Topical Bleomycin-dimethylsulfoxide in AIDS Kaposi's Sarcoma

Sir,

The treatment of Kaposi's sarcoma in the acquired immunodeficiency syndrome (AIDS) requires systemic chemotherapy or interferon for disseminated disease. In patients with few lesions, such a treatment is difficult to consider. Many alternatives have been proposed, including radiotherapy, laser, intralesional vinblastine or bleomycin and, recently, liquid nitrogen and sclerotherapy (1, 2). Cosmetics may also add to the treatment of the psychological aspect of the disease.

We tried a topical treatment with bleomycin (BLM) diluted in dimethylsulfoxide (DMSO), firstly to reduce systemic toxicity, secondly to have the maximal concentration of the drug at the tumor site and thirdly to have the potential dedifferentiating effect of DMSO.

We used the same dosage of BLM as in systemic chemotherapy, i.e. a total of 5 mg per day during 3 days, repeated every 2 weeks until total disappearance of the lesions. BLM was diluted in DMSO and applied on patch test devices (Leukotest, BDF Medical, Le Plessis Robinson, France), which were applied to the skin lesions for 12 h and then removed. Regular blood examination was performed during the treatment.

The determination of bleomycin metabolites A2 and B2 in the patient's sera was performed by using a liquid chromatographic method with UV spectrophotometry according to the technique of Shiu et al. (3). DMSO and dimethylsulfoxide ($DMSO_2$) in serum were quantified by gas chromatography employing a flame ionization detector according to the technique of Mehta et al. (4). Each dosage was performed before and 5, 15, 30, 45 min, and 1, 2, 3, 6, 9, 12, 24 h after the application of the BLM-DMSO mixture. Using these chromatographic methods, we were able to detect serum concentrations of BLM A2, BLM B2, DMSO and $DMSO_2$, respectively equivalent to 0.1 mg l^{-1}, 0.2 mg l^{-1}, 25 mg l^{-1} and 25 mg l^{-1}.

CASE REPORTS

Case 1

A 30-year-old man, serologically positive for the human immunodeficiency virus in 1989, was included in the Concorde protocol (Inserm, France). He first developed biopsy-proven Kaposi's sarcoma in December 1989 and presented 3 maculopapular lesions of the thighs after 2 months. He gave his informed consent to the treatment. Five mg of BLM diluted in 0.5 ml DMSO were applied per day during 3 days. After a total of 6 courses, we observed the clinical disappearance of Kaposi lesions (lightly pigmented macules). Histopathology showed less important lesions. A clinical recurrence of the lesions appeared in September 1990. The topical treatment was then reintroduced, with good results. However, he developed a pulmonary infection due to atypical mycobacteria and died in May 1991.

Case 2

A 34-year-old man had been HIV-positive since 1987. He presented with 5 Kaposi's sarcoma papular lesions in December 1990, and he gave his informed consent to the treatment. BLM was diluted in 1 ml of DMSO and applied in February 1991 as described in Case 1. He received a total of 5 courses with a disappearance of the violaceous hue and of the infiltration of the lesions, but a pigmentation of the test area was observed. A widespread eruption of Kaposi lesions appeared in July 1991, and BLM was given by the intramuscular route with stabilization of the lesions. The lesions primarily treated by topical BLM were again papular in January 1992. The subsequent worsening of the Kaposi's sarcoma led to the patient's death in May 1992.

BLM A2 and BLM B2, DMSO and $DMSO_2$ serum concentrations measured in both patients were never present above the lower limit of quantification.

DISCUSSION

In many patients, Kaposi's sarcoma begins with few lesions and its treatment is actually not standardized. Many therapies have been proposed. Our aim was to use topically a chemotherapeutic agent which is known to be active in a systemic form. We tried BLM in a vehicle also known for enhancing skin penetration. DMSO is used in treating extravasation of anthracyclin and vinca alkaloids alone or with alpha tocopherol with good therapeutic effects and without local and systemic toxicity (5–7). The quantity of DMSO was different in our two patients because we needed to treat all the lesions; 0.5 ml was used to treat 3 lesions in the first patient and the double quantity to treat 5 lesions in the second patient. Systemic toxicity was not observed in our two patients, as shown by regular blood examination, and we did not find BLM A2, BLM B2, DMSO and its metabolite in their different serum samples.

We observed a good therapeutic effect which lasted some months. The recurrence of the disease could be due to an incomplete effect, as shown by histopathology in our first patient, or to the rapid evolution of the disease, as in our second patient. A problem was the pigmentation we observed with topical BLM. It is a well-known side-effect with systemically used BLM, of unknown mechanism. The role of BLM is evident in our case by the pigmentation of all the device area, and it cannot be regarded as pigmented sequelae of treated Kaposi lesions.

This method is actually of limited value because of its temporary effect, but its efficacy and feasibility are important to consider. It may represent a new way of treating Kaposi's sarcoma, but many immunosuppressive drugs may have pigmenting side-effects.

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