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Neutropenia induced by paraquat poisoning

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Paraquat is a synthetic, nonselective, contact herbicide, which causes injury to tissues following contact. When ingested in sufficient amounts, paraquat has life-threatening effects on the gastrointestinal tract, lungs, kidney, liver, heart and other organs. This is a case report of a 15-year-old girl from an agricultural area who was admitted to hospital for treatment. She presented with discomfort, nausea and vomiting. She had drunk a small wine glass full of paraquat. After 18 days in the hospital, the girl developed neutropenia. This is the first reported case of paraquat poisoning-induced neutropenia. Human & Experimental Toxicology (2001) 20

Keywords: paraquat poisoning; neutropenia

Case report

A 15-year-old girl from an agricultural area was admitted to our hospital with discomfort, nausea and vomiting. The girl seemed in good condition, but was rather overweight. Her ability to recall personal details was normal. She did not drink alcohol. On examination, her temperature was 36.6°C, pulse rate 98/min, arterial blood pressure 130/70 mm Hg. The girl started to cry and to complain of pain and swelling in her mouth. A discussion with the girl without the presence of her parents revealed that she had drunk a small wine glass full of paraquat, about 150 mL of paraquat 20% aqueous solution around 2 h before admission. Gastric lavage was performed immediately. She was given 500 mL of bentonite as liquid suspension every 4 h for 2 days, and a charcoal hemoperfusion was initiated. Methylprednisolone 16 mg/day for 15 days, was administered, then gradually reduced and stopped. Chest X-ray, blood and biochemical examinations were normal, while paraquat plasma levels on the first day during the hemoperfusion session were 1 μg/mL. On the second day before the start of the hemoperfusion session, paraquat levels were 0.7 μg/mL, while on the third day they were 0.03 μg/mL. Paraquat levels were determined using liquid chromatography as described earlier. After the sixth day, no paraquat was detected. Because the patient was unco-operative behaviorally, it was decided to extend her stay for further observation.

During hospitalization, the patient presented normocytic anemia, which we believed was a result of the various blood samples taken and hemoperfusion. After 18 days in the hospital, the girl developed neutropenia (blood hematocrit 30%, platelets 526 000/mm³, leukocytes 3000/mm³, neutrophils 1%,
lymphocytes 43%, myelocytes 31%, eosinophils 21%, basophils 2%, plasmacytes 2%). The girl's medical history did not reveal any abnormalities from previous blood examinations or any chronic diseases. There was no evidence of bacterial infection, viral infection or splenomegaly; HIV and autoimmune disorders tests were negative. As there is no existing literature to support methylprednisolone as a causative factor of neutropenia and as the patient had been administered no other medication suspected of causing neutropenia, it was considered that her neutropenia could not, therefore, have been considered drug-induced. A bone marrow biopsy revealed increased cellularity with hyperplastic and dysmorphic erythroblasts and megakaryocytes. There was an augmentation in early neutrophilic precursors and lack of mature neutrophils. Haemosiderin was normal. She was treated with recombinant human granulocyte colony-stimulating factor (G-CSF), 5 μg/kg per day for 8 days. She was discharged after 40 days of hospitalization in good health. She returned to our outpatient department for regular check-ups, and a year later, there was no evidence of cyclic neutropenia. She was healthy and her blood tests were normal.

Discussion

The toxic effects of paraquat are largely the result of a metabolically catalyzed single electron, which reduces oxidation reaction, resulting in depletion of cellular NADPH and the generation of potentially toxic forms of oxygen, such as the superoxide radical.

Immediately after ingestion, vomiting and diarrhea occur. Painful erosions of oral and pharyngeal mucosa and the gastrointestinal tract become evident. The lung selectively accumulates paraquat from the plasma by an energy-dependent process. Because the secretion of absorbed paraquat occurs mainly via the kidneys, the early onset of renal failure following intake of toxic doses will have a marked effect on paraquat elimination and distribution, and consequently on its accumulation in the lungs, leading to pulmonary fibrosis. Hypoxemia due to pulmonary edema and alveolitis occurs within a few days of ingestion. Central nervous system disturbances do not develop until severe hypoxemia progresses. If the amount of paraquat ingestion is significant, patients die of cardiac failure within a few days. Ingestion of as little as 10–20 mL of concentrated 20% paraquat solution has resulted in death.

The most important single determinant of survival is early intervention. Decontamination by either induction of vomiting or gastric lavage is of some value if performed during the first hour after ingestion. Bentonite treatment, activated charcoal, aimed at neutralizing paraquat in the gastrointestinal tract, should be administered in consideration of the fact that although its efficacy has not been proven, in relation to morbidity or mortality, it might be helpful in limiting absorption. In addition, attempts to remove absorbed paraquat from the circulation by haemoperfusion, or aid its excretion by the kidneys with diuresis, should be performed. There is no antidote, and efforts to diminish lethal effects continue to be of limited success. Oxygen administration should be restricted as far as possible to avoid excessive superoxide formation. Many therapies, including corticosteroids, immunosuppressive treatment, superoxide dismutase, have proven to be of no significant importance in human paraquat poisoning. In our case, the treating physician, in his/her attempts to aid the patient as far as possible, administered methylprednisolone, despite there being no previous specific indications of its value in treating paraquat poisoning, because of its general anti-inflammatory effects. The World Health Organization published a health and safety guide to basic precautions that should be observed with paraquat use, but with little impact, and paraquat continues to be a source of mortality in some agricultural communities.

In our case, although the quantity of paraquat ingested was high, the patient was successfully treated. This was due, in part, to the speed of confrontation of each of her symptoms and complications. As rapid initiation of vomiting (a nonspecific feature of poison ingestion) occurred in the patient within a short time of ingestion; this may have reduced the absorption of the poison. This factor, along with the rapid initiation of charcoal hemoperfusion, was perhaps the most significant factor contributing to a successful outcome. The examination of bone marrow cells did not reveal anything specific but may have been indicative of toxicity due to a chemical agent. This is the first description, to our knowledge, of paraquat poisoning-induced neutropenia. From the medical history, clinical and laboratory examinations that were conducted during hospitalization, as well as the regular check-ups for the following 1 year, no other probable cause for neutropenia was evident. With regards to the patient’s anemia, it was apparent that this was due to the various blood samples taken and hemoperfusion performed. A series of five patients, where a progressive, normochromic anemia developed after paraquat intoxication, has been described previously in literature. This commenced a few days after taking paraquat and was followed by aplasia of erythropoiesis in the bone marrow, but other cell systems were unaffected. However,
findings with regard to bone marrow examination in our case did not agree with this.

Physicians working in agricultural areas such as Crete should be aware of the possibility of paraquat poisoning and its treatment, where speed is vital. Our case also shows that poisoning by such herbicides can cause previously unknown effects such as neutropenia. Paraquat poisoning is a little known enemy of which we should be beware constantly.

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