CASE REPORT

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Paraquat Myocarditis and Adrenal Cortical Necrosis

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ABSTRACT: A patient is described in whom a peracute paraquat intoxication caused a toxic myocarditis and an adrenal cortical necrosis.

KEYWORDS: toxicology, paraquat, myocarditis, adrenal cortical necrosis

Paraquat is a commonly used herbicide (chemically: 11-dimethyl 44 bi-pyrillium chloride) which has been in use since 1958 and has caused a considerable number of accidental and intentional deaths.

The most characteristic changes caused by the more chronic toxic action are the well known pulmonary alveolar cell proliferations which are responsible for the respiratory insufficiency and death in many patients.

Other toxic changes, which might as well cause death, have been described less frequently. We saw a patient who died within two days with an extensive myocarditis and a diffuse bilateral adrenal cortical necrosis following intentional ingestion of paraquat.

Case Report

A 24-year-old Beduin male employed as a tractorist was admitted urgently to the hospital after he drank about 1 L of fluid thought to contain Tionex, a known insecticide. At the time of admission he was in a satisfactory general condition except for a psychomotor restlessness. Some redness of the larynx was found, otherwise the physical examination was normal.

The patient received symptomatic therapy: gastric lavage and infusions. He was given laxatives and was sent for observation to the internal medical department. About 6 h after admission to the hospital his condition worsened considerably, the restlessness became worse, and marked hyperventilation appeared. The patient was anuric and catheterization revealed only a small amount of urine.

Laboratory findings were: arterial blood gas oxygen of 100 mm Hg; arterial blood gas carbon dioxide of 25 mm Hg; pH of 7.18; hemoglobin, 15 g/100 g; hematocrit 47%; leukocytes

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5000; thrombocytes 150 000; prothrombin time 49%; marked decrease in coagulation factors 5, 7, and 10; glucose, 11.2 mmol; urea 6.3, mmol; sodium, 146 meq; potassium, 3.3 meq; and the chest X-ray was normal.

As the clinical and laboratory pictures were not compatible with Tionex poisoning, investigation of the ingested material was begun. The urine examination was positive for the weed killer paraquat. Also in the gastric contents paraquat was identified. Further analysis revealed that the patient had ingested Dukatalon®, which contains 130 g of paraquat and 70 g of diquat per litre (which equals a 20% solution).

About 10 h after admission the patient was transferred to the general intensive care unit. He was now in poor general condition with marked restlessness, fast and deep respirations, a regular pulse of 100/min, and blood pressure of 70/40. The abdomen was distended without peristalsis. Abdominal puncture revealed a yellow fluid. Immediately upon admission to the unit he was given fuller's earth through the gastric tube and canulation of the femoral vein and hemodialysis was begun as well as intubation and artificial respiration. The blood flow decreased further and at the same time the central venous pressure was zero. Inspite of large amounts of intravenous fluids the systolic pressure went up only to 70 whereas the central venous pressure increased to 12 cm of water. At this stage dopamine was given in increasing amounts without influence on the blood pressure. The electrocardiogram (ECG) showed a complete block between atrium and ventricle. The patient died 8 h after admission to the general intensive care unit (18 h after admission to the hospital).

At postmortem examination the pertinent gross findings included a marked pulmonary edema and acute congestion, a moderate bilateral pleural effusion, and dilatation of stomach and small intestine with diffuse petechial hemorrhages in the gastric mucosa. The liver appeared somewhat pale. In the abdominal cavity 300 cm^3 of a clear yellowish fluid were present. The only other findings were some cerebral edema and a few subendocardial hemorrhages in the left ventricle.

On histological examination two findings were especially outstanding and unsuspected. The first was an acute (polymorphonuclear) myocarditis. These infiltrations occurred in foci within the interstitial tissue, without evidence of muscle fiber destruction, in both the right and left ventricular wall (Fig. 1). A fat stain proved to be negative.

Another unexpected finding was a diffuse bilateral adrenal cortical necrosis involving primarily the zona fasciculata (Figs. 2 and 3). Other, apparently less specific findings were a decrease in the number of the cerebellar Purkinje's cells with degenerative changes in other preserved cells and an increase in chronic inflammatory cells in the lamina propria of the

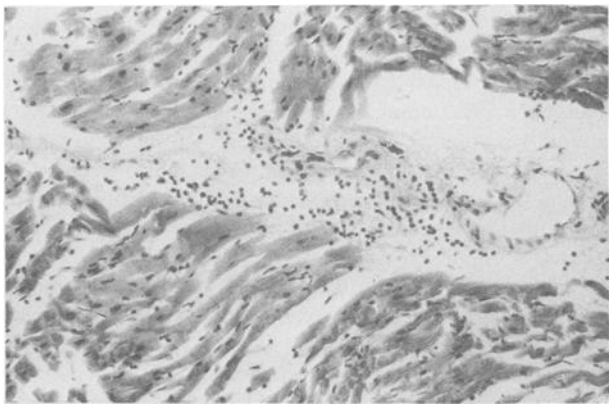

FIG. 1—*Interstitial myocarditis with leukocytic infiltration, lematoxylin and eosin, No. 160.*

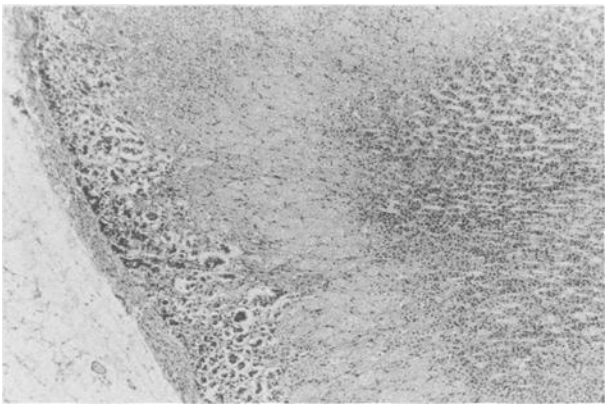

FIG. 2—*Adrenal cortical necrosis involving the zona fasciculata, hematoxylin and eosin, No. 60.*

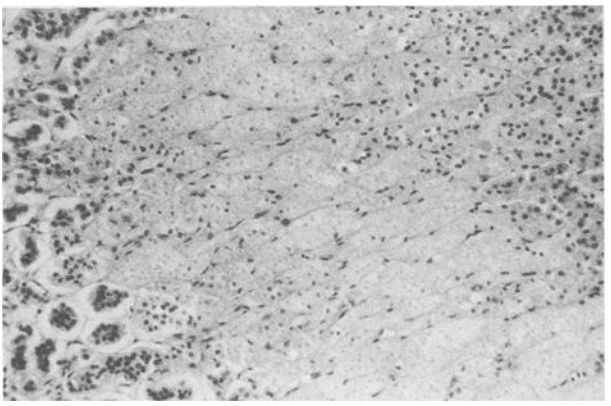

FIG. 3—*Recent necrosis of the zona fasciculata, hematoxylin and eosin, No. 160.*

small intestine, central hepatic necroses, and megakaryocytes in lung capillaries. A fat stain of liver tissue was negative.

Discussion

Myocarditis has been suspected clinically in a number of patients with paraquat intoxication according to their ECG findings [*1-6*]. These changes occurred between less than the second and up to the sixth day after ingestion of the paraquat.

Bullivant [*1*] found in a patient on the sixth day after paraquat ingestion clinically an ECG conduction bundle defect with associated toxic myocarditis. At autopsy on the same day, changes pertaining to the heart were "a soft and discolored myocardium and on section showed a mild myocarditis." The patient had ingested about half a glassful (114 mL) of a 20% solution of paraquat in water.

A second patient of the author, who was believed to have taken only a mouthful of the liquid (and most of which was said to have been rejected immediately) developed during his clinical course a partial defect of conduction on ECG and evidence of a possible (toxic) myocarditis with widespread effects of some congestive heart failure. The patient died on

Day 15 after ingestion. He showed, as did the previous patient, the characteristic proliferative pulmonary changes but no myocardial pathology.

McKean [2] described an eleven-year-old boy who took a mouthful of a Paraquat solution which was, however, immediately ejected. Four days later the ECG showed T-wave inversion in leads II and III, a ventricular fibrillation and a sinus tachycardia. Five days later the ECG showed extensive T-wave inversion in the standard and limb leads and across the precordium. Eventually these changes receded, and one month later there was T-wave inversion in leads III and VI only. The patient recovered without evidence of lung changes.

Nagi [3] found in a patient at autopsy focal neutrophilic infiltration in the myocard with the question of toxic myocarditis as cause of death. No lung changes were found but the patient did have adrenal cortical necrosis in addition to the myocardial changes.

Lanzinger et al [4] described an elderly patient who took one swallow of Gramoxone® (paraquat solution) which was ejected immediately. On the fourth day the ECG revealed a sinus tachycardia, left type, antesystolic with incomplete Wolff-Parkinson-White Syndrome as well as left precordial inner layer changes. An X-ray on the fifth day showed a heart without dilatation. The patient died on the eight day. No myocardial changes are described, only diffuse pulmonary proliferative changes.

Schoenborn et al [5] described a patient who ingested two to three swallows of an undiluted paraquate solution and who died on the seventh day. At autopsy the heart showed focal fatty changes, sometimes degenerative changes of single muscle fibers, and some activation of the mesenchyme.

Malone [6] saw a patient after ingestion of a small amount of paraquat. He showed on the fifth day on ECG widespread inversion of T-waves consistent with toxic myocarditis. Nine months later the ECG was normal.

As Malone [6] points out in his review: when the paraquat was taken intentionally it was usually a larger amount and death occured relatively early (after two to three days) with cellular necrosis in liver, kidney, and heart and only unspecific lung changes. Paraquat taken accidentally usually involved smaller amounts and a longer survival. In these latter patients enough time elapsed to develop the characteristic lung changes.

According to the clinical history and the postmortem findings in the above patients, proliferative lung changes were present only in one patient at the time of the clinical myocarditis; in the others the lung changes occurred later, or not at all because the patient died too soon. As the amount of paraquat ingested can usually not be specified, there is no possibility to draw any conclusions as to the amount necessary to cause myocardial changes.

The second finding of possible importance in our patient was a diffuse bilateral adrenal cortical necrosis which involved practically only the zona fasciculata. No evidence of vascular thrombosis or diffuse intravascular coagulation were found.

Adrenal necrosis in paraquat intoxication has been described only rarely although the high incidence in 1 series (7) in 12 out of 23 fatal cases indicates a higher true incidence. The question of whether to give these patients, following intoxication, supportive steroid therapy has been discussed by Fitzgerald [7]. The extent of the adrenal necrosis in his review was not related to the quantity of paraquat ingested. On the other hand, signs of adrenal insufficiency may be difficult to detect and, thirdly, practically all patients do receive steroid therapy anyhow.

References

[1] Bullivant, C. M., "Accidental Poisoning by Paraquat. Report in 2 Cases in Man," *British Medical Journal*, No. I, May 1966, pp. 1272-1273.

[2] McKean, W. I., "Recovery from Paraquate Poisoning," *British Medical Journal*, No. 3, Aug. 1968, p. 292.

[3] Nagi, A. H., "Paraquat and Adrenal Cortical Necrosis," *British Medical Journal*, No. 2, June 1970, p. 669.

[4] Lanzinger, G., "Akute interstitielle Lungenfibrose bei Paraquat-Vergiftung," *Muenchener Medizinische Wochenschrift*, Vol. 111, No. 16, April 1969, pp. 944-949.
[5] Schoenborn, H., Schuster, H. P., and Kossling, F. K., "Klinik and Morphologie der akuten peroralen Diquatintoxikation," *Archiv Fuer Toxikologie*, Vol. 27, March 1971, pp. 204-216.
[6] Malone, J. D. G., "Paraquate Poisoning: A Review of 19 Cases," *Journal of the Irish Medical Association*, Vol. 64, Feb. 1971, pp. 59-68.
[7] Fitzgerald, G. R., Barniville, G., Fitzpatrick, P., Edwards, A., Silke, B., Carmody, M., and O'Dwyer, W. F., "Adrenal Abnormalities in Paraquat Poisoning," *Irish Journal of Medical Science*, Vol. 146, Dec. 1977, pp. 421-423.

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