

Suicide Death from Paraquat Auto-Inoculation: A Case Report

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Abstract

We examine a case involving a 34-year-old man who died of complications following the self-inoculation of Paraquat for suicidal purposes. During the crime scene investigation were seized all the paraphernalia were analyzed and were positive for Paraquat. At the autopsy were found an area of hemorrhagic infiltration on the inside face of the abdominal wall, in correspondence of the right peri-umbilical region, following the self-inoculation of the Paraquat performed. The aspects of greatest interest of the particular case under examination have been analyzed. In particular, we have taken into consideration the biochemical and toxicological aspects of Paraquat and the medico-legal problems related to the inoculation of the compound.

Keywords: *suicide, autopsy, forensic toxicology.*

Introduction

Although poisoning or drug intake are the most common suicidal conducts in Italy, Paraquat poisoning is relatively rare in our country compared to others (especially in Asia)^{1,2,3,4,5}. From the case here reported emerged that, even small quantities of the compound taken for suicidal purposes, may have a rapid fatal course, with the progressive onset of renal failure and pulmonary fibrosis. The relative impact of medical-pharmacological treatment following these events is not clear; however, given the importance of an early diagnosis of the picture, it is possible to insert more often this particular harmful practice in the differential diagnostic reasoning in the presence of pulmonary, gastrointestinal and renal signs and symptoms, so as to be able to undertake elimination therapy, as soon as possible. In this paper, we examined a case involving a 34-year-old male subject who died of complications following the self-inoculation of Paraquat for suicidal purposes. Once the aspects of greatest interest of the particular case under examination have

been analyzed, we have systematically considered the biochemical and toxicological aspects of this substance, with specific attention to the medical-legal problems connected to it.

Case Report

The case examines the death of SA, a male subject aged 34 at the time of the facts, who, after access to the Emergency Department reported the self-inoculation of an herbicide not better specified in the abdomen, in the right peri-umbilical region; it should be added that the anamnesis was positive for a previously diagnosed schizophrenia, and that the subject was in pharmacological treatment at the local Center of Mental Hygiene. The subject's conditions, at the entrance to the emergency room, appeared characterized by a relative clinical stability, with a normal range in routine blood tests and in the vital parameters. However, due to suicidal behavior, the health care workers considered prudent to keep the patient under observation, arranging for admission to the Department of Surgery. Toxicological analysis on the syringe used for self-inoculation were positive for Paraquat. The subsequent course was characterized by a relative clinical stability, although on the 4th day it was observed a progressive alteration of the renal function parameters (in particular hyper-azotemia and hyper-creatininemia), evolved in a frank Acute Renal Failure

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picture, together with hyperglycemia. Therefore, the health care workers arranged a necessary hemodialysis session. Meanwhile, in addition to the specialist advice of a psychiatrist due to the schizophrenic framework shown by the patient, the Poison Center's opinion was also required, which provided specific indications about the therapy. The next day (the fifth day of hospitalization) the clinical picture was aggravated by the appearance of a severe hypoxia and desaturation, so that the Resuscitation Consultant considered advisable to arrange the moving of the patient to the Intensive Care Unit; here the chest radiographic examination showed signs of severe interstitiopathy, and the blood gas test provided data to support hypoxemia and ventilatory deficit; therefore, the patient was subjected to Oro-Tracheal Intubation in order to connect him to the Mechanical Ventilator. On the following days, the conditions remained stable in their gravity: in addition to a persistent hypoxia, the blood glucose, azotemia, creatinine, transaminase and gamma GT values remained high, making up for a picture of multi-organ suffering. Despite the help of the mechanical ventilator and of the oro-tracheal intubation, bilateral pleural effusion and pulmonary parenchymal alterations radiologically documented, also occurred. Finally, on the 22nd day of hospitalization there was a definitive aggravation of clinical picture with the appearance of hypotension and massive desaturation, despite the help of the automatic respirator and circulation deficit and despite the attempt of inotropic drugs administration to support hemodynamic (sympathomimetic amines); in the early hours of the following day, after the appearance of severe involuntary bradycardia evolving in asystole, despite the resuscitation maneuvers, the death of S. A. occurred.

Autopsy Findings

The autopsy subsequently performed found:

- an area of hemorrhagic infiltration on the inside face of the abdominal wall, in correspondence of the right peri-umbilical region, following the self-inoculation of the Paraquat performed by S. A.

- a very marked picture of congestion and multiple-visceral edema, with greater expression at the encephalic and pulmonary levels;

- aspects of pulmonary parenchyma congestion, with large areas of inflammation as well as a marked fibrotic pattern of the bronchial tree.

These data, although relatively non-specific, thus allowed to identify the cause of death of S. A. in an acute cardio-circulatory and respiratory failure, as terminal epiphenomena of a Multi-Organ Failure Syndrome secondary to acute intoxication by exogenous substances, in particular Paraquat.

Hystopathological Findings

Upon histological examination of the samples collected in the autopsy site, the most interesting findings were as follows:

- Edema and Encephalic congestion;
- Acute pulmonary emphysema;
- Massive congestion of every examined parenchyma.

Discussion

Paraquat dichloride (1,1'-dimethyl-4,4'-bipyridinium dichloride) is a contact herbicide widely used in this chemical form in agriculture; it is the most important compound of the dipyridyl herbicide family⁶. In most of Paraquat-based herbicides available on the market, it is associated with other herbicides (such as Diquat); usually, for this type of formulations (in which the percentage of Paraquat never exceeds 2.5%), the harmful effects are limited to nausea and / or vomiting, which may or may not be associated with alterations in the main functional parameters of respiratory mechanics, however without lethal effects⁷. The clinical effects of this substance are usually related to the ingested dose: in the majority of cases with an (oral) dose intake equal to 20-40 mg of Paraquat / kg, the death occurs within 2 or 3 weeks from the ingestion, while for larger doses (> 40 mg / kg) the death occurs 1 to 7 days after exposure^{8,9}. Although accidental deaths from Paraquat exposure by inhalation or transdermal absorption are reported^{10,11}, the oral intake (either accidental or deliberate) is the most commonly involved; this substance is not significantly absorbed, in fact, in the absence of continuous skin solutions¹². Studies related to cases of Paraquat poisoning have shown that this substance has a toxic action developing with some delay compared to the intake ; the lesion, in fact, manifests itself during the following days (as mentioned, the times vary mainly according to the ingested dose) with dramatic changes at pulmonary level, with the appearance of pathological changes associated with dyspnoic symptomatology, until to produce a ARDS framework due to the destruction of alveolar epithelial

cells¹³; the main pathophysiological mechanism is the liberation of free radicals with oxidative damage of the pulmonary tissue. While pulmonary edema and pulmonary damage may be acute, within a few hours from a quantitatively severe exposure, late toxic damage can lead to a picture of pulmonary fibrosis, which is the most frequent cause of exitus¹⁴. The lung, therefore, is the typical target of the Paraquat: here the chemical products resulting from the reactions of oxygen are in fact available, which, reacting with Paraquat, produce free radicals.

Lung damage follows a two-phase pattern¹⁵: a) Pneumocytes concentrate the chemical compound thanks to the active membrane transport mechanism, with the destruction of the alveolar epithelium; b) Progressive inflammation and fibroblastic proliferation lead to widespread pulmonary fibrosis. In some cases, pneumothorax or pneumomediastinum may also derive from the progressive action of the inflammatory process, extending up to the esophagus¹⁶. The toxic action of Paraquat also occurs in the kidney: here, the necrosis of proximal tubule cells causes renal failure, but this clinical spectrum is sometimes reversible by forced hydration protocols^{17,18}. In addition, the direct effects of Paraquat on the ocular, cutaneous or on mucous membranes should not be forgotten, where it can lead to irritation or ulceration in case of direct contact^{19,20}. The treatment of Paraquat poisoning is based on measures aimed to modify both the kinetics and the toxic dynamics²¹. Toxicokinetic can be modified by reducing its absorption, removing the poison from the plasma, inhibiting its penetration into the cells of the alveolar epithelium and integrating a pharmacological therapy in order to reduce the onset of pulmonary fibrosis, improving gaseous exchanges. Among the treatment modalities used to increase its renal elimination or removal from the circulation (forced diuresis, peritoneal dialysis, hemodialysis, continuous arterio-venous hemofiltration, hemoperfusion), haemoperfusion is considered the most effective procedure in order to remove the herbicide from the blood circulation²². The percentage of the therapeutic success of this method is directly proportional to the timeliness of its application; nevertheless, the studies conducted showed that the extraction efficacy (measured based on the dose of paraquat removed from the circulation) is however limited in relation to the absorbed dose²³. A critical role is assumed, in cases of ingestion for suicidal purposes, by the methods of early

diagnosis of Paraquat intoxication: blood or urinary levels (usually tested by mass spectrophotometry) of this substance can confirm its presence in toxic quantities in the blood, also providing a survival index especially when dosed in the first 24 hours after the event^{24,25}. In this regard, a urinary value of Paraquat metabolites <1.0 g / mL suggests an increased risk of mortality. In order to prolong this range of prognostic predictability, some nomograms have also been developed, for example about the role of electrolytes and/or pancreatic enzymes alteration on prognosis^{26,27,28,29}. It should be remembered how, a few months before the facts under review, in particular in January 2010, the European Commission, with the EC regulation n. 15/2010, decided to ban the use of Paraquat substance as a pesticide and to include it in the list of chemical substances listed in parts 1 and 2 of the Annex I of the EC Regulation n.689 / 2008, among those substances subject to export notification requirement and among those submitted to the PIC notification^{30,31}. The case brought to the attention showed some aspects of uncertainty, above all from the point of view of the temporal trend of the clinical picture: in fact, the patient's condition at the entrance to the emergency room appeared stable, with normal hematochemical parameters. Nonetheless, the Healthcareers prudently contacted the Poison Control Center and retained the patient, arranging for admission to the Department of Surgery, also due to the particular site of the poison auto-inoculation (abdominal region, right paraumbilical site) with possible involvement of the peritoneal serosa and relative risk of acute abdomen. The particularity of the auto-inoculation site carries out, in the exposed case, a very important role also from a medico-legal point of view; in fact, as at the time of clinical diagnosis, also in the subsequent medical-legal process, it brought to light further elements of difficulty in the analysis of the causes and the pathophysiological mechanisms related to the patient's death. During the 5th day of hospitalization there were signs of initial acute renal failure, with hyperazotemia and hypercreatininemia, involving after a day also the respiratory system, with increasing hypoxia and desaturation, for which the patient was transferred to Intensive care. Here, from the chest radiograph, a picture of severe interstitiopathy emerged, and a hemogasalytic examination confirmed hypoxemia and ventilatory deficit, for which it was subjected to oro-tracheal intubation and connection to the Mechanical Ventilator. Recalling what it has been said previously about Paraquat and its toxic action that can be expressed

in varying but unpredictable times (from a few days to 2 - 3 weeks), we can understand as, also in the case in question, after a period of relative stability of the general patient's clinical conditions, both a respiratory and renal failure progressively worsened the condition, and ultimately led the patient to death.

Conflict of Interest: The authors have no conflicts of interest to declare.

Ethical Clearance: Informed consent was obtained from legal guardian for uses of the case materials for research purposes and publication findings.

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