Case Report

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Intravenous Immunoglobulins as Pre-Operative Management in a Case of Hereditary Spherocytosis

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Since 1981 high doses of human intravenous immunoglobulin (IVIG) were used for the treatment of different haematologic diseases [1–5]. The most accepted hypothesis for the mechanism of IVIG action claims that the binding of immunoglobulins to Fc receptors of reticulo-endothelial macrophages inhibits the clearance of opsonized cells. This Fc-receptor blockade is attributed to a direct binding of injected IgG or, alternatively, to a binding of IVIG-coated red blood cells [2, 6]. The use of IVIG in nonimmune haemolytic anaemias has not been so far referred.

We describe the case of a patient suffering from a severe hereditary spherocytosis (HS) treated with IVIG before splenectomy.

B.C., a 40-year-old white male, was admitted in September 1987 to our Hospital for severe haemolytic anaemia, jaundice, elevated fever (40°C), dyspnea and tachycardia. Similar episodes of anaemia and jaundice were frequent in his clinical history since the age of 20.

Physical examination revealed remarkable hepatosplenomegaly, cardiomegaly, and pulmonary findings of bilateral high-pitched end-inspiratory crackles. Chest X-ray showed basal bilateral pneumonitis.

Biochemical assays showed: haemoglobin ranging from 4 to 5 g/dl, PCV 13%, reticulocyte count $200 \times 10^9/l$, leucocyte count $2.5 \times 10^9/l$, PLTS $140 \times 10^6/l$; serum bilirubin $256.5 \mu\text{mol/l}$, 90% of which was unconjugated. Peripheral blood smear showed marked anisopoikilocytosis, schistocytes and spherocytes, while bone marrow presented marked hyperplasia of the erythroid series.

The search for autoantibodies, the antiglobulin test (direct and indirect), Ham and Sugar tests were negative. The red cell enzyme activities were normal. The erythrocytic osmotic fragility (OF), studied both by acidified glycerol lysis test [7] and 'pink test' [8] were increased, whereas autohaemolysis test was normal.

To ascertain the role of the spleen as a site of extravascular haemolysis, ^{51}Cr kinetic studies using patient's red cells, were performed according to the method of Early and Sodee [9]. The results showed a shortened erythrocyte life span and an elevated splenic/ hepatic ratio of radioactivity, as typically found in HS.

No familial study was possible because parents and relatives were not alive.

Clinical history, behaviour of osmotic fragility tests, ⁵¹Cr data, negative tests for autoimmune haemolytic anaemia and other haemolytic anaemias suggested the diagnosis of HS according to Dacie[10].

We treated the patient by antibiotic therapy (ampicillin plus tobramycin), obtaining the complete resolution of pneumonitis. However, the severe anaemia forced us to transfuse him at short intervals (7–8 units/week) in order to counterbalance the continuous rapid fall of haemoglobin level (fig. 1).

Therefore we decided to submit the patient to splenectomy. Before this, in an attempt to reduce the sequestration of erythrocytes and the size of the spleen, we administered two cycles of IVIG at a dosage of 0.4 g/kg/day for 5 days.

During and after each cycle a progressive recovery of haemoglobin values with a significant decrease of the transfusional need was noted (fig. 1). Moreover, the ⁵¹Cr kinetic study dramatically changed (fig. 2), showing a biphasic curve: before IVIG infusion the disappearance of ⁵¹Cr erythrocytes was very rapid, corresponding to a mean life span of 4 days; after IVIG infusion the clearance of labelled erythrocytes was much slower, corresponding to a life span of 32 days. Also the splenic/hepatic ratio of radioactivity decreased from 4.66 to 2.6 after IVIG infusion. We documented the progressive reduction of the splenic radioactivity and size with the scintigrams of the spleen, scanned at different times before and after IVIG.

After this double treatment the splenectomy was performed at Hb level of 11.8 g/dl, without complications.

Six and twelve months later the patient was in good health and showed complete normalization of all haematological parameters, except for OF and peripheral blood smear, where spherocytes were still present.

This finding opens the possibility of therapy in HS, particularly as a preoperative procedure for splenectomy.

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Blood transfusions

Fig. 1. Changes of haemoglobin levels before and after IVIG cycles; transfused blood units are listed on top.

0 4 Time, days

Fig. 2. Disappearance of ⁵¹Cr erythrocyte radioactivity before and after IVIG (arrow): the first steep slope of the curve corresponds to a mean cell life span of 4 days; the second slower slope to a mean life span of 32 days.

Time, days

References

Imbach P, d'Apuzzo V, Hirt A, et al: High-dose intravenous gammaglobulin for idiopathic thrombocytopenic purpura in childhood. *Lancet* 1981;i:1228–1230.

Bussel JB, Kimberly RP, Inman RD, et al: Intravenous gammaglobulin treatment of chronic idiopathic thrombocytopenic purpura. *Blood* 1983;2:480–486.

Newland AC, Treleaven JG, Minchinton RM, et al: High-dose intravenous IgG in adults with autoimmune thrombocytopenia. *Lancet* 1983;i:84–87.

Bussel J, Cunningham-Rundles C: Intravenous gammaglobulin in the treatment of humoral immunodeficiency disease and autoimmune hematologic disease. *Rat Drug Ther* 1984;18:1–7.

McGuire WA, Yang HH, Bruno E, et al: Treatment of antibody-mediated pure red-cell aplasia with high-dose intravenous gammaglobulin. *N Engl J Med* 1987;317:1004–1008.

Fehr J, Hofman V, Kappeler U: Transient reversal of thrombocytopenia in idiopathic thrombocytopenic purpura by high-dose intravenous gammaglobulin. *N Engl J Med* 1982;306: 1254–1258.

Zanella A, Izzo C, Rebulli P, et al: Acidified glycerol lysis test: a screening test for spherocytosis. *Br J Haemat* 1980;45:481–486.

Vettore L, Zanella A, Molaro GL, et al: A new test for the laboratory diagnosis of spherocytosis. *Acta Haemat* 1984;72:258–263.

Early PJ, Sodee DB: Principles and practice of nuclear medicine. St. Louis, Mosby, 1985, part 2, pp 828–847.

10 Dacie J: Hereditary spherocytosis: in Dacie J (ed): *The Haemolytic Anaemias*. Edinburgh, Churchill Livingstone, 1985, vol 1, part 1, pp 134–215.