Ascorbic Acid-Induced Hemolysis in G-6-PD Deficiency

THOUGH THE ORIGINS of erythrocyte glucose-6-phosphate dehydrogenase (G-6-PD) deficiency are rooted in human antiquity, the presence of drug-induced hemolysis in individuals subsequently felt to have G-6-PD deficiency was first reported in 1926 and the biochemical lesion responsible for this phenomenon elucidated in 1956 (1). In the United States, hemolysis induced by infection or drugs is the most common clinical manifestation of G-6-PD deficiency (2).

Ascorbic acid (vitamin C), an essential vitamin, is commonly used in pharmacologic doses for the prevention of the common cold and to promote the healing of wounds. We report here an individual with G-6-PD deficiency who developed intravascular hemolysis and acute renal failure after being treated with large amounts of ascorbic acid.

The G-6-PD isoenzyme present in the vast majority of people of African descent with G-6-PD deficiency, GdA-, is characterized by rapid electrophoretic mobility, moderate deficiency in activity, and increased in-vivo lability (2). The details of the procedures used for the detection of G-6-PD deficiency have been previously described (3).

A 68-year-old black man was admitted to the University of Mississippi Medical Center for treatment of acute renal failure. Six days before admission he suffered second-degree burns of the hand. He was hospitalized for treatment and received 80 g of ascorbic acid intravenously on each of 2 consecutive days. Before treatment the urinalysis and hemoglobin concentration were normal. On the third hospital day he became oliguric; the urine was noted to be dark in color and the serum red. The creatinine concentration was 3.9 mg/100 ml and the hemoglobin concentration 5.8 g/100 ml. He was transferred to a regional hospital, given 2 units of blood and corticosteroids, and transferred to the University Medical Center. Upon admission the patient was comatose and in respiratory distress. Physical examination showed a right-sided hemiparesis. The liver and spleen were not enlarged and there was no purpura. The last three digits of his left hand were involved with a second-degree burn. Laboratory data showed a hemoglobin concentration of 11.8 g/100 ml, leukocyte count of 26 000/mm^3, and platelet count of 45 000/mm^3. The reticulocyte count was 5.9%. The peripheral blood film showed schistocytes, poikilocytic cells, nucleated erythrocytes, and diminished numbers of platelets. The serum creatinine was 13.8 mg/100 ml. The patient was anuric. The erythrocyte G-6-PD level was 1.76 lU/g hemoglobin (normal, 8.4 ±1.3 IU). Electrophoresis of G-6-PD showed a rapidly moving component (GdA-) as well as a band of normal mobility (GdB). Cytochemical tests of the patient's erythrocytes showed about 50% of cells lacking G-6-PD activity (normal, < 5%). The patient was begun on hemodialysis with little change in his status. The platelet count rapidly returned to normal. The fibrinogen level, prothrombin time, and partial thromboplastin time were normal suggesting that a possible episode of disseminated intravascular coagulation, likely precipitated by intravascular hemolysis, had abated. His neurologic status deteriorated requiring tracheostomy. An electroencephalogram showed no activity, hemodialysis was discontinued, and he died on the 22nd hospital day.

Glucose-6-phosphate dehydrogenase is a key link in the hexose monophosphate shunt-glutathione system whose prime function in the erythrocyte appears to be the protection of this metabolically deprived cell from oxidative damage (2). The cell deficient in G-6-PD cannot respond appropriately to oxidative stress and under such conditions is susceptible to hemolysis. Infection and a diverse group of drugs has been associated with hemolysis in patients with G-6-PD deficiency (2).

Ascorbic acid is an essential vitamin for man, which has recently been used in the treatment of wounds and prophylaxis of colds. Large doses are employed; however, unequivocal evidence supporting its value in these disorders is lacking (4). Although generally considered to be harmless, ascorbic acid is a potent reducing agent and has been associated with mild degrees of hemolysis when individuals with G-6-PD deficiency were given doses of 1500 mg[5], and with oxidative denaturation of hemoglobin, and a fall in erythrocyte glutathione level when incubated with enzyme-deficient cells in vitro (1). In our patient, it appears as if unusually large intravenous doses of ascorbic acid led to intravascular hemolysis that precipitated disseminated intravascular coagulation and acute renal failure. Although blood transfusions were given before testing for G-6-PD deficiency, the large number of circulatihg enzyme-deficient cells and low level of enzyme activity suggest that G-6-PD deficiency existed in this patient before transfusion.

The pharmacologic use of ascorbic acid has received much publicity in both the lay and medical press. Though our patient was given this drug intravenously, and in amounts greater than those usually employed, our experience suggests that caution and appropriate testing be used before the administration of large doses of ascorbic acid to individuals who might be susceptible to G-6-PD deficiency.

G. DOUGLAS CAMPBELL, JR., B.A.
MARTIN H. STEINBERG, M.D., F.A.C.P.
JOHN D. BOWER, M.D., F.A.C.P.

Mr. Campbell and Drs. Steinberg and Bower:
Divisions of Hematology and Nephrology
Department of Medicine
University of Mississippi School of Medicine
Jackson, Mississippi 39216

Dr. Steinberg:
Special Hematology Laboratory
Veterans Administration Hospital
Jackson, Mississippi 39216

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