European Journal of Cancer, Vol. 34, No. 7, p. 1133, 1998

Printed in Great Britain
0959-8049/98 $19.00+0.00

Letters

PII: S0959-8049(97)10137-X

A Case of Ototoxicity in a Patient with Metastatic Carcinoma of the Breast Treated with Paclitaxel and Vinorelbine

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NEUROLOGICAL TOXICITY due to paclitaxel and/or vinorelbine is common and characterised by paraesthesia and, less commonly, by a reduction of sensibility in the extremities.

We report a case of ototoxicity in a patient with metastatic carcinoma of the breast treated with paclitaxel and vinorelbine.

A 54-year-old woman with locally advanced left breast carcinoma was treated in 1992 with eight courses of chemotherapy (cyclophosphamide 600 mg/m^2 intravenous (i.v.) bolus, epirubicin 60 mg/m^2 i.v. bolus, 5-fluorouracil 600 mg/m^2 i.v. bolus; every 21 days) followed by radiotherapy and tamoxifen 20 mg per day. The patient remained free of disease until July 1996, when a liver ultrasound showed multiple diffuse liver metastases. Therefore, the patient started chemotherapy with paclitaxel 135 mg/m^2 in 3-h infusions on day 1 and vinorelbine 25 mg/m^2 i.v. bolus on days 1 and 3; the courses were repeated every 3 weeks. A premedication regimen was used before the paclitaxel infusion which consisted of intramuscular (i.m.) orfenadrine 40 mg 30 min before, ranitidine 50 mg i.v. 30 min before and dexamethasone 20 mg i.v. 10 min before the paclitaxel infusion. We also administered granisetron 3 mg i.v. and metoclopramide 20 mg i.v. on days 1 and 3 of the course, respectively. The patient had a normal electrocardiogram before treatment.

At the nadir of the first cycle, grade 3 (WHO) mucositis and febrile neutropenia were observed; as a result the patient received antibiotic therapy with ciprofloxacin 1 g per day and fluconazole 100 mg per day orally, and the doses of both chemotherapeutic drugs were administered at 75% of the dose in the subsequent two courses. During the second cycle, the patient reported grade 1 (WHO) peripheral neurotoxicity consisting of mild paraesthesia in the extremities and bilateral mild hearing loss with bilateral acute tone tinnitus that increased after the third course of chemotherapy. No changes in taste were reported.

The patient then underwent an ear, nose and throat examination. Otomicroscopic examination was negative bilaterally. Pure tone audiometry showed a bilateral symmetrical sensorineural hearing loss at the middle and high frequences (2–4 kHz, 35 dBHL bilaterally). Impedance audiometry was negative, the stapedius reflex threshold performed to 0.5–1–2–4 kHz with contralateral stimulus was within normal range bilaterally. Brain stem response audiometry (B.A.E.P.) showed a bilateral cochlear pattern. The cerebral magnetic resonance imaging study before and after the administration of a standard dose of gadolinium was negative. For these reasons and despite the reduction of liver metastases, chemotherapy was discontinued after the third cycle.

Peripheral neuropathy is well recognised as the most important non-haematological side-effect associated with paclitaxel and/or vinorelbine therapy. The peripheral neurological symptoms reported consist chiefly of numbness, tingling, and burning pains in the extremities. The incidence and the severity of neurological symptoms are generally affected by cumulative exposure to the drugs. Some sporadic cases of central nervous system toxicity consisting of convulsions during paclitaxel therapy and reversible visual disturbances were recently reported consisting of scintillating scotomata and loss of visual acuity. Visual evoked potential studies suggested a toxicity of paclitaxel to the optic nerve [1]. Ototoxicity was reported in a retrospective review in 2 diabetic patients treated with paclitaxel [2] and in 2 patients treated, in a phase I study, with 4-day continuous infusion of paclitaxel followed by cisplatin [3]. To date, ototoxicity in patients treated with vinorelbine has not been reported.

We report a case of ototoxicity in a non-diabetic patient with metastatic carcinoma of the breast treated with a 3-h infusion of paclitaxel and vinorelbine. In this patient any other possible cause of hearing loss was excluded, including prior exposure to aminoglycosides, furosemide, or to other risk-factors for ototoxicity. The patient reported hearing loss and tinnitus after the second cycle of chemotherapy.

The hearing loss was sensorineural and bilateral and the site of the lesion was cochlear as showed by B.A.E.P. and the acoustic impedance test (the Metz test was positive at 2 kHz bilaterally). In this case, although the chemotherapy was discontinued, the hearing loss and tinnitus did not recede because irreversible damage of the sensorineural structure of the inner ear had occurred.

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Received 21 Jul. 1997; revised 6 Nov. 1997; accepted 3 Dec. 1997.

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