normal cell counts. Nerve biopsy showed a mixture of both axonal degeneration and segmental demyelination. A second treatment with ^{131}I (100 mCi) was administered. In the following year, the neuropathy improved remarkably. The level of the IgA-λ spike did not increase and no plasmacytosis was found in bone marrow biopsy. Total body ^{131}I scan disclosed no ectopic uptake of radioiodine; CT scan showed the disappearance of lung nodules and the serum thyroglobulin level became undetectable.

In 1989, a stage I melanoma (Clark's level III) was excised in the right scapula. At that time, the Poems syndrome was completed with the discovery of endocrinopathies: low follicle stimulating hormone and luteinising hormone levels in spite of menopause, and a peripherical adrenal deficiency with low serum level and urinary excretion of cortisol and elevated adrenocorticotrophic hormone and lipotropic pituitary hormone levels. A substitutive treatment with hydrocortisone was given. In 1991, she developed two basal cell carcinomas in the neck inside the irradiated field. In 1992, a pleural and pericarditic effusion resolved with symptomatic treatment. A skin biopsy showed histological features of glomeruloid haemangioma as already described [2]. A skeletal survey detected no abnormality. Serum IgA spike remained stable and IL6 and IL1β serum levels were still elevated. Neurological examination was unchanged.

Our patient presented all the signs of Poems syndrome. In this context, osteosclerotic bone lesions without plasmacytosis are rare [3]. No B-cell proliferation appeared during a follow-up of 8 years, despite repetitive evaluation with bone marrow biopsies and skeletal surveys. To our knowledge, 4 patients with Poems have also presented with a malignancy, either a carcinoma of the lung (1), thyroid (1), vulva (2) or a bone mastocytoma diagnosed at autopsy (4). In these cases, no myeloma or plasmacytoma was reported, but in some cases a Castleman's disease was present [2, 4]. In our patient, the only evidence of a relationship between the Poems syndrome and the two cancers was a parallel improvement of neuropathy and thyroid carcinoma, and a synchronous appearance of endocrinopathies and melanoma. Of note is the partial regression of the neuropathy without treatment of myeloma or plasmacytoma, nor corticosteroid therapy, which is uncommon.

High IL6 and IL1β serum levels were recorded at various times during the course of the disease. Serum IL6 levels have been found elevated in Poems syndrome associated with Castleman's disease [5], but undetectable in 9 cases of Poems syndrome without Castleman's disease [6]. Our results suggest that IL6 may be present in the serum of patients with Poems syndrome without Castelman's disease. To our knowledge, high serum IL1β levels have not been reported in Poems syndrome. This cytokine production may originate from the thyroid carcinoma or the melanoma, since the secretion of IL6 and IL1β by thyroid and melanoma cell lines has been demonstrated [7–9]. Nevertheless, the presence of these cytokines in this case supports their putative role in the pathogenesis of Poems syndrome.

When associated with myeloma or plasmacytoma, Poems manifestations may be considered as a paraneoplastic syndrome. Only accumulating data will determine whether a greater frequency of neoplasms is linked to this syndrome, with clinical implications for follow-up it would involve.

1. Nakanischi T, Sobue I, Toyokura Y, *et al.* The crow fukase syndrome: a study of 102 cases in Japan. *Neurology* 1984, **34**, 712–720.
2. Chan JKC, Fletcher CDM, Hicklin GA, Rosai J. Glomeruloid hemangioma. A distinctive cutaneous lesion of multicentric Castleman disease associated with Poems syndrome. *Am J Surg Pathol* 1990, **14**, 1036–1046.
3. Bardwick PA, Zvaifler NJ, Gill GN, Newman D, Greenway GD, Resnick DL. Plasma cell dyscrasia with polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes: the Poems syndrome. Report on two cases and a review of the literature. *Medicine* 1980, **59**, 311–322.
4. Myers BM, Miralles GD, Taylor CA, Gastineau DA, Pisani RJ, Talley NJ. Poems syndrome with idiopathic flushing mimicking carcinoid syndrome. *Am J Med* 1991, **90**, 646–648.
5. Mandler RN, Kerrigan DP, Smart J, Kuis W, Villiger P, Lotz M. Castleman's disease in Poems syndrome with elevated interleukin-6. *Cancer* 1992, **69**, 2697–2703.
6. Emile C, Danon F, Fermand JP, Clauvel JP. Castleman's disease in Poems syndrome with elevated interleukin-6. *Cancer* 1993, **71**, 874.
7. Kennedy RL, Jones TH, Davies R, Justice SK, Lemoine NR. Release of interleukin-6 by human thyroid epithelial cells immortalized by Simian virus 40 DNA transfection. *J Endocrinol* 1992, **133**, 477–482.
8. Lee JD, Sievers TM, Skotzko M, *et al.* Interleukin 6 production by human melanoma cell lines. *Lymphokine Cytokine Res* 1992, **11**, 161–166.
9. Bennicelli JL, Elias J, Kern J, DuPont Guerry IV. Production of interleukin 1 activity by cultured human melanoma cells. *Cancer Res* 1989, **49**, 930–935.

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Use of Erythropoietin in the Management of the Haemolytic Uraemic Syndrome Induced by Mitomycin C/Tamoxifen

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THE HAEMOLYTIC uraemic syndrome (HUS) is an acquired syndrome consisting of intravascular haemolysis, thrombocytopenia and acute renal failure with hypertension, neurological symptoms, pulmonary oedema and intolerance to blood transfusions. Patients receiving combination chemotherapy with mitomycin C, methotrexate and mitozantrone (3M) with tamoxifen have an increased incidence of HUS due to a probable interaction between mitomycin C and tamoxifen [1]. The anaemia of the HUS is complicated by reactions to the required blood transfusions. These reactions theoretically are due to a response to foreign red blood cells and can result in an increase in the ongoing intravascular haemolysis and, in turn, a deterioration in the renal function, anaemia and thrombocytopenia. For this reason, blood transfusions should be used sparingly in these patients, and washed red cells should be given using a filter and with hydrocortisone cover.

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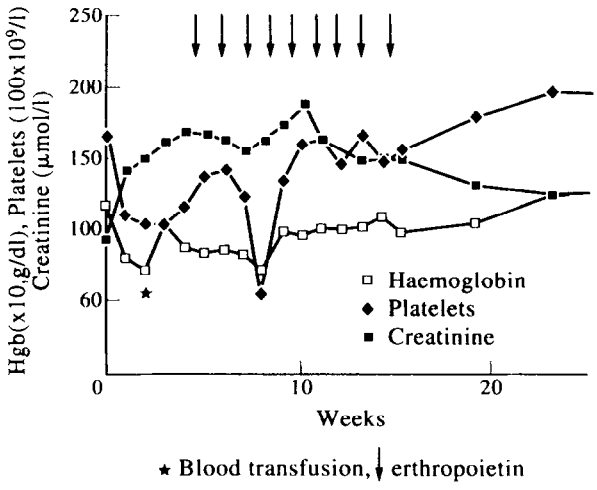

Figure 1. Haematological and renal responses to erythropoietin—patient 1.

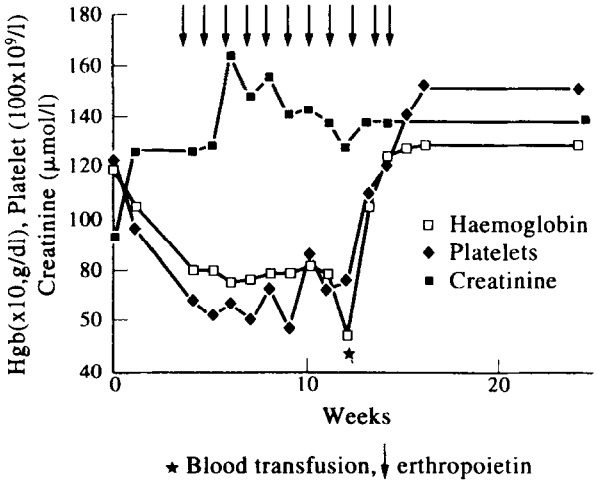

Figure 2. Haematological and renal responses to erythropoietin—patient 2.

2 patients who were symptomatic with anaemia from HUS were treated with erythropoietin (Boehringer Mannheim, U.K.) in our hospital, and this was associated with marked improvements in the haemaglobin values, platelet counts and renal function.

A 44-year-old woman, currently on tamoxifen, presented with anaemia, thrombocytopenia, impaired renal function and hypertension 9 months after completing chemotherapy with 3M. Tamoxifen was stopped and antihypertensives introduced. She had one blood transfusion, but the haemaglobin increment was not maintained and she became symptomatic from anaemia again. Her creatinine was rising and platelet count falling, and we were, therefore, reluctant to give further blood transfusions. She was started on erythropoietin (2000 U, twice a week increasing to 5000 U, twice a week). Thereafter, the haemaglobin, platelets and renal function improved (Figure 1) and this was maintained on stopping erythropoietin.

The second patient, a 61-year-old woman, also taking tamoxifen, presented in the same way, 5 months after completing 3M chemotherapy. Tamoxifen was stopped, antihypertensives were commenced, erythropoietin (2500 U, twice a week) was given subcutaneously, and the haemaglobin, platelet count, urea and creatinine monitored over the next few weeks (Figure 2). There was little improvement, although her haematological and renal function did not initially deteriorate. She became symptomatic with dizziness and associated abdominal pain, epigastric tenderness and her haemaglobin dropped suddenly to 5.4 g/dl. However, no melaena was ever documented. A single blood transfusion of 3 U of washed red blood cells with intravenous ranitidine was given and the erythropoietin dose was increased to 5000 U twice a week. No platelet transfusion was given. Both haematological and renal function improved thereafter and were maintained unsupported after discontinuation of the erythropoietin after 10 weeks.

Our patients with mitomycin C/tamoxifen HUS display, in many cases, a subacute form of this syndrome which may become acute or continue in a chronic phase. As the treatment is symptomatic and the main problem in these two cases was anaemia, we used erythropoietin to alleviate this symptom with a view to minimising the requirement for blood transfusions. Patient 2 remained asymptomatic despite anaemia, and for this reason, the erythropoietin dose was not increased briskly as in patient 1. When it was increased the recovery was rapid. Although we did not measure serum erythropoietin levels prior to treatment in our 2 patients, it is possible that, due to renal dysfunction, these patients had an impaired erythropoietin response to anaemia, and thus we were in fact replacing an associated deficiency. The data we present suggest that erythropoietin is of value in the HUS by decreasing the need for blood transfusion, and thereby preventing the intravascular haemolysis associated with blood transfusions, which contributes to both platelet consumption and deterioration in renal function.

1. Montes A, Powles TJ, O'Brien MER, *et al.* A toxic interaction between mitomycin C and tamoxifen causing the haemolytic uraemic syndrome. *Eur J Cancer* 1993, **29A**, 1854–1857.

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