Acute Cardiac and Renal Failure after 5-FU and Cisplatin Treatment

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Dear Sir,

Cardiotoxicity is a rare side effect of 5-FU [1] and cisplatin (CP) therapy [1, 2]. We report herein one observation of cardiac and renal failure after treatment with 5-FU and cisplatin.

In 1987, a 42-year-old woman presented with uterine carcinoma. Initial treatment associated surgery and radiotherapy. Intravenous urogram and renal function were normal (serum creatinine $82 \mu\text{mol/l}$). In August 1989, an intravenous urogram showed obstruction of the left ureter. A left nephroureterectomy was performed which showed an extension of the carcinoma to the ureter. After surgery, renal function remained normal (serum creatinine $75 \mu\text{mol/l}$). Chemotherapy was started 1 month after surgery with CP 60 mg/day , 5-FU $1,500 \text{ mg/day}$ for 4 days associated with a unique 12-mg dose of mitomycin. CP was given preceded by intravenous hy-dration. On the fourth day of treatment she presented with an acute renal and cardiac failure, with arterial hypotension ($70/40 \text{ mm Hg}$), oliguria and an increase in serum creatinine from 75 to $416 \mu\text{mol/l}$ 5 days after CP administration. Treatment with furosemide, dopamine and dobutamine produced a rise in systolic blood pressure, a diuresis of $1,500 \text{ ml/day}$, but no change in renal function. The EKG, displayed sinus tachycardia without ischemic lesions. The chest radiograph was consistent with pulmonary edema and the echocardiogram showed diffused hypokinesis. Ten days later, the echocardiogram showed an amelioration (resting left ventricular ejection fraction was 25%) and 1 month later the resting left

ventricular ejection fraction was up again to 50%. In contrast, renal function did not improve and hemodialysis was started. Six months after CP infusion the patient is still on dialysis.

Our patient presented an acute and definitive renal failure after CP therapy. This complication is exceptional since prehydration is systematically associated with CP [5]. In our patient, cardiac failure and reduced kidney mass are probably aggravating factors. It must be outlined that although it has been suggested that fractional administration of CP may lessen the nephrotoxicity of this drug [6], there is no conclusive evidence on this issue.

Cardiotoxicity of 5-FU is rare, being 1.6% in a review of 1,083 patients [4]. Known predisposing risk factors for 5-FU cardiotoxicity are a previous cardiac history or a history of left ventricular irradiation [7], which were not present in our patient. In our patient a possible contributing factor was the concomitant administration of CP. To our knowledge only 4 cases of cardiac failure secondary to the administration of 5-FU and CP have been recently reported [1, 3]. Including our

patient, 4 patients out of 5 had a reversibility of their cardiac failure. In these patients, the small cumulative dose of CP (160 vs. 300–600 mg/m² reported in the literature) distinguish them from those previously reported for cardiotoxicity when CP was given alone. A synergistic or permissive effect of CP on 5-FU cardiotoxicity can therefore be suspected. Although these observations represent a small percentage of the patients who have received concomitantly 5-FU and CP therapy, they reaffirm a potential toxicity which should be monitored and thus far cannot be prevented.

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