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Case Report

Paraphenylenediamine Poisoning in Tunisia: A Case Report

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Abstract

Paraphenylenediamine (PPD) represents the main active substance in the color of hair dyes. In Tunisia, PPD poisoning is very common, especially in rural areas where the consequences linked to this toxic substance are still unknown. In this paper, we report a case of PPD poisoning and confirm the diagnosis by a qualitative method of analysis. We discuss the clinical manifestations and study the kinetics of biological parameters during the monitoring of the poisoning. The main complication was renal failure and the treatment was basically symptomatic.

Key words: p-Phenylenediamine, PPD, Hair dyes, Renal failure, Poisoning

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حالة تسمم بمادة البارافينيلين داي أمين في تونس: تقرير حالة

تمثل مادة البارافينيلين داي أمين Paraphenylenediamine PPD المادة الفعالة الرئيسية في لون صبغات الشعر. ويعتبر في تونس التسمم بمادة البارافينيلين داي أمين أمر شائع جداً، لا سيما في المناطق الريفية حيث العواقب المرتبطة بهذه المادة السامة لا تزال غير معروفة. في هذه الورقة، تم تسجيل تقرير عن حالة تسمم بمادة البارافينيلين داي أمين، حيث تم تأكيد التشخيص من خلال طريقة التحليل النوعي. وتم مناقشة المظاهر السريرية، ودراسة حركية المعايير الحيوية خلال مراقبة حالة التسمم، وكانت المضاعفات الرئيسية لهذه الحالات هي الفشل الكلوي، وتم التركيز على معالجة الأعراض فقط.

Introduction

p-Phenylenediamine (PPD), also known as 1,4-Diaminobenzene (C6H8N2), has many industrial applications. In cosmetology, it is generally added to hair dyes (Henna, Lwasonia inermis) and is used as a permanent body dye (Black Henna or Harkous) to produce a darker shade [1, 2]. Henna is a flowering plant belonging to the Lythraceae family. Harkous (Black Henna) is a mixture of many compounds including nut gal, clove, and tannins and is used as a permanent tattooing dye[2]. Both Henna and Harkous are traditionally and widely used in North Africa [2]. In Tunisia, these are freely sold, which increases their use, especially by young women.

PPD is not known to be carcinogenic but it has been linked to several health problems. Exposure routes are

through inhalation, skin absorption, ingestion, and skin and/or eye contact. Symptoms of exposure include throat irritation (pharynx and larynx), bronchial asthma, and sensitization dermatitis, and in more serious cases it causes angioneurotic edema, rhabdomyolisis, and even renal failure [1, 3, 4]. PPD is suspected to be responsible for many cases of poisoning whether by accidental ingestion or attempted suicide [5, 6]. Its commercialization should therefore be strictly regulated.

In this paper, we report a case of accidental ingestion of PPD in Tunisia reviewing chemical, clinical, biological, and analytical features.

Case Report

A 33-year-old woman was brought to the emergency and intensive care center (Tunisia) with an alleged history of accidental unknown poisoning. On inquiry, it was revealed that a day before this incident she ingested a black powder mixed with water. The suspected product was brought by the patient's mother to be investigated in our laboratory. This product was identified as a black stone and is shown in the Figure 1.

Figure 1- *Black stone of suspected product*

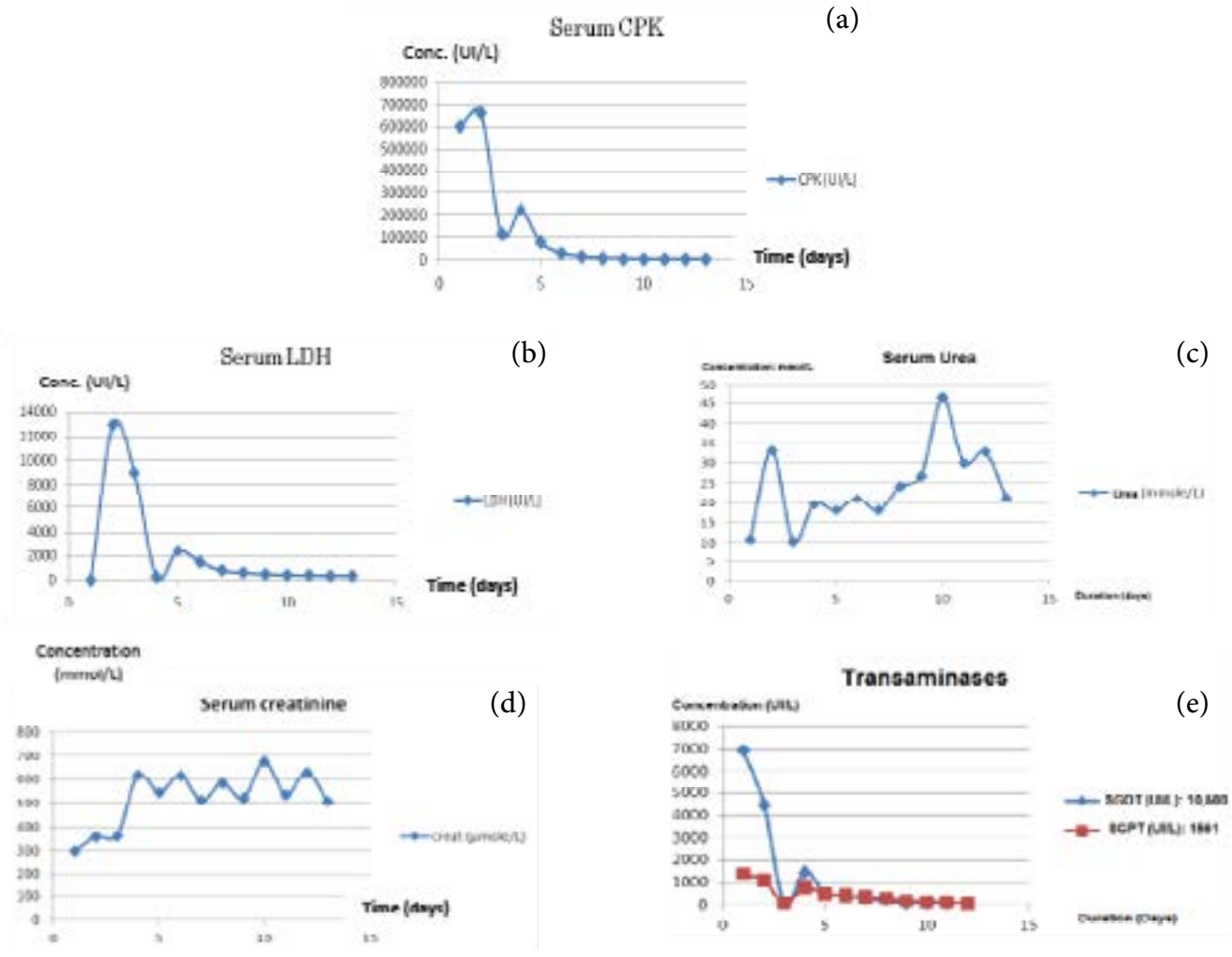

Figure 2- *Kinetics of serum parameters during hospitalization: (a) CPK, (b) LDH, (c) urea, (d) creatinine, and (e) transaminases*

On admission, the patient was conscious, eupneic, and had complaints of nausea, vomiting, muscle pains, a lower limb disability, parasthesia and conjunctival discoloration. Her body was covered by papules and her urine was black colored. Systemic examination was normal.

Biological investigations showed a rhabdomyolysis with an increasing of serum CPK (600 000 UI/L) and serum LDH (15 000 UI/L). Her hepatic enzymes were high (10500 UI/L for glutamic-oxaloacetic transaminase GOT and 1561 UI/L for glutamic-pyruvic transaminase GPT), suggestive of a hepatic cytolysis. Her blood urea and serum creatinine were 297 µmol/L and 10.9 mmol/L, respectively, revealing an acute renal failure. The evolution of these biological parameters during her hospitalization is presented in Figures 2 (a, b, c, d, e).

Her hematological parameters showed hyperleucocytosis and a platelet count of 562,000/mm3. She also had hyperkalemia, hypocalcaemia and hyperphosphatemia. Metabolic acidosis was confirmed by arterial blood gas analyses. The urine of the patient had a black color. Its examination revealed proteinuria, hemoglobinuria, and hemosiderinuria. A gastric lavage was done and the patient was managed with symptomatic therapy based on oral calcium and sodium bicarbonate. Alkalization of urine was performed to facilitate the elimination of the toxic substances and metaboloites. Because of her persistent oliguria, she was started on haemodialysis on the second day of hospitalization. In view of the non-improvement of the renal function, three other dialysis sessions were performed on the 5th, 7th and 9th day (4 hours per session) after admission.

Based on clinical and biological symptoms, toxicological investigations were directed towards a possible PPD intoxication. The suspected black stone was analyzed by thin layer chromatography (TLC) and gas chromatography coupled with mass spectrometry (GC/MS). TLC was performed by an alkaline liquid-liquid extraction with ether as an extraction solvent.

A mixture of ammonia/methanol (0.75:50; v/v) was used as a migration bath. Results showed an Rf of 0.7, equivalent to that obtained by a pure PPD standard, thereby suggesting intoxication by PPD. The TLC plate for the suspected substance is given in Figure 3.

The results were confirmed by GC/MS [7] using a DB-5MS capillary column (Agilent). High-purity helium was used as the carrier gas with a constant flow at 1 mL/min; splitless injection was performed at a purge time of 2 min and a purge flow of 20 mL/min. The oven temperature was

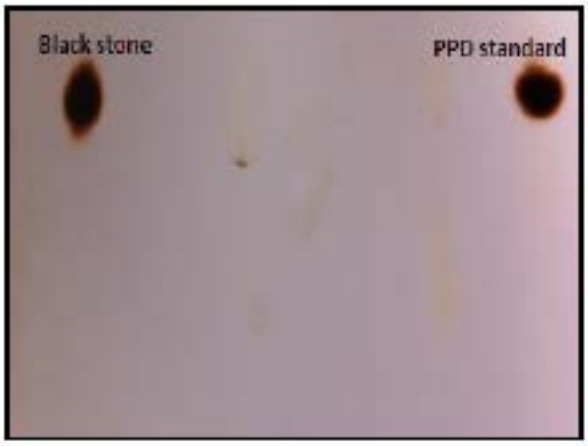

Figure 3 - *Thin layer chromatography plate for the suspected substance (the black stone)*

programmed from 100°C to 290°C at 25°C/min in the scan mode. The equilibration time was 0.5 min. Using these conditions, the parent compound (PPD) was identified in the suspected stone ingested by the patient with a chromatographic peak at a retention time of 5.6 min (Figure 4-a). For urine, the chromatogram revealed a peak at 10 min linked to N, N'- diacetyl paraphenylenediamine, the main metabolite of PPD (Figure 4-b).

Toxicological monitoring was performed in order to establish the elimination kinetic of this poison. N,N'-diacetyl paraphenylenediamine persisted even after the first dialysis and disappeared only after the second one, a week after the admission.

To rule out any possible intoxication by heavy metals such as lead and cadmium, blood lead and cadmium levels were determined by graphite furnace atomic absorption spectrometry (GF AAS). No significant levels of heavy metals exposure was found.

Discussion

PPD (C6H8N2) is a substance presented as uncolored crystals which become brown and then black under UV radiation. It has an aromatic structure derivatized from aniline. It is obtained by reduction of aminobenzene with hydrogen sulphide [1]. PPD is considered as a lesional toxic substance. The formation of oxidized derivatives of PPD such as benzoquinone diimide is responsible for the destruction of muscle cells by a mechanism of membrane lipid peroxidation leading to muscle necrosis and severe rhabdomyolisis.

In the present investigation, the patient suffered from

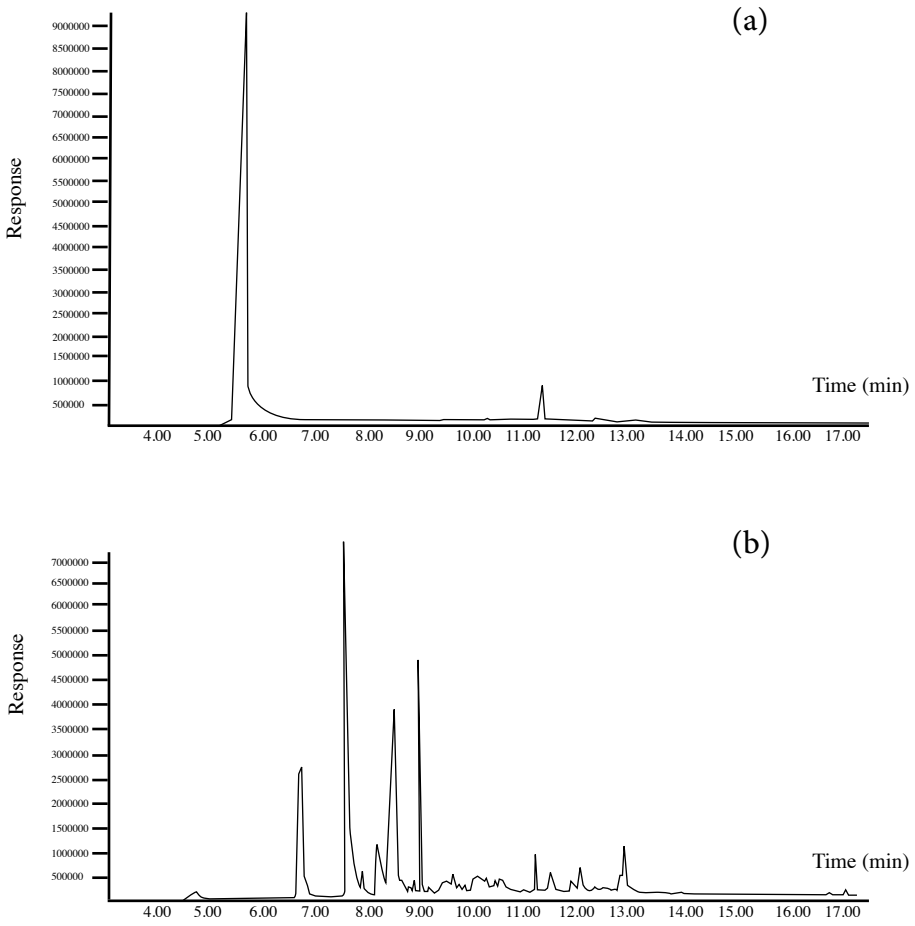

Figure 4- *PPD in the suspected stone (a) and its metabolite in urine (b) chromatograms*

muscular tension and myalgias due to rhabdomyolisis with an increase in plasma concentrations of LDH and CPK, about 1000 times the average values in the 48th hour after ingestion (Figures 2-a, b).

Serum transaminases levels were also high, from 30 to more than 100 times the highest limits of normal values (< 45.0 UI/L), explaining the hepatic cytolysis. This injury can be argued histologically by a micro and macro vesicular steatosis with portal inflammatory and hepatic impairment [7]. Moreover, clinical features were mainly marked by severe renal failure with very high serum levels of creatinine and urea. These parameters reached their upper values on the 10th day of hospitalization with levels of 46.4 mmol/L and 677 µmol/L for urea and creatinine, respectively (Figures 2-c and d). Plasma levels of lead (30 – 169 µg/L) and cadmium (< 1 µg/L) were considered to be normal, making PPD the only cause of nephrotoxicity.

The cause of acute tubular necrosis in PPD poisoning is due to concentration of PPD in renal tubules. This occurs due to the aromatic structure of PPD which makes it readily absorbable and concentrated in the tubules [4].

Hyperleucocytosis could be explained by the formation of substances with inflammatory activity deriving from the oxidation of PPD. This would increase the permeability of blood vessels, explaining the occurrence of oropharyngeal edema, one of the first manifestations of acute poisoning [8].

Besides renal injury, respiratory distress and muscular symptoms were also observed at the beginning of PPD poisoning. Patients who are not treated immediately may develop severe complications which can be fatal.

Regarding the treatment, there is no known antidote for PPD and the therapy is purely symptomatic [4]. In our case, the patient was ventilated, sedated and treated with dialysis. Her clinical condition improved within two weeks. PPD was totally eliminated within 7 days but the renal fail-

ure has persisted which showed the huge impact this toxic substance can have on renal function.

Conclusion

Clinical features of PPD poisoning are mainly dominated by renal failure, respiratory distress and muscular syndrome. A symptomatic and evacuator therapy must be rapidly applied in order to avoid respiratory and cardiac complications. The prevention of renal failure requires hemodialysis and alkaline diuresis.

In Tunisia, PPD is sometimes used as an excipient during the preparation of traditional cosmetics to maintain the fixation of dark color. This substance can cause serious health problems. Therefore, a regulatory decision should be taken by the government to control the use of PPD in cosmetic products.

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