CLINICAL RESEARCH

Pure red cell aplasia and thymoma associated with high levels of the suppressor/cytotoxic T lymphocyte subset

J P MILNES, B P GOORNEY, T B WALLINGTON

Abstract

A 64 year old man admitted to hospital with increasing effort dyspnoea and lethargy was found to have a thymoma and pure red cell aplasia. Lymphocytes accounted for 20-30% of marrow cells, and numbers of T8 suppressor/cytotoxic cells in peripheral blood were greatly increased. He remained anaemic after removal of the thymoma despite blood transfusions, and immunosuppression with prednisolone 60 mg and cyclophosphamide 50 mg daily was started. The dose of prednisolone was reduced to 15 mg owing to steroid myopathy and the risk of opportunistic infection. He went into remission, and the dose was further decreased to 10 mg daily.

Introduction

Cell mediated inhibition of erythropoiesis has recently been reported in patients.^{1,2} We describe the successful treatment of a patient with pure red cell aplasia and thymoma in whom extremely high numbers of T lymphocytes of the T8 suppressor/cytotoxic subset were found in the peripheral blood.

Case report

A previously healthy 64 year old retired docker was admitted to hospital in 1983. For two months he had suffered from increasing effort dyspnoea and lethargy. His general practitioner had diagnosed atrial fibrillation and cardiac failure and prescribed digoxin, but his

condition had not improved. Cardiac failure had persisted, and he had developed pallor.

Initial investigations showed haemoglobin concentration 4.7 g/dl, white cell count $14.8 \times 10^9/l$, mean corpuscular volume 119 fl, and reticulocyte count less than 1%. A chest x ray film showed a lobulated anterior mediastinal mass. Bone marrow examination showed greatly reduced erythropoiesis with lymphocytes accounting for 20-30% of marrow cells; megakaryocytes and granulopoiesis were normal. Lymphocyte surface marker studies were performed on cells isolated from heparinised venous blood on a Ficoll/Isopaque (Triosil) density gradient. Monoclonal antisera (Ortho) were used as follows: OKT3 (total T), OKT4 (helper/inducer T cells), and OKT8 (suppressor/cytotoxic T cells). Counts were performed with an epi-illuminated fluorescence microscope. The number of OKT8 reactive cells was greatly increased with a slight reduction of OKT4 reactive cells (table). Neither antinuclear antibodies nor antiacetylcholine receptor

T lymphocyte subsets before and after treatment

	Normal range	February	June	August	October
T4 positive helper/inducer cells ($\times 10^3/l$)	0.54-1.59	0.36	0.02	0.20	0.15
T8 positive suppressor/cytotoxic cells ($\times 10^3/l$)	0.29-0.86	4.98	0.26	0.73	0.49
T4+:T8+	1.4-2.5	0.07	0.08	0.27	0.31
Dosage of prednisolone (mg/day)			60	15	10
Dosage of cyclophosphamide (mg/day)			50	50	50

antibodies were detected. A Coombs test gave a negative result. The following were normal: urea, electrolyte, glucose, calcium, albumin, and bilirubin concentrations; alanine aminotransferase and alkaline phosphatase activities; thyroxine, immunoglobulin, C3, and C4 concentrations; immune complexes (C1q binding); and vitamin B₁₂ and folate concentrations.

He was treated initially with digoxin, diuretics, and blood transfusion and underwent thoracotomy. An encapsulated tumour, roughly 4 cm $\times$ 5 cm $\times$ 6 cm, was removed. This was a benign thymoma of predominantly spindle cell type. His postoperative progress was uneventful, but after six weeks he was again anaemic, the reticulocyte count remaining less than 1%. Further blood was given and immunosuppression with prednisolone 60 mg and cyclophosphamide 50 mg daily started.

Two months later he was readmitted to hospital with severe proximal myopathy, anaemia, and a right lower lobe pneumonia. His

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condition improved after treatment with amoxycillin, physiotherapy, and blood transfusion. At this time a 10% reticulocytosis developed; the peripheral lymphocyte numbers including OKT4 reactive cells were extremely low. In view of the considerable risk of opportunistic infection and the steroid myopathy the dose of prednisolone was reduced to 15 mg. From that time his condition improved appreciably. No further blood transfusion was required, and in October 1983 the dose of prednisolone was reduced to 10 mg. He subsequently remained in remission taking cyclophosphamide 50 mg plus prednisolone 10 mg a day.

Discussion

Idiopathic acquired pure red cell aplasia is associated with thymoma in about one third to one half of cases. Its occurrence with other autoimmune disorders and reports of successful responses to thymectomy, immunosuppressive drugs, and plasmapheresis³ have suggested an immunological basis. In some cases the suppression of erythropoiesis appears to be mediated by humoral agents, thought to be antibodies. Putative antibodies have been shown against erythropoietin and mature erythroblasts.³ Recent reports have shown that inhibition of erythropoiesis can be effected by suppressor T lymphocytes.^{1,2}

Monoclonal antibodies are available to identify T cell subsets.⁴ The T8 positive population contains both suppressors and cytotoxic cells. Our patient had an excess of lymphocytes in his bone marrow and high numbers of T8 positive cells in

peripheral blood before treatment. Thymectomy followed by immunosuppression with prednisolone and cyclophosphamide effected a considerable reduction in T8 positive cells and clinical remission. Although functional studies were not performed, we think it probable that these cells played a part in the suppression of erythropoiesis.

Bacigalupo *et al* indicated that in severe aplastic anaemia the detection of suppressor T cells in the bone marrow correlates with successful responses to immunosuppressive regimens.⁵ Our observation would lend support to a similar assertion regarding pure red cell aplasia.

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A sensitive immunoradiometric assay for serum thyroid stimulating hormone: a replacement for the thyrotrophin releasing hormone test?

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Abstract

The value as a thyroid function test of a new, rapid, and highly sensitive immunoradiometric assay for thyroid stimulating hormone (TSH) was assessed in 188 consecutive new patients with suspected hyperthyroidism. The diagnosis was made on clinical grounds and on the basis of serum total triiodothyronine and thyroxine concentrations and the response of TSH to thyrotrophin releasing hormone (TRH) as measured by radioimmunoassay. In all except one patient the basal TSH concentration by immunoradiometric assay predicted the response of TSH by radioimmunoassay to TRH, an undetectable value being recorded in patients with a subnormal

response and a measurable value in those with a normal test result. This clear relation was not observed for basal TSH concentrations as measured by radioimmunoassay. In a series of 39 hospital inpatients with acute or chronic non-thyroidal illness, of whom 11 had low concentrations of total thyroxine or triiodothyronine, or both, basal TSH concentrations were detectable by both radioimmunoassay and immunoradiometric assay in all cases and were associated with normal responses to TRH.

The immunoradiometric assay for TSH, which is commercially available, may therefore obviate the need for the more time consuming TRH test and simplify the approach to thyroid function testing in patients with suspected hyperthyroidism.

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Introduction

Measurement of the basal serum concentration of thyroid stimulating hormone (TSH) is an essential test in the investigation of suspected hypothyroidism. A raised concentration confirms a primary cause of the disease, while a normal or low concentration excludes it or, more rarely, indicates a pituitary or hypothalamic cause. Except in thyrotoxicosis induced by TSH, which is extremely rare, the basal serum TSH concentration is suppressed in hyperthyroidism. These low TSH concentrations, however, are of little diagnostic value as most