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Letter to the Editors

Clotting Activation after Blood Transfusion in Patients Receiving 5-Fluorouracil and Mitomycin-C Treatment

Giancarlo Agnelli[1], Paolo Gresele[1], Giuseppe G. Nenci[2]

[1] Istituti di Clinica Medica and
[2] Semeiotica Medica, Università di Perugia,
I-06100 Perugia, Italy

A syndrome of intravascular haemolysis and renal failure in two patients receiving long-term 5-fluorouracil (5-FU) and mitomycin-C (Mit-C) treatment, as adjuvant chemotherapy in gastric adenocarcinoma, has recently been reported by Jones et al. [2]. More recently Lempert described a similar case [4]. Indeed, microangiopathic haemolytic anaemia and uraemia have already been reported to occur after treatment with 5-FU and Mit-C [1, 3]. However in Jones' and Lempert's patients the syndrome was in some way strikingly exacerbated by RBC transfusions.

We studied a patient with pancreatic carcinoma who, after 1 month of treatment with 5-FU, Mit-C, and doxorubicin according to the schedule proposed by McDonald et al. [5], developed marked anaemia requiring RBC transfusions. No haemolysis and no impairment of renal function was evident at that time. Coagulation studies were performed before and after transfusions to verify whether a disseminated intravascular coagulation (DIC) would be elicited or worsened by blood transfusions. The addition of their effect to that of the disease and/or of cytotoxic therapy would thus be the cause of the supervention of a haemolytic-uraemic syndrome. Three 250-ml RBC transfusions were performed one day apart. Just before the third transfusion, 2,500 IU of heparin was given IV in rapid bolus.

Prothrombin time (PT), activated partial thromboplastin time (aPTT), thrombin clotting time (TCT), fibrinogen assay (Fibr.), a latex test for fibrinogen-fibrin degradation products (FDP), protamine sulphate test for fibrin monomers (FM), and platelet count were performed: (I) before RBC transfusions; (II) 24 h from the end of first transfusion and immediately before the second one; (III) 2 h from the end of second transfusion; (IV) 24 h from the end of the second transfusion and immediately before the heparin infusion and the third transfusion; (V) 2 h from the end of the third transfusion; (VI) 48 h from the third transfusion.

The following results were obtained:

Samples	PT (s)	aPTT (s)	TCT (s)	Fibr (g/l)	FPD (μg/ml)	FM	Platelets ($\times 10^3/\mu l$)
I	17.5	47.0	16.0	4.2	< 10	–	104
II	22.0	55.0	19.5	3.5	10–40	–	88
III	25.0	59.0	28.1	3.5	> 80	+	60
IV	26.2	61.0	25.1	4.2	10–40	–	58
V	21.9	47.8	23.0	3.8	10–40	–	60
VI	26.0	61.5	28.2	3.2	10–40	–	66
Control	14.0	45.5	16.0	2.4–4.0	< 10	–	170–400

Our data suggest that RBC transfusions play a critical role in evoking a clotting activation, which could initiate a haemolytic-uraemic syndrome in patients treated with 5-FU and Mit-C. A low dose of heparin was able to prevent or minimize this post-transfusional activation of a DIC, thus providing a measure that could reduce the potential hazard of blood transfusion in patients treated with 5-FU and Mit-C. How RBC transfusion triggers DIC remains to be established. If this effect is due to the residual plasma present in RBC preparation, the same result obtained with heparin could be attained by using washed RBC concentrates.

Reprint requests should be addressed to: G. G. Nenci

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