after taxol treatment (rHu IFN-β postincubation), or treated with the drug alone for 24 h. In all cases, the modulation of drug toxicity by rHu IFN-β was evaluated by clonogenicity assay. Colonies were allowed to develop for up to 14 days, then harvested, stained and analysed using an image analyser (Ibas20;Zeiss/Kontron, Germany).

Figure 1 shows the effect of pre- and postincubation with rHu IFN-β on the cytotoxicity of taxol on the four different cell lines. The cell lines differed in their sensitivity to taxol. Incubation with 1000 U/ml rHu IFN-β alone for 24 h did not reduce the clonogenic potential of the cells. Taxol, however, produced a clear, dose-dependent reduction in clonogenicity. In the SW626 cell line, consistent synergy was seen with both pre- and post-incubation with IFN-β ($P < 0.01$), for the IGROV1 cell lines, both pre- and post incubation with rHu IFN-β antagonised ($P < 0.01$) the effects of taxol. SK-OV-3 was highly sensitive to taxol treatment (panel C). OVCAR 3, in contrast, was comparatively resistant to taxol treatment (panel D). IFN-β post-incubation showed no evident interaction in these two cell lines.

It is thus apparent that IFN-β, at least at 1000 U/ml concentration, can either enhance or reduce the cytotoxicity of taxol in different cell lines, even though all are derived from human epithelial ovarian neoplasms. All four cell lines were growing almost at similar rates (doubling time around 22 h); SW626, in which IFN-β enhanced taxol cytotoxicity, showed an intermediate sensitivity to taxol compared to the other cell lines, SK-OV-3 and IGROV1 being more sensitive and OVCAR 3 less so. Therefore, the enhancement appears to be unrelated to either the cell kinetic features or the sensitivity to taxol. These data suggest the need for caution in generalising interpretations from single cell lines to clinical practice, and underline the likely complexity of the interactions between IFN and antineoplastic drugs.

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Poems Syndrome With High Interleukin (IL)6 and IL1β Serum Levels, in a Patient With Thyroid Carcinoma and Melanoma

E. Tartour, D. Adams, J.-F. Besancenot, W.H. Fridman and M. Schlumberger

POEMS SYNDROME, a rare systemic disease, is characterised by a combination of polyneuropathy, organomegaly, endocrinopathies, monoclonal protein and skin changes. Myeloma and extra-medullary plasmacytoma are often found in the course of the disease [1]. Only anecdotal cases of Poems have been reported in patients with other malignancies. We report a documented Poems syndrome with elevated interleukin (IL)6 and IL1β serum levels, in a patient with thyroid carcinoma and melanoma. In 1955, a 27-year-old woman, with a follicular thyroid carcinoma, underwent a right lobectomy and lymph node dissection, followed by neck irradiation. She was then lost to follow-up. However, in 1982, her serum thyroglobulin level was elevated, a ^{131}I total body scan showed an uptake in the right lung and a computed tomography (CT) scan showed lung micronodules. She was treated with ^{131}I (100 mCi), and L-thyroxine treatment (100 μg/day) was given. At that time, tendon reflexes were diminished in her upper limbs and absent in lower limbs. In 1984, she was admitted for malaise and progressive neuropathy. Examination revealed symmetric motor and sensory deficits in the limbs, worse distally. A bilateral papilloedema, a hepato-splenomegaly and skin changes with hyperpigmentation and hypertrichosis were also noted. Serum immunoelectrophoresis disclosed a weak monoclonal IgA-λ spike, and urine immunoelectrophoresis was positive for λ light chains. Serum IgG and IgM levels were normal. Small sclerotic lesions were seen in the L2 lumbar vertebrae and in the right ischiopubic branch. A bone marrow biopsy and aspirate showed no plasma cytosis and a L2 vertebra biopsy, under CT guidance, discovered no plasmacytoma. At that time, a thrombocytosis (6.8×10^8/ml) was also present. No hormonal abnormality was found. Serum IL6 levels were moderately elevated (28 pg/ml, normally less than 15 pg/ml) and serum IL1β levels were high (120 pg/ml, normally less than 60 pg/ml). Cerebrospinal fluid (CSF) analysis showed high protein levels (120 mg/ml) with

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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.

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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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