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LETTER TO THE EDITOR

The cumulative incidence of gemcitabine-induced thrombotic microangiopathy

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To the Editor

Thrombotic microangiopathies (TMAs) are characterised by thrombocytopenia, microangiopathic hemolytic anemia, renal insufficiency and, in some cases, hepatic or central nervous system involvement. TMA may be idiopathic or caused by factors such as infections, malignancies or drugs, cytotoxic drugs in particular [1]. The nucleoside analog gemcitabine, a relatively new but widely applied cytotoxic drug, has recently been associated with TMA [2–4].

At the oncology department of our hospital, three patients have been diagnosed with TMA during gemcitabine therapy (Table I). All of them manifested the typical laboratory findings: anemia, thrombocytopenia, schistocytosis, renal insufficiency and a reduced serum haptoglobin concentration. They were managed by discontinuation of gemcitabine therapy and plasma exchanges leading to regression of the TMA in two patients who had mild renal insufficiency at diagnosis and irreversible renal failure in one patient who had more advanced renal disease. The diagnosis was made 6–9 months after the start of gemcitabine therapy and the patients had not been treated with other drugs known to cause TMA. Thus, it seems likely that TMA was induced by gemcitabine in these cases.

The three patients represent 1.4% of the 224 patients who, according to the hospital pharmacy, have been treated with gemcitabine at the hospital since 2002. This is the same cumulative incidence of TMA in gemcitabine-treated patients as reported by Müeller et al. in 2005 but it is definitely higher than that found by Humphreys et al. in 2004 (0.31%) which, in turn, was much higher than the initial estimate in 1999 (0.015%) [2–4]. Taking only into account the 55 of our patients who received gemcitabine for 6 months or longer, the cumulative incidence was 5.5%. Accordingly, this serious complication of gemcitabine therapy seems to be much

Table I. Clinical information about three patients who developed thrombotic microangiopathy during gemcitabine treatment.

	Patient 1	Patient 2	Patient 3
*Age (years)	65	59	61
Cancer (organ)	Urinary bladder	Oesophagus	Unknown
Duration of G (months)	9	9	6
Total dose of G (g)	31.8	11.3	24.8
*B-Platelets ($\times 10^9$/l)	85	66	123
*S-Creatinine (μmol/l)	157	389	165
Outcome of TMA	Regression	Hemodialysis	Regression
*Survival (months)	7	4	2
Cause of death	Cancer	Cancer	Cancer

*At the time of diagnosis of the thrombotic microangiopathy. G = gemcitabine.

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more common than previously thought, particularly during long-lasting treatment.

Oncologists should be well aware of the risk of TMA during gemcitabine therapy. It would seem wise to include analysis of haptoglobin, for detection of hemolysis, in the regular check-up of patients who receive prolonged gemcitabine therapy e.g., those who are treated for a longer period than 6 months. This would facilitate early diagnosis of TMA and, thereby, increase the quality of life in these often very ill patients. It is possible that simply stopping gemcitabine therapy leads to reversal of the TMA process and organ damage provided that this is done early enough.

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