Chlorpropamide-induced haemolytic anaemia

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Summary

A newly diagnosed diabetic patient, recently started on chlorpropamide, required emergency admission because of sudden onset of weakness and syncope. *In vitro* testing confirmed the diagnosis of chlorpropamide induced haemolysis, and withdrawal of the drug resulted in clinical recovery.

Introduction

Chlorpropamide is widely used in the treatment of diabetes. Chlorpropamide-induced haemolytic anaemia has been reported only once before (Logue, Boyd and Rosse, 1970).

Case report

A 64-year-old white woman was admitted to Nassau Hospital, Mineola, New York, because of lightheadedness and syncope for 2 days. She had been well until about 5 months before admission when she began noting progressive weakness associated with polyuria and polydipsia. She was found to have diabetes mellitus by her private physician and was started on chlorpropamide 300 mg daily one week before her admission. Her weakness and malaise continued and she was brought to the Emergency Room after 2 syncopal episodes.

There was no prior history of anaemia or other serious illness. She denied taking any medication apart from the chlorpropamide.

On examination, she was weak and lethargic but orientated. Pulse was 96/min and regular, BP was 135/80 mmHg and temperature 38°C. The skin was pale and the sclera were icteric. There was no adenopathy or hepatosplenomegaly. Faeces were haemoccult negative.

Initial laboratory measurements were as follows: Hb 11.3 g/dl, haematocrit 32%, WBC $27.0 \times 10^9/l$, platelet count $230 \times 10^9/l$, glucose 15.6 mmol/l, BUN 6.9 mmol/l, lactic dehydrogenase $9.2 \mu\text{mol/sec/l}$, total serum bilirubin $169 \mu\text{mol/l}$, of which 119.8

$\mu\text{mol/l}$ was indirect. The urine contained occult blood (3+), glucose (1+), and protein (2+).

On the 4th day in hospital, the patient's condition worsened. She became profoundly weak and her urine was now deep brown in colour. Her temperature was 39°C, Hb 5.6 g/dl, haematocrit 15%, reticulocyte count 5%, haptoglobin 0 g/l and the direct Coombs' test was strongly positive. Peripheral smear revealed spherocytosis, polychromasia, marked agglutination of red cells and erythrophagocytosis.

The probability of drug-induced haemolysis was considered and chlorpropamide was discontinued. The diagnosis was confirmed by *in vitro* tests. These showed that the antibody in the patient's serum was an IgG and that lysis of complement-sensitive paroxysmal nocturnal haemoglobinuria cells occurred when the patient's serum was incubated with normal fresh serum and chlorpropamide.

In addition, a positive Coombs' test was reproduced by incubating chlorpropamide, patient's serum and normal red blood cells, as shown in Table 1.

The patient was then given 2 units of packed red blood cells. Seven days later, her Hb was 11.5 g/dl, haematocrit 31% and the reticulocyte count 19%. One month after discharge she was progressing well. Her Hb was 13.1 g/dl and the haematocrit 41%.

TABLE 1. Results of incubating drug, patient's serum and normal serum

Fresh serum O-positive red blood cells normal donor (ml)	Fresh patient serum (ml)	Chlorpropamide (5 mg/ml) (ml)	Antiglobulin test
0.2	0.2	0.2	+++
0.2	0.2	0	-
0.2	0	0.2	-

Her diabetes mellitus was brought under control with 20 units of isophane insulin injection daily.

Discussion

Drug-induced, antibody-mediated haemolytic anaemia has been shown to be initiated by a variety of chemicals and drugs (Worlledge, 1969; Petz and Fundenberg, 1966).

Haemolytic anaemias have been classified as 'immune' when the antigen (e.g. a drug) is identified and 'autoimmune' when the antibody does not react specifically with an identifiable exogenous antigen (Croft *et al.*, 1968).

In the autoimmune variety, haemolysis is rarely acute and often persists for several weeks after cessation of therapy. Haemolysis induced by α -methyldopa is of this variety (Worlledge, 1969).

Chlorpropamide-induced haemolytic anaemia has been reported only once previously (Logue *et al.*, 1970). In the present patient, haemolysis was acute, related to drug ingestion and primarily intravascular—all features suggestive of an immune haemolytic process. Prompt clinical recovery was associated with drug withdrawal.

In vitro tests showed clearly that haemolysis oc-

curred only in the presence of chlorpropamide. In addition, erythrophagocytosis seen in this patient may partly explain the intravascular haemolysis.

Chlorpropamide has been widely used in the treatment of diabetic patients. Hence, one should consider chlorpropamide-induced haemolysis as one of the possible aetiologies of sudden-onset anaemia in a diabetic patient receiving this oral hypoglycaemic agent.

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