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Feasibility of Paclitaxel in a Patient with Anthracycline-induced Congestive Heart Failure

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PACLITAXEL HAS been demonstrated to be an active drug in the treatment of pretreated breast cancer [1]. The drug induced objective responses in 20–40% of women who failed to respond to prior treatment with anthracyclines [1–3]. There is no clear definition of the best dose to administer in monochemotherapy since a randomised trial failed to observe a significant difference between 135 and 175 mg/m^2 [2]. Although cardiotoxicity does not represent the most frequently encountered side-effect, the drug has been associated with cardiac disturbances [4]. In particular, congestive heart failure (CHF) has been described in a woman who died soon after paclitaxel infusion and who had been previously treated with a high cumulative dose of anthracyclines [5]. However, there are no data on the feasibility of paclitaxel in patients with severe concomitant cardiopathy.

We report the case of a woman with anthracycline-induced CHF that was subsequently given paclitaxel. In 1994, a 55-year-old woman with a previous history of breast cancer with bone metastases presented with progressive painful bone disease. The patient had received prior radiotherapy to the left thoracic area, vertebrae and skull. Ovariectomy followed by three lines of hormonotherapy (tamoxifen, 4-hydroxyandrostenedione, megestrol acetate) had been performed and, starting in December 1993, the patient received six cycles of the FEC schedule (5-fluorouracil, 750 mg/m^2, epirubicin, 75 mg/m^2 and cyclophosphamide, 500 mg/m^2). The patient presented no obesity or hypertension.

A staging workup revealed mild normochronic, normocytic anaemia and altered baseline CA 15.3 and CEA values. A bone scan found diffuse disease deposits on the chest, skull and vertebrae, and a bone X-ray defined multiple sites of bone lysis. Owing to the presence of increasing bone pain, the patient started, in October 1994, treatment with vinorelbine. After two doses of chemotherapy, she presented peripheral neuropathy requiring treatment interruption. Therefore, in November 1994, the patient was treated with L-leucovorin (100 mg/m^2 days 1–5), 5-fluorouracil (370 mg/m^2 days 1–5), and mitoxantrone (10 mg/m^2 day 1), with cycles repeated every 21 days.

In March 1995, the patient presented with asthenia, dyspnoea, hepatomegaly, ascites and tachycardia. An electrocardiogram revealed tachycardia and increased left atrial dimensions. A chest X-ray was positive for congestive lung circulation. Echocardiography revealed dilatative cardiomyopathy with hypokinesis and depressed left ventricular ejection fraction (30%). The patient started therapy with furosemide, digoxin and vasodilatators, with regression of the symptoms. Cardiac monitoring was then performed every 2 months and showed stability of disease.

Eleven months later, new bone lesions were observed on follow-up bone scan and the patient presented with pain on lumbar vertebrae. On the basis of the previous treatment, the patient started paclitaxel at a dose of 135 mg/m^2, repeated every 21 days. Premedication with steroids and antihistamines was performed. Cardiac therapy was left unchanged. A baseline echocardiography revealed stability of the cardiomyopathy with a left ventricular ejection fraction of 25–30%. After two cycles of therapy, a new echocardiograph was performed and was defined as unchanged. The patient had no symptoms or side-effects related to the treatment, so that two new cycles were given.

Disease re-evaluation was performed in June 1996 and revealed progressive bone disease with new lesions on the left pelvis with associated pain. On the basis of these results, treatment was stopped and the patient submitted to palliative radiotherapy. A new cardiac evaluation revealed average stable myocardial functions with a left ventricular ejection of 30%. No worsening of the dimensions of the left ventricle was noted.

Paclitaxel is known to be associated with cardiac disturbances. It may cause rhythm alterations including bradycardia, atriventricular block, ventricular tachycardia and ischaemia [4]. Albeit rarely, it has been associated with CHF [5]. The mechanism has not been entirely clarified, although selective activation of histamine receptors in cardiac tissue has been indicated as a possible explanation for paclitaxel-induced rhythm alterations, and peculiar structural myocardial abnormalities have been detected in myocardial cells of a patient who died of CHF after paclitaxel infusion [5, 6]. In our case, no signs of worsening of left ventricular ejection fraction were noted and no symptoms attributable to the treatment were observed, thus indicating that the taxane had no further negative effect on depressed heart contractility.

In conclusion, although our results should be interpreted with caution since they were observed only in a single case, they indicate the feasibility of paclitaxel at the dose of 135 mg/m^2 in a patient with previous anthracycline-induced CHF. Assiduous monitoring of cardiac function is mandatory.

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