increasing incidence of lithium poisoning. It can be prevented by preliminary assessment of renal function and monitoring of the serum lithium especially if there is any change in the patient's condition. As renal excretion is the only route of elimination of lithium, acute renal failure is a serious complication of an already hazardous condition.

Acknowledgments

We thank Professor A. Polak for his advice, Dr J. Burston for the histological report and the nurses of the Wessex Regional Renal Unit for their skilled attention.

References

- AMDISEN, A. & SKOLDBORG, H. (1969) Haemodialysis for lithium poisoning. *Lancet*, ii, 213.
- GLESINGER, B. (1954) Evaluation of lithium in treatment of psychotic excitement. *Medical Journal of Australia*, 41, 277.
- HAWKINS, J.B. & DORKEN, P.R. (1969) Lithium. *Lancet*, i, 839.
- RADOMSKI, J.L., FUYAT, H.N., NELSON, A.A. & SMITH, P.K. (1950) Toxic effects, excretion and distribution of lithium chloride. *Journal of Pharmacology*, 100, 429.
- ROBERTS, E.L. (1950) A case of chronic mania treated with lithium citrate and terminating fatally. *Medical Journal of Australia*, 37, 261.
- SCHOU, M. (1958) Lithium studies. I. Toxicity. *Acta pharmacologica et toxicologica*, 15, 70.
- SCHOU, M., AMDISEN, A. & TRAP-JENSEN, J. (1968) Lithium poisoning. *American Journal of Psychiatry*, 125, 520.
- THOMSEN, K. & SCHOU, M. (1968) Renal lithium excretion in man. *American Journal of Physiology*, 215, 823.
- VERBOV, J.L., PHILLIPS, J.D. & FIFE, D.G. (1965) Case of lithium intoxication. *Postgraduate Medical Journal*, 41, 190.
- WILSON, J.H.P., DONKER, A.J.M., VAN DER HEM, G.K. & WIENKJES, J. (1971) Peritoneal dialysis for lithium poisoning. *British Medical Journal*, 2, 749.

Postgraduate Medical Journal (April 1973) 49, 279-281.

Haemolytic anaemia in myelomatosis

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Summary

A case of IgA myelomatosis with a haemolytic anaemia is described. No auto-antibodies could be found and the mechanism of the haemolysis was obscure.

Haemolytic anaemia is a rare complication but a search of the literature has revealed a few cases with a comparable shortening of red cell life-span, most without auto-antibodies but some with a positive Coombs' test.

Introduction

Myelomatosis is not a rare disease. Anaemia, leucopenia and thrombocytopenia are common complications, the cause usually being accepted as due to bone-marrow invasion with the abnormal plasma cells. Haemolytic anaemia has been described, but commonly amounts to no more than a mild to moderate degree of shortening of the red cell life-span. Twelve such cases are described by Cline & Berlin (1962) with a minimum half-chromium time ($T_{\frac{1}{2}}^{151\text{Cr}}$) of 16 days all with negative Coombs' tests and another by Bowdler & Prankerd (1962) with a

red cell life-span of 15 days. These patients showed no evidence of the presence of auto-antibodies, but Pirofsky (1969) discusses nine patients with auto-immune haemolytic anaemia and myelomatosis and Dacie (1967) refers to seven patients in the literature with myelomatosis and positive Coombs' tests.

We report here a patient with IgA myelomatosis, overt clinical and laboratory evidence of haemolysis, a red cell life-span of about 30 days and an absence of demonstrable auto-antibodies.

Case report

Mr William D., aged 79, a retired wireman, previously healthy, was admitted to a local cottage hospital on 15 January 1971 with bilateral bronchopneumonia. This was treated with ampicillin but was slow in resolving and the patient was referred to a chest physician (Dr M. Pemberton) who found anaemia (Hb 7.0 g/100 ml) and a very high ESR (71 mm/hr Wintrobe). Plasma proteins showed a high globulin level and immunoelectrophoresis a very high IgA level and sternal marrow examination

confirmed myelomatosis. The patient was transferred to the Grange Hospital, Weaverham, on 8 February 1971, and afterwards referred to one of us (C.D.R.P.) for further management.

On examination he was pale and dyspnoeic. There was no jaundice or abnormality in the cardiovascular system and BP was 140/85 mmHg. No enlarged lymph nodes were palpable. Bronchial breathing and coarse rales were present at both lung bases. Urine was normal.

Investigations. Hb 6.2 g/100 ml. MCHC 26%. WCC 8600/mm³, polymorphs 86%, lymphocytes 12%, monocytes 2%. ESR 71 mm in 1 hr. Blood film showed marked rouleaux formation.

Serum protein 9.6 g/100 ml., albumin 1.8 g/100 ml, globulin 7.8 g/100 ml. Electrophoresis showed decreased albumin and a paraprotein band in alpha 2 position. Immunoglobulin estimations showed a very marked increase in IgA (approx. 1000 mg/100 ml), IgG 1000 mg/100 ml, and IgM 40 mg/100 ml (normal).

Serum alkaline phosphatase 16 KA units/100 ml. Serum bilirubin 0.5 mg/100 ml. Blood urea 39 mg/100 ml. Serum electrolytes normal.

Bone marrow: cellular marrow. Normoblasts and myeloid precursors were well represented and there was an occasional megakaryocyte. About 40% of nucleated cells were of abnormal plasma cell type. The appearances were typical of myelomatosis.

Sputum culture showed normal flora. Faecal occult blood tests were negative on three occasions. Chest X-ray confirmed bilateral bronchopneumonic changes. X-rays of skull and pelvis were normal.

Treatment for the pneumonia consisted of ampicillin 2 g/day for 7 days. Cyclophosphamide 100 mg daily and oxymetholone 50 mg daily were started on 15 February 1971. On 20 February his haemoglobin was only 4.4 g/100 ml, but white cell count and platelets were normal. Three units of whole blood were transfused on 22 February and prednisolone 5 mg thrice daily was started. Cyclophosphamide was reduced to 50 mg daily on 23 February because of a fall in platelets to 83,000/mm³ and they were 117,000/mm³ on 26 February (Fig. 1). At this time his general condition was satisfactory and he was discharged home on cyclophosphamide 50 mg daily, oxymetholone 50 mg daily and prednisolone 15 mg daily. On March 10 his blood picture showed: Hb 7.4 g/100 ml, WCC 8200/mm³, platelets 88,000/mm³. Prednisolone was reduced to 10 mg daily, but oxymetholone 50 mg daily and cyclophosphamide 50 mg daily were continued.

His general condition deteriorated and he was re-admitted to hospital on 19 March 1971. He was anaemic and jaundiced, and had gross oedema of both ankles. JVP was raised, pulse 100/min and regular. BP 170/90 mmHg. Heart sounds were

FIG. 1. Summary of progress.

normal. Coarse rales were present at both lung bases. The liver was enlarged to 3" below the costal margin and the spleen to 2" below the costal margin. Urine contained an excess of urobilinogen. His heart rapidly became normal with bed rest, digoxin and frusemide therapy, and he was free from oedema or neck vein congestion in 10 days.

Further investigations. Hb 5.5 g/100 ml, WCC 3000/mm³, platelets 30,000/mm³, reticulocytes 8%. Direct Coombs' test negative. Blood group O Rh positive. No atypical iso- or auto-antibodies detected in his serum (Manchester Blood Transfusion Service). Haptoglobins (two estimations) 15 mg and 40 mg of Hb binding power/100 ml. Glucose-6-phosphate dehydrogenase in red cells and red cell osmotic

fragility test normal. Ham's test negative. Liver function tests: Serum bilirubin 2.1 mg/100 ml; thymol turbidity 1 unit; zinc turbidity 10 units; serum alkaline phosphatase 6.3 KA units/100 ml. Electrophoresis: marked decrease in albumin. Paraprotein in alpha 2 position, slight increase in gamma-globulin. Blood urea 133 mg/100 ml. Three tests for occult blood in faeces were negative. Mid-stream urine showed coliforms on culture. Electrophoresis of urine: most plasma proteins seen. Paraprotein band seen in alpha 2 position. No sharp band of Bence Jones proteinuria seen in gamma position. Red cell survival test: half-chromium time ($T_{\frac{1}{2}}^{51Cr}$) was 12 days (equivalent to red cell life-span of about 30 days, calculated by method A of Mollison (1956)). Marrow: cellular marrow with myeloma cells still predominating. No abnormality of erythropoiesis.

Three days after his admission he developed purpuric spots on the abdomen and became more icteric, and blood urea rose to 280 mg/100 ml. He had a further blood transfusion of 2 units. Cyclophosphamide and oxymetholone were discontinued for a short time but prednisolone was continued (10 mg daily) (Fig. 1). His general condition remained poor. Blood count: Hb 6.8 g/100 ml, WCC 5000/mm³, platelets 92,000/mm³. Two weeks later he developed epistaxis and his prednisolone was increased to 30 mg daily, but he gradually deteriorated and died on 22 April 1971.

Necropsy (Dr H. Allison). There was no congestive heart failure, jaundice or enlargement of lymph nodes, and no gross bony lesions were present. There was mild coronary atheroma with some left ventricular hypertrophy and bilateral terminal bronchopneumonia was present.

The liver, spleen and kidneys were macroscopically normal.

Histological examination of the vertebrae showed extensive infiltration with myeloma cells and the kidneys showed moderate tubular atrophy and hyaline casts in many of the distal tubes.

Liver and spleen were histologically normal.

Discussion

We have described a patient with myelomatosis, a considerably reduced red cell life-span and clinical evidence of haemolysis. Dacie (1967) emphasizes the rarity of haemolysis in this condition and states that the Coombs' test is rarely positive, though he does refer to seven such cases in the literature. In our patient a thorough search for antibodies both in the serum and adsorbed onto the red cells by the Manchester Blood Transfusion Service was negative, and this seems to have been the case in those patients described by Cline & Berlin (1962). It is therefore not surprising that there was no response of the haemolysis to prednisolone in our patient.

The mechanism of the haemolysis, as in many cases of malignant disease both haematological and non-haematological is not completely clear (Hyman, 1954; Hyman, Gellhorn & Harvey, 1956; Pengelly & Wilkinson, 1962). Auto-immune haemolytic anaemia is most commonly associated with lymphatic leukaemias and malignant lymphomas, and is less usual in association with other forms of malignancy. But it is perhaps surprising that in a malignant disorder of the plasma cells in which there is often a gross alteration in the plasma proteins involving the immunoglobulins, haemolytic anaemia of auto-antibody type does not occur more often. This is probably because the protein abnormalities are usually monoclonal in myelomatosis and not polyclonal as are red cell auto-antibodies produced by the lymphatic tissues (Pirofsky, 1969; Hobbs, 1971).

The abnormal globulin in our patient was in the alpha 2 position on paper electrophoresis, although the excess immunoglobulin was clearly of the IgA variety. This phenomenon is known, though not very common, occurring in only 1% of cases, most being found in the gamma, or, more rarely, in the beta position (Ritzmann & Levin, 1968; Snapper & Kahn, 1971).

Acknowledgments

We are grateful to Dr M. Pemberton for referring this patient to us for further investigation, and to Dr H. Allison for carrying out the necropsy investigation. Our thanks are also due to Mrs V. McKenzie for preparing the chart, and to Mrs J. White for typing the manuscript.

References

- BOWDLER, A.J. & PRANKERD, T.A.J. (1962) Anaemia in the reticuloses. *British Medical Journal*, **1**, 1169.
- CLINE, M.J. & BERLIN, N.I. (1962) Studies of the anaemia of multiple myeloma. *American Journal of Medicine*, **33**, 510.
- DACIE, J.V. (1967) *The Haemolytic Anaemias: Congenital and Acquired, Part III*, 2nd edn., pp. 754-755. Churchill, London.
- HOBBS, J.R. (1971) Immunocytoma o' mice an' men. *British Medical Journal*, **2**, 67.
- HYMAN, G.A. (1954) Studies on anaemia of disseminated malignant neoplastic disease. I. The haemolytic factor. *Blood*, **9**, 911.
- HYMAN, G.A., GELLHORN, A. & HARVEY, J.L. (1956) Studies on the anaemia of disseminated malignant neoplastic disease. II. Study of the life-span of the erythrocyte. *Blood*, **11**, 618.
- MOLLISON, P.L. (1956) *Blood Transfusion in Clinical Medicine*, 2nd edn, p. 139. Blackwell Scientific Publications, Oxford.
- PENGELLY, C.D.R. & WILKINSON, J.F. (1962) The frequency and mechanism of haemolysis in the leukaemias, reticuloses and myeloproliferative diseases. *British Journal of Haematology*, **8**, 343.
- PIROFSKY, B. (1969) *Autoimmunisation and the Autoimmune Hemolytic Anemias*, pp. 127-131. Williams and Wilkins, Baltimore.
- RITZMANN, S.E. & LEVIN, W.L. (1968) In: *Laboratory Notes for Medical Diagnostics*, p. 19. Hoechst Pharmaceuticals.
- SNAPPER, I. & KAHN, A. (1971) *Myelomatosis. Fundamentals and Clinical Features*, p. 52. Karger, Basel.