Acute Renal Failure Due to (+)-Cyanidanol-3-Induced Hemolytic Anemia

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Dear Sir,

Recently (+)-cyanidanol-3, a drug widely used in Italy for liver diseases, has been removed from sale by the national health authorities because of severe adverse effects seen in 3 patients at the Naples Hospital. Although some cases of hemolytic anemia had already been reported [1–3], the drug had been considered devoid of severe side effects until now. We wish to report a case of acute renal failure due to hemolytic anemia, induced by this drug.

A 47-year-old woman was admitted to our hospital for severe hypotension, diffuse abdominal pain, diarrhea and oliguria occurred a few minutes after the ingestion of 500 mg tablet of (+)-cyanidanol-3. The patient had been given the drug 1 month before because of digestive disturbances, without any adverse reactions. On admission, hematocrit was 23%, RBC 2.7×10^6 and free hemoglobin was observed in plasma and urine. Plasma haptoglobin was undetectable. The direct Coombs test was strongly positive with both multispecific serum and sera-specific for IgG, IgM, IgA, C3 or C4. The indirect Coombs test was negative and there were no cold or warm agglutinins in the serum. Signs of intravascular coagulation were also observed, with fibrinogen 136 mg/dl, partial thromboplastin time 94 s, (n.v. 35 s) FDP 40 µg/ml. The patient was treated with fluid replacement, heparin infusion, 1 g hydrocortisone in a single pulse, 600 mg cimetidine and 25 mg furosemide intravenously twice daily for the first 3 days. Hypotension and diuresis rapidly recovered, but serum creatinine progressively increased to 12 mg/dl and plasma urea to 149 mg/dl. Fibrinogen and haptoglobin reached normal values within a few days. The direct Coombs test became negative on the 10th day, after which creatinine clearance improved and was normal 4 weeks after admission.

Osmotic fragility of RBC, hemoglobin electrophoresis and ⁵¹Cr-labeled survival were normal. Glucose-6-phosphate dehydrogenase activity was normal in the patient and in her 2 daughters and 1 son. Three months after the hemolytic episode, patient's serum mixed with a (+)-cyanidanol-3 saturated solution in buffered saline strongly agglutinated ABO-Rh compatible RBC at 37 °C (titer 1,024). No hemolysis was observed. Pretreatment of serum with 2-

mercaptoethanol decreased the titer of agglutinating activity (1:16). Sera from 6 normal donors used as controls always gave negative results.

Our case confirms that immune hemolytic anemia may be a severe adverse reaction of (+)-cyanidanol-3. Since the drug has been shown to be of only marginal benefit in liver diseases [4], the risk benefit ratio should be estimated whenever this drug is to be used.

References

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