Fatal toxic myocarditis induced by Paraphenylene Diamine. A case report

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Abstract: Para phenyl diamine (PPD) is an aromatic amine derivative of Aniline that is widely used as a cosmetic product, particularly in hair dye preparations. PPD acute poisoning leads to respiratory distress, rhabdomyolysis, muscle necrosis and renal failure. Cardiac complications are rarely reported in the literature. We will present a case of PPD poisoning presenting as myocarditis, associated to rhabdomyolysis with a fatal outcome. A 22-year-old man was hospitalized for ingestion of a hair dye. At admission it had a severe edema of the face and neck. Laboratory exams showed renal failure, increased serum lactate deshydrogenase, creatine phosphokinase and troponine T. Toxicological screening showed the presence of Paraphenyl Diamine in blood and stomach. The patient died in the tenth day due to a cardiogenic shock. A forensic autopsy was performed. The pericardium was spotted by multiple hemorrhagic petechiae. The myocardium and the epicardium had multiple hemorrhagic areas. Histological examinations revealed the presence of acute inflammation of the myocardium and epicardium associated with severe ulceration of the endocardium. Inflammatory infiltrate consisted mainly of neutrophils with frequent micro abscesses in the myocardium and epicardium. Death was attributed to Paraphenyl Diamine poisoning complicated with rhabdomyolysis and acute myocarditis.

Key Words: para phenyl diamine, poisoning, hair dye, myocarditis.

Paraphenylene diamine (PPD) or black dye is an aromatic amine derivative of the Aniline, which is traditionally used as cosmetic product, particularly in hair dye preparations in the Maghreb countries and India [1]. PPD poisoning is emerging as an important etiological factor of suicide worldwide [2].

Acute hair dye poisoning leads to respiratory distress, rhabdomyolysis, muscle necrosis and renal failure. Mortality rate is high and especially related to respiratory and renal complications [3]. Cardiac complications, such as myocarditis and arrhythmias, have been rarely reported in the literature.

In this paper, we report a lethal case of PPD poisoning causing myocarditis associated to rhabdomyolysis.

CASE REPORT

A 22-year-old man, without any medical history, came at the Emergency Department with complains of hematemesis that appeared after ingestion of hair dye.

On examination, he was drowsy with a Glasgow Coma Scale of 13. He had a severe face and neck edema, a pulse of 100/min, a blood pressure of 90/40 mmHg and a respiratory rate of 24/min. The electrocardiogram showed sinus tachycardia without arrhythmia or atrioventricular conduction abnormalities. The patient was immediately ventilated mechanically, with oro-tracheal intubation. Laboratory exams showed renal failure (serum urea at 10,5 mmol/L; serum creatinine at 256 µmol/L, hyperkalemia - 8,2 mmol/L), increased serum...
lactate dehydrogenase (LDH) - 16416 UI/L [normal value = 135-220 UI/L], creatine phosphokinase (CPK) 127890 UI/L and troponine T - 4,59 ng/L [normal value < 0,02 ng/L]. Arterial blood gas analysis revealed metabolic acidosis. Initial treatment consisted of diuretics, sodium bicarbonate, oral calcium and alkalinization. In view of his persistent oliguria and deranged metabolic parameters, he was put on hemodialysis. The toxicological screening showed the presence of Paraphenyl Diamine in blood and stomach. Death was caused by cardiogenic shock in the tenth day after admission.

At the autopsy we found moderate bilateral pleural effusion (600 mL). Lungs were heavy, weighing 1550 and 1170 g with a massive hemorrhagic edema. The heart weighed 344 g. The pericardium was spotted by a multiple hemorrhagic petechiae some of which had centrally a white spot (Figs 1, 2). The myocardium and epicardium had multiple hemorrhagic area. The maximal myocardial wall thickness was 15 mm on the left ventricle and 5 mm on the right ventricle (Fig. 3). Histological examinations revealed the presence of acute inflammation of the myocardium and epicardium (Fig. 4) associated with severe ulceration of endocardium (Fig. 5). Inflammatory infiltrate consisted mainly of neutrophils sometimes organized in micro abscesses in the myocardium and epicardium (Fig. 6). Death was
attributed to Paraphenyl Diamine poisoning followed by rhabdomyolysis and acute myocarditis.

**DISCUSSION**

Paraphenylenediamine (PPD) is an aromatic amine, in which at least one hydrogen of the cycle has been replaced with an amine substitute. It is a brown or black coloured solid substance, easily soluble in hydrogen peroxide and not in water. It’s widely used in the Maghreb as a cosmetic product.

Absorbed orally for suicidal intention or for criminal purposes, PPD causes both local and systemic toxicity. By electron oxidation, PPD is metabolized to an active radical by cytochrome P 450 peroxidase to form a reactive compound called benzoquinone diamine. This can be further oxidized to a trimer, known as Bandrowski’s base, which is reported to cause anaphylaxis as well as being strongly mutagenic [4]. The toxic effect consists of a direct attack on striated muscle, but there is no indirect toxicity by metabolic or neuromuscular abnormalities. In humans, the toxic dose is estimated at 3 g and the onset of symptoms usually is between 4 and 6 hours; 15 to 120 minutes in the series of 56 PPD poisoning reported by Zeggwagh [5]. Complications of acute PPD poisoning are usually secondary to rhabdomyolysis and usually include hyperkalemia, hypocalcemia, hyperphosphatemia and hyperuricemia [6], all causing acute kidney injury. Myocarditis, pericarditis, arrhythmias are reported as rare complications of PPD poisoning [7].

Typically, myocardium is rarely injured in toxic rhabdomyolysis. The mechanism of myocardial lysis in PPD poisoning is not clear yet. It could be a direct involvement of the myocardial fiber by membrane lipids peroxidation, and a storage inhibition of calcium in the sarcoplasmic reticulum responsible for calcium overload [8]. For myocarditis, although it is reported since 1969 [9], it remains poorly documented and it seems difficult to accurately determine its frequency, as the myocardial function is not always affected. In 1996, Zeggwagh _et al._ [5] described two cases of toxic myocarditis due to PPD. Referring to Dallas criteria, the diagnosis of myocarditis requires the presence of an inflammatory cellular infiltration on conventionally stained myocardial tissue sections with or without associated myocytes necrosis [10, 11].

The diagnosis of myocarditis after PPD is difficult. The clinical features are extremely variable, ranging from asymptomatic disease, to heart failure with cardiogenic shock. Cardiac injuries may be aggravated by circulatory and metabolic complications of rhabdomyolysis. The myocardial involvement is dose dependent [12]. The sensitivity of electrocardiogram for myocarditis is only 47% and the most common ECG findings are nonspecific T-wave changes [13]. Cardiac biomarkers of myocarditis also lack specificity, but they may help to confirm the diagnosis [14,15]. Increased serum concentrations of troponin I (TnI) or troponin T (TnT) are more frequent than increased levels of creatine kinase [14,15], and occur in 32–49% of patients due to myocytes damage [6]. The troponin elevation in PPD poisoning can also occur due to rhabdomyolysis, sepsis, renal injury and heart failure [4].

Sometimes it is impossible to differentiate between myocarditis and myocardial infarction [16]. Transthoracic echocardiography was proposed to confirm the diagnosis of myocarditis due to hair dye poisoning [17]. It may show regional wall motion abnormality and decreased left ventricular ejections fraction. The value of coronary angiography in diagnosis of myocarditis was revealed by Brahmi _et al._, who reported a case of myocarditis with myocardial infarction induced by PPD and where the diagnosis was confirmed by angiography showing septoapical hypokinesia due to the spasm of the

![Figure 5. Ulceration of the endocardium (haematoxylin and eosin stain x 40).](image)

![Figure 6. This high magnification view shows the inflammatory infiltrate consisting mainly of neutrophils (haematoxylin and eosin stain x 400).](image)
left anterior descending coronary artery [1].

Mortality of PPD poisoning is high, ranging from 25-33% depending on the series. The most frequent causes of death are renal failure and respiratory distress. The mortality related to myocardial injury appears high [4]. In clinical practice, myocarditis diagnosis is difficult and it’s often a postmortem finding. At autopsy, the appearance of the myocardium is very evocative and histology confirms the diagnosis.

CONCLUSION

PPD poisoning is often used for suicidal attempt. Its main acute toxic effects are rhabdomyolysis with renal failure and respiratory distress. Myocarditis may be only found at the autopsy but it can also be a direct cause of death. With regards to treatment, there is no specific antidote available and the management of PPD poisoning.

References