

Letter to the editors

Idiosyncratic reaction to bleomycin in an epithelial tumor

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Sir,

Blenoxane (sterile bleomycin sulfate) is a mixture of cytotoxic glycopeptide antibiotic isolated from a strain of *Streptomyces verticillus*. This drug is being administered in the treatment of a large variety of tumors. The most familiar of its side-effects are pulmonary fibrosis. Also known are fever, shivering, and a detrimental influence on the skin, the hair, and the mucous membranes.

In about 1% of lymphoma cases treated with bleomycin, an anaphylactic-like reaction is described, though no similar reaction has been described in patients suffering from epithelial tumors treated with bleomycin.

The report below concerns a patient with bronchogenic anaplastic carcinoma who developed an anaphylactic reaction to bleomycin.

Case report

Z. A., aged 52, had always enjoyed good health. In May 1982 pain started in the chest and the back. After 4 months a chest X-ray demonstrated dimness in the right lower lobe, with a dim right sinus. Bronchoscopy revealed an anaplastic carcinoma. Bone scan revealed an increased concentration in the area of the upper sternum and the D4 vertebra. The liver function tests were normal. An elevated alkaline phosphatase of 148 IU of bony origin was noticed.

On physical examination the patient was found to be in a very poor general condition, being weak with shallow breathing and suffering from severe bone pains.

Chemotherapy was started, including cyclophosphamide 500 mg/m², vincristine 1.0 mg/m², and methotrexate 50 mg/m², every 21 days. The combination was administered three times, with no improvement. The lung tumor increased and substantial damage to the sternum and the ribs developed.

At the end of December 1982 the combination treatment as per the Hill and Price protocol [9] was applied. It was started by infusion of 15 U of bleomycin in 150 cm³ normal saline. Immediately this infusion was started the patient became short of breath and felt faint; he was pale and confused, shivering, and in a cold sweat, despite a rise in temperature up to 39° C. The pulse was thready and the pulse rate was 120/min. Blood pressure was 70/40; the ECG was normal. Following the administration of steroids, promethazine, and liquids the

reaction ceased, and after 20 min he regained the same state as before the treatment.

It was decided to find out whether the reaction was hazardous, and after a week IV bleomycin infusion was resumed. After about 0.5 U of the drug had been infused the shortness of breath, feeling of weakness, paleness, cold sweat, and fever appeared again.

This time no confusion appeared. The blood pressure was 90/70 and tachycardia 100. After treatment with Ultracorten 100 mg IV and promethazine 25 mg IV the symptoms observed disappeared within 15 min.

In view of the anaphylactic reaction to bleomycin the chemical protocol was changed to a combination of vincristine, methotrexate, and adriamycin, but again this brought no improvement, and the patient died at the end of January 1983 with symptoms of severe respiratory insufficiency.

Discussion

Bleomycin is an anticancer antibiotic that has attained a prominent place in the chemotherapeutic treatment of cancer over the last 12 years. Its main application is in squamous cell carcinoma of head and neck [1, 2, 9, 14, 15]. The drug is also widely used for the treatment of tumors of the skin, the penis, the cervix uteri, and the vulva [1, 2, 6, 7].

It is administered in combination with other drugs in nonseminomatous germ cells tumors of the testes [4, 7, 8, 11], and in other combinations in Hodgkin's lymphoma [1, 3] and in non-Hodgkin's lymphoma [1, 3, 10, 12].

Yagoda [15] describes the main side-effects of bleomycin, comprising fever (60% of all cases), shivering (40%), alopecia (35%), nausea (35%), fatigue (30%), vomiting (28%), loss of weight (25%), and rash, headache, itching and pulmonary fibrosis, each appearing in about 10% of cases in various degrees of severity [2, 5, 7, 13, 15].

Blum [2] describes four patients, representing 2.6% of the total lymphoma cases he reviewed, who developed a reaction similar to the anaphylactic reaction, manifesting itself in fever, fall in blood pressure, and various grades of shortness of breath.

A similar reaction was described by Yagoda [15] in a patient with Hodgkin's disease. It is generally supposed that 1% of lymphoma patients treated with bleomycin might develop such a reaction [1, 5, 13], and therefore it is advisable to give a trial dose of 1–2 mg bleomycin and to wait 24 h before administering the entire dose of the agent [1, 5, 13].

As pointed out, this adverse reaction, for which we have no clear explanation as yet, has so far been confined to lymphoma patients. A survey of the literature has not revealed any reports of similar reactions in patients being treated for epithelial tumors.

We have described here the case of a 52-year-old male suffering from bronchogenic anaplastic carcinoma, who developed an anaphylactic reaction even with a very tiny quantity of bleomycin, which disappeared after treatment with steroids and antihistamines.

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