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Treatment of Interleukin-2-induced Thrombocytopenia by Intravenous Immunoglobulin

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Thrombocytopenia (TP) is one of the common side-effects of intravenous interleukin-2 (IL-2) [1–3], some of the patients requiring transfusional platelet support and/or treatment discontinuation. We report a case of IL-2-induced TP which was treated with intravenous immunoglobulin (Ig), allowing the continuation of IL-2 therapy.

A clear cell renal adenocarcinoma has been found in a 66-year-old man. An extended nephrectomy was performed. The perirenal fat and one of the resected nodes were involved. The CT scan performed 1 month after the surgical procedure showed a centimetric pulmonary nodule and two metastatic lesions in the liver. The patient was included in a multicentric randomised phase II study [4], and received recombinant IL-2 (Eurocetus, France) 18×10^6 IU/m^2/day as a continuous infusion for 5 days, in combination with interferon-α2a (Roche, France) 18×10^6 IU by subcutaneous injection every 3 days for 17 days. The IL-2 regimen was repeated at days 12, 29 and 40, and the interferon regimen at day 29. Partial response was achieved at day 70.

It was decided to pursue therapy by four maintenance courses of treatment. Each course consisted of IL-2 18×10^6 IU/m^2/day as a continuous infusion for 5 days at days 78, 107, 123 and 137, in combination with interferon-α2a. During the second and the third maintenance courses, a grade 3 TP occurred (Table 1), and IL-2 had to be interrupted, respectively, after 53 and 24 h of IL-2 infusion. No symptoms of haemorrhaging were noted. The platelet count was normal 4 days later in each case. Because of the occurrence of the TP, each time more severe and earlier after the start of the infusion, we administered polyvalent Ig (400 mg/kg daily for 3 days) prior to the last course of IL-2 treatment. The platelet count remained greater than 90×10^9/l even after 4 days of treatment. Since the patient developed some mental confusion after 90% of the planned dose of IL-2 was administered, therapy was interrupted. A CT scan evaluation was performed 4 weeks later, showing the disappearance of all known tumour lesions. The patient remains disease-free 12 months after this treatment has been discontinued.

In this patient, intravenous Ig reduced IL-2-induced TP and allowed continuation of therapy. Corticosteroid treatment and platelet transfusion were not required. The rapid recovery of platelet counts after IL-2 ceased, and the presence of hyperplastic megakaryocytopoiesis during the treatment suggest a peripheral mechanism for IL-2-induced TP [3]. Polyvalent intravenous Ig are commonly used in the treatment of TP of peripheral origin, mainly related to immune disorders [5]. This treatment may inhibit the capture of platelets by the reticulo-endothelial system and the peripheral destruction. Further studies are needed to assess its efficacy as prevention or treatment of IL-2-induced haemorrhaging.

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Table 1. Relationship between platelet count and maintenance courses of IL-2

	IL-2 infusion		Platelet counts (10^9/l)	
Day Number	Planned dose	Administered	Before IL-2	After IL 2
78	90×10^6 IU/120 h	90×10^6 IU/120 h	?	116
107	90×10^6 IU/120 h	40×10^6 IU/53 h	186	40
123	90×10^6 IU/120 h	18×10^6 IU/24 h	188	31
137	90×10^6 IU/120 h	72×10^6 IU/96 h*	134	90

*Polyvalent immunoglobulin, 400 mg/kg/day for 3 days, were administered prior to IL-2 treatment.

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