

Acute Renal Failure in Glucose-6-Phosphate Dehydrogenase (G6 P.D.) Deficiency

Pages with reference to book, From 192 To 196

Manoharlal, S.A. Jaffar Naqvi (Department of Nephrourology, Jinnah Postgraduate Medical Centre, Karachi.)

Abstract

A total of 103 cases of Acute Renal Failure of varied aetiology were seen in the Department of Nephrourology, Jinnah Postgraduate Medical Centre, Karachi, during the period 1975-82. Four cases presented with history of jaundice, anaemia, fever with or without rigors and oliguria and on investigation were found to have G-6 P.D. deficiency. The 4 patients were young males of age group 16-25 years. They were given some drugs e.g. anti-malarials, by their family physicians before admission in the Renal Unit.

They were managed by Haemodialysis, peritoneal dialysis or conservatively. All recovered and renal function became normal.

Whenever a patient presents with mild jaundice, severe anaemia and acute renal failure, a great degree of suspicion of G-6-P.D. deficiency is required. Such cases do recover after proper management (JPMA 33:192,1983).

Introduction

Acute Renal Failure associated with massive intravascular haemolysis in G-6-P.D. deficient individuals is relatively less common. Whereas the incidence of G-6 P.D. deficiency in Pakistan varies from 2.6 - 8.0% (Saleem, 1966; Hashmi et al., 1976; Mc Curdy and Mahmood, 1970). These individuals are always at risk as anti-malarial drugs e.g. primaquin, pamaquin and chioroquin; Antituberculous drugs e.g. Isoniazid, PAS & Streptomycin; Acetylsalicylic Acid, antibiotics e.g. Chloramphenicol, Nitrofurantoin, Sulphonamides are commonly used for various ailments in our country. Also infections e.g. Urinary tract infection, Lobar pneumonia, Infective hepatitis and Typhoid can cause haemolysis in these individuals.

This preliminary report of 4 cases of G-6-P.D. deficient individuals presenting as acute renal failure is being reported for the first time in Pakistan to increase the awareness of this problem, so that they may be managed and treated early and properly.

Material and Methods

Patients with acute renal failure are admitted in the Department of Nephrourology, Jinnah Postgraduate Medical Centre, Karachi on referral from units of Medicine, Surgery and Obstetrics of JPMC, other hospitals in Karachi and interior of Sind, and from family physicians, because of high urea.

The four (4) patients in this study were young males, average age being 20 years (16-25 years). They presented with symptoms of fever, jaundice, vomiting, oliguria, haematuria and pain in the renal angles. The tests carried out were: Hb%, PCV, Platelets, Prothrombin time, Reticulocyte count, BUN, Sugar, Creatinine, S. Electrolytes, Liver function tests, Calcium, In. Phosphorous, Alkaline phosphatase, S. Urate, Total Proteins, Hepatitis BsAntigen, Urine D/R and Culture and Sensitivity, 24 hours Creatinine clearance, Urinary protein, Urinary urea, Sodium and Potassium, KUB and chest x-ray were done to exclude Calculus Disease or respiratory infection.

G-6-P.D. estimation was done by the method of Jacob & Jandi's Ascorbate Cyanide Screening Test.

Coomb's test and Bone-marrow biopsy was done only in one patient.

Patients were managed by peritoneal dialysis (2 cases), peritoneal and haemodialysis (one case) and conservatively (one case).

Case Report

Mr. M.I., 25 years, male, Electrician by profession, residing in Drigh Colony, Karachi was admitted on 26th October, 1982 with complaints of:

- i) Pain in the epigastrium -
- ii) Fever with rigors - 6 days
- ni) Vomiting 15-20/day -5 days.
- iv) Pain both flanks, colicky
- v) Haematuria - 1 day
- vi) Less urine - 1 day

He had been taking Basoquin on advice of family physician. He was transferred to renal unit, having been in medical unit prior two days.

On examination, looking ill, pale, fully conscious, jaundice present, anaemia present. Oral hygiene poor, Temp. 100°F, Pulse 88/min. regular, B.P. 90/40 mmHg, Weight 45 Kg., tenderness both hypochondria present, Liver 3 finger enlarged, smooth, tender, spleen just palpable, other systems were normal.

Investigations showed: Hb 10.2G%, PCV 32%, ESR 20 mm, Reticulocyte count 3%, BUN 80 mg%, Creatinine 12.6 mg%, Urinary sodium 104 mEq/L and urinary potassium 25 mEq/L, G-6- P.D. partially deficient. Other tests could not be done because of haemolysis. Haemoglobinuria present. Peritoneal dialysis (with Pen solution Ostuka Indonesia) was done on 27th October, 1980. A total of 60 cycles (each cycle of 2 litres) till- 30th October, 1980 and again 26 cycles on 1st November, 1980. His Hb% fell to 5.1 G% on 30th October, 1980, 3 units of packed cells were transfused (Blood group A+ve.)

As condition did not show any improvement and he remained oliguric, an a-V shunt was put in the arm and haemodialysis was done on six occasions from 2nd November, 1980 to 20th November, 1980. His urine out-put increased gradually to 3-4 litres in 24 hours. He developed Urinary Tract Infection (E. Coli) which was treated with Nalidixic acid successfully. He was discharged on 4th December, 1980 when his results were: Hb 6.8G%, PCV 23%, BUN 25mg%, S. Creatinine 1.4mg%, Tests repeated on 16th February, 1982 were: Hb. 14.2 G%, BUN 12mg%, S. Creatinine 0.8mg%, Creatinine clearance 100 ml/min.

Results

Out of 103 patients of Acute Renal Failure of varied aetiology only 4 patients were proven to be having G-6P.D. deficiency. First patient (M.I.) had severe haemolysis and hepatosplenomegaly and remained severely oliguric for 17 days. Other patients were passing urine 1-1.5 litres in 24 hours. All had mild jaundice (haemolytic) 1-5 mg%, SGPT was mildly increased 40-50 units/ml. Normal Alkaline phosphatase, Reticulocyte count varied from 3-6%. All were Hepatitis Bs Antigen Negative. All were severely anaemic, Hb% varied from 4.6%. In two cases whose initial Hb% was raised were transfused blood before admission to renal unit. Anaemia was haemolytic in type. BUN initially ranged from 80-240 mg% and Serum creatinine 9-38 mg%.

One case (M.I.) underwent haemodialysis and peritoneal dialysis, two (G.R. & M.A) peritoneal dialysis and one (M.A.) was managed conservatively. Three patients were transfused blood and then treated with haematinics. Three patients developed UTI, which could possibly be due to catheterisation. It was treated successfully with suitable antibiotics.

All patients improved and were discharged within 2-5 weeks when BUN and Serum Creatinine became normal. Renal functions were repeated afterwards and were found normal. Hb% was also more than 11 G% in all cases.

Discussion

Glucose-6-Phosphate Dehydrogenase (G-6 P.D.) is the first enzyme in the Hexose mono-phosphate shunt pathway. It was discovered in 1956, to be deficient in the erythrocytes of individuals who were susceptible to acute intravascular haemolysis induced by the administration of Primaquin (Carson et al., 1956).

G-6-P.D. deficiency probably occurs in more than 100 million people in the world (Carson and Tarlov, 1962), with a frequency of 2-35 percent (W.H.O., 1967).

It is genetically transmitted by a sex-linked gene of intermediate dominance (De Leeuw et al., 1963; Marcolongo and Contu, 1961). Its frequency is particularly high among Negroes of North America and West Africa, and among the Caucasians of Mediterranean area and of the Middle East. The G-6-P.D. deficiency of affected negroes is different from that of caucasians. In negroes the activity of the enzyme is about 15% of normal, whereas in caucasian males it is less than 1% (Zinkhan and Lenhard, 1959).

Thus the clinical effects are greater in the non-negro type of deficiency.

An important aspect of correlation between enzymatic deficiency and susceptibility to drug induced haemolysis is furnished by the clinical course and kinetics of haemolytic reactions. In negroes the haemolysis is generally moderately severe and self limited; only the older cells being destroyed. The younger cells which have a greater G-6-P.D. activity, are insensitive to drugs. For this reason, the recovery from haemolytic crisis takes place even if drug administration is not discontinued. In caucasians, haemolysis is usually more severe and does not seem to be self limited. This is in accord with the fact that the younger cells, as well as mature cells are G-6-P.D. deficient too (Burka et al., 1966).

It is now established that people with erythrocyte G-6-P.D. deficiency, may develop an acute haemolytic state after exposure to certain drugs, chemicals, infections, fava beans (Dausett and Contu, 1967; Dacie and Lewis, 1968; Beutler, 1969).

More than 40 drugs have been incriminated and some are commonly used: Chloroquin, Pamaquin, Primaquin, Acetylsalicylic acid, Nitrofurans, Sulphones, Sulphonamides, Chloramphenicol, PAS, Quinidine, Streptomycin, Water soluble analogues of Vit. K, Isoniazid, Ascorbic Acid.

Regarding the infections that can cause intravascular haemolysis are Urinary Tract Infection (Owusu et al., 1972), Infectious Hepatitis (Salen et al., 1966), Rickettsial infections (Whelton et al., 1968), Pneumonia, Metabolic acidosis, viral infections (Burka, 1969), Typhoid (Adu et al., 1976).

Mengel et al. (1967) has found that Negro G-6-P.D. deficient patients do not normally have significantly lowered haematocrits. During an acute infection, however, these patients experience a haematocrit level drop of 11.8% in comparison to drop of only 4.1% in non G-6-P.D. patients.

The haematologic manifestations in our patients are similar to those seen in susceptible individuals with drug induced haemolytic anaemia of Primaquine type causing oxidative destruction of the red cells. These were characterised by a rapid decline in haemoglobin concentration accompanied by reticulocytosis. All patients had mild jaundice (haemolytic) and slightly raised SGPT (40.50 I.U.) indicating no severe damage of liver. After recovery the haemoglobin increased to almost normal levels and also normal Bilirubin and SGPT was noted.

Acute Renal Failure is an important and potentially lethal complication of intravascular haemolysis (Whelton et al., 1968; Adu et al., 1976; Phillips and Silvers, 1969) but is relatively less common in comparison to the frequency of G-6-P.D. deficiency. While the pathogenesis of this event is not clear, a combination of renal ischaemia and intratubular obstruction is likely. Several studies indicate the

importance of dehydration (Harrison et al., 1947; Maluf, 1949), renal ischaemia (Yuile et al., 1945) or acidosis (Baker and Dodas, 1925) for the induction of renal lesions during infusion of haemoglobin or haemolysed red cells in vivo.

Goldberg (1962) using a technique of aortic infusion of haemolysed RBCs demonstrated acute reduction of urine flow, and decreased clearance of creatinine, Hippuran and Para.amino hippuric acid in the dog. These events occurred in the absence of generalised ischaemia, suggesting that acute intra-tubular obstruction was an important factor in the observed oliguria and altered clearances.

Thus a combination of physical obstruction, renal ischaemia and possibly direct nephrotoxicity may lead to tubular damage and subsequent leakage of tubular fluid into the interstitium. Sequentially a rise in intra-renal tension, further mechanical obstruction to renal blood flow, reduction in glomerular filtration and oliguria may result in acute renal failure.

In our four cases, only one has severe oliguria persisting for 17 days, other three were passing 1-1.5 litres of urine in 24 hours. It may be due to direct nephrotoxicity being major factor in later three cases and intratubular obstruction in the first one. All the four patients had taken antimalarial drugs, Chloroquin or Basoquin. Chloramphenicol and Acetyl salicylic acid are also used commonly. No infections such as UTI, Typhoid, Infectious hepatitis or Pneumonia can be implicated in these patients. The results are encouraging i.e. all the four patients recovered after management with pentoneal or haemodialysis and one after conservative management by giving large dose of Frusemide and correcting fluid electrolyte imbalance.

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