Vinorelbine Therapy in a Hemodialyzed Patient

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Sir,

Navelbine (vinorelbine) is a new semi-synthetic vinca alkaloid exhibiting better he-matologic tolerance and weaker neurotoxici-ty than the older drugs of the same family. Its indications are non-small cell lung cancer, breast carcinoma (K), Hodgkin's lymphoma and osteosarcoma. It can be used in mono-therapy or in association with other chemotherapeutic drugs [1].

Its metabolism is essentially hepatic, and less than 8% of the drug is found in urine 72 h after administration [1]. No study concerning the kinetics of the drug has been performed in dialyzed patients as far as we know; the manufacturers suggest caution in use with these patients but no specific dose reduction is advised.

We prescribed this drug to a patient with end-stage renal disease (ESRD) on hemodia-lytic treatment with no remaining diuresis for a relapse of breast K.

A lobular breast K was diagnosed in 1980, when the patient was 67 years old. Staging was T1a, NO, MO according to TNM classification of the UICC.

The first protocol applied was tumor resection and axillary lymph node dissection and local radiotherapy (6,000 rad on the scar + 5,600 rad on the breast and on the internal mammarian lymph nodes). An adjuvant chemotherapy was performed including 6 monthly courses of teniposid 100 mg, mitomy-cin C17 mg and methotrexate 2×15 mg. After 6 courses, hemolytic-uremic syndrome secondary to mitomycin C [patient No. 9 of a previous work [2] appeared, which rapidly led to ESRD. In September 1981, hemodia-lytic treatment was started.

In November 1986, a cutaneous relapse of the lobular K occurred. Because of the histological type, though hormonal markers were negative, a hormonal treatment with tamoxifen 20 mg/day was started. However, in June 1987, mastectomy was performed.

In 1988, a new cutaneous relapse led to starting other treatments: tamoxifen 20 mg/ day + aminogluthimide 500 mg/day, hy-drocortisone 20 mg/day, then medroxypro-gesterone 400 mg/day and at last bromo-criptine 5 mg/day. Despite the different approaches made, cutaneous lesions worsened, and in March 1990, chemotherapeutic courses with doxorubicin 10 mg/m²/week were given.

In August 1990, a carcinomatous lymphangitis of the lung appeared and diffuse bone metastatic involvement was found. Treatment with vinorelbine was then decided.

A dose of 25 mg/m² once a week was first employed, i.e., 40 mg, administered at the end of hemodialytic sitting.

One week after the first injection, leuko-penia occurred (1,700 leukocytes/mm³, fig. 1). A 2nd dose was given, and leukocytes sank to 700/mm³. This leukopenia was then complicated by pulmonary infection. Leukocytes rose to normal values 5 days afterwards, and pneumonia rapidly recovered.

As a drug blood measurement was not available, it was decided to reduce the dose to 12.5 mg/m² once per week. The patient was then given 20 mg/week from December 1990 to March 1991 (12 injections on the whole) without appearance of leukopenia, with a stabilization of the clinical situation and a subjective improvement of dyspnea due to lymphangitis.

In conclusion, little experience exists until now concerning the use of vinorelbine in

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10,000-1

8,000

6,000

250

4,000

200

- 150 $\frac{7}{8}$

2,000

-100 $\frac{3}{8}$

50

Fig. 1. Leukocyte and platelet count during vinorelbine therapy.

Nov. 19 t t

Jan. 19 1991

Dec. 19 1990

Feb. 19 Mar. 19 Apr. 1

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25 mg/m² = 40 mg 12.5 mg/m² = 20 mg Vinorelbine

patients with ESRD. In particular, dose adjustment is suggested by the producer but no specific criteria are advanced.

We used this chemotherapeutic drug as a single drug therapy for end-stage breast lob-ular K in a woman of 77 years on hemodia-lytic treatment. The normal dose proved to be toxic, even though the prevalent metabolism of the drug is hepatic. The dose was then modified after 2 leukopenic episodes complicated by infections according to empiric criteria. The drug was then well tolerated from a hematologic point of view, and leukopenic episodes occurred no more. No other side effects, particularly neurotoxicity and hepatotoxicity, were observed. Subjective improvement and objective clinical stabilization were

observed. However, the absence of even the slightest leukopenia induces us to question the possibility of an insufficient dose choice.

A future pharmacokinetic study of vinorelbine in hemodialyzed patients is suitable, and a systematic evaluation of the blood concentration will allow a more scientific adaptation of the dose in these patients.

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