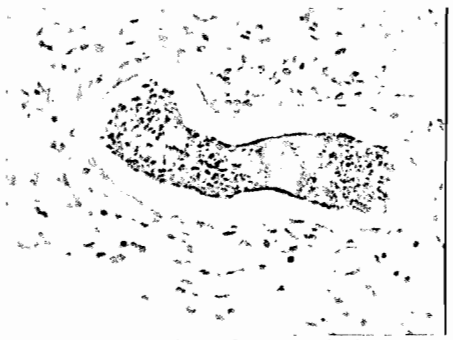

Fig 4. Features suggestive of acute tubular necrosis

Fig.5. Features suggestive of acute tubular necrosis

Immuneflourescense tests were negative for immunoglobulins, fibrinogen and compliments.

Peritoneal dialysis was immediately started. This was shortly followed by short daily sessions of haemodialysis for 10 days. Then he was considered for alternate day haemodialysis. Haemodialysis continued for 3 weeks when the patient regained normal renal function. Referring the patient for fascitomy was considered initially but abandoned because of the remarkable improvement of his lower limbs after initiation of dialysis.

Discussion

Toxicity of paraphenylenediamine (PPD) (synonyms: p-Diaminobenzene, "Para", p-Phenylenediamine) has been recognized for over a century[1-3]. PPD [C6HiNH2)2; M.W.=108.1] is a derivative of paranitroaniline. It is also used to stain animal furs, in photochemical measurements, in accelerating vulcanization of rubber, and to manufacture azo dyes[4, 5, 6]. PPD is thought to be oxidized in vivo to a quinine di-imine and then acetylated to form a diacetyl derivative. The quinine diimine of PPD is the toxic derivative.

Skin exposure to PPD has been considered to cause exfoliative dermatitis, contact eczema and asthma. After ingestion concomitant gastritis may develop. It may also lead to anemia, cyanosis, cardiac toxicity, hepatitis, vasculitis, vertigo, rise in blood pressure, tremors, convulsions, coma and death. Symptoms generally start 4 – 6 hrs after ingestion and the patient shows characteristic face presentation: face is swollen and oedematous with oedematous bull neck, bulging eyes, open mouth with oedematous wooden and heard protruded tongue. Urine is characteristically chocolate brown. Urine microscopy shows gross or mild albuminurea with haematurea: PPD can be detected by thin layer chromatography. Early major cause of death is asphyxia and irreversible ventricular fibrillation[6, 7].

Severe acute tubular necrosis was the definite histopathological pattern seen in this patient. However, some degree of mesangial glomerulopathy which we think is reactive and secondary to severe tubular damage has also been observed[8]. ARF may result from prerenal (hypovolaemia), intrarenal (ATN) and postrenal causes. Severe rhabdomoylsis was indicated clinically by severe muscle tenderness and development of compartment syndrome of the legs. Very high level of creatinine kinase (50130 u/l) was seen in our patient. These levels were disprortionate to levels seen in cases of acute tubular necrosis not associated with rhabdomyolysis. Severe muscle damage is one of the additional contributory factors to the severity of acute tubular necrosis as myoglobin is toxic to tubules.

The clinicalopathological set up in this patient is consistent with rhabdomyolysis, acute renal failure and compartment syndrome of lower limbs due to severe PPD intoxication.

Henna coloring when used alone is a lengthy and tedious procedure. PPD may be added

to the mixture to accelerate the process, to darken, and to give more precision to the design. That is why the agent attracted attention when it became a regular additive to hair dyes containing Henna, and led to a variety of severe intoxications[5, 6, 9-11].

Henna is a traditional dye in the Middle East, the Indian subcontinent, China and Africa. It consists of the dried leave of *Lawsonia alba,* The coloring matter is 2-hydroxy-1, 4-naphthoquinone. It may also be prepared synthetically. There has never been any evidence that Henna itself might be toxic. Thus toxicity of the combination of Henna and PPD, known as "black powder" is solely associated with PPD[6, 12-15].

Fatal cardiac arrest in a 22-month-old child three hours after PPD ingestion was described by Bowen in 1963[16].It is estimated that about 4% of apparently normal subjects are allergic to the agent. In this context, the leading symptom is an angioneurotic edema. In the early 1980's, few cases of acute and chronic renal failure following the use or ingestion of Henna/ PPD were published. Chugh et al.[13] reported the first acute renal failure in two women in India after suicidal ingestion of hair dye (PPD and Henna). Suliman reported 17 cases with acute renal failure in Sudan after accidental, suicidal or homicidal ingestion of PPD. 12 of these patients died within 48 h after ingestion. Similar reports were published from India, Morocco, Tunisia and other African countries[6, 15].

Early tracheostomy is life saving and gold standard management on presentation. No antidote is known for PPD, and there is no experience regarding active toxin removal. However, haemoperfusion in early hours of intoxication might help in the treatment of acute PPD intoxication and improve the outcome[6].

Acute haemodialysis has to be avoided on presentation because of the haemodynamic instability of these patients due to the cardiac toxicity of the dye. Continuous renal replacement therapy is not available as yet in this country as well as in most other developing countries. Acute peritoneal dialysis was considered because of convenience, availability and safety. Our patient had short frequent haemodialysis sessions with excellent recovery.

To the best of our knowledge, this is the first time for compartment syndrome of the legs to be reported as a consequence of acute PPD poisoning.

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