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UKRAIN MONOTHERAPY IN MALIGNANT MELANOMA (CASE REPORT)

HAMLER F., HIESMAYR W., KORSH O.*, MELNYK A.

Ukrainian Anti-Cancer Institute, Margaretenstrasse 7, 1040 Vienna, Austria.

Summary: *A patient with a metastasizing malignant melanoma (stage III) was treated with Ukrain monotherapy. Before and during the first Ukrain course of treatment the patient excreted melanin in the urine. After the third course melanin was no more detectable and the patient has been without any symptoms of disease for the last 12 years.*

Introduction

Ukrain, a semisynthetic alkaloid derivative from *Chelidonium majus L.*, has shown tumourostatic and tumourocidal properties, both by direct action on cancer cells and mediated via lymphocyte subsets of the immunological apparatus (1). Malignant melanoma is considered to be more sensitive to immunological treatments than to chemotherapy, but in fact the results to date are controversial and this tumour is still one of the most aggressive, with growing incidence because of meteorological changes world-wide. Research even includes thermal neutrons (2). In a test panel from the National Cancer Institute, Bethesda, Maryland, USA, all eight human melanoma cell lines were sensitive to Ukrain, reaching GI_{50} values between 1.2 and 3.5 µM; TGI values between 4.7 and 10.3 µM and IC_{50} values between 15.6 and 77.1 µM (3).

Patient and methods

In the summer of 1983 a 43 year-old man complained of pain in the right deltoid muscle. At the keloid a small, dark, exophytically growing node developed which was very sensitive to even small traumata and bled easily. A cloudy pigmented area 3 cm x 2.5 cm developed later. The patient noted swelling of the lymph nodes in the right axilla which persisted despite antibiotic therapy. A biopsy of the axillary lymph node done in July 1983 revealed a "metastasis of a malignant melanoma with intact but thickened capsule. The tumour cells show pale nuclei with partly broad, partly small, pale cytoplasm. Much melanin is seen within the tumour cells. The lymph nodes show small-to-extensive invasion of tumour cells with necrosis in the larger". The right axilla was evacuated surgically of lymph nodes. *Histological diagnosis*: lymph node metastases of a malignant, primary, suspected nodular melanoma. No other surgical, radiological or cytostatic treatments were carried out.

* *Author to whom correspondence should be addressed.*

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X-ray examinations of the abdomen and thorax showed no abnormalities. In the ultrasound scanner some echo reflexing zones were seen in the right segment of the liver. The Thormaehlen test showed melanin in the urine on two occasions in July 1983 and in September 1983. 10 mg/ml Ukrain was given intravenously in four series every second day: 17 times in the first three series and 12 times in the fourth series. Two more series: 7 injections of 10 mg/ml Ukrain twice a week, were carried out. Treatment began in July 1983 and ended in March 1985. The superficial malignant area was examined in the dark under ultraviolet light at 254 and 366 nm to study the accumulation of the fluorescent Ukrain (4).

Results

According to the first examinations, the patient was in stage III with massive lymph node metastases and suspected diffuse metastases because of the positive tests for melanin even after the operation. These tests were positive in July 1983 and September 1983 but negative in March 1984 and September 1984. During the first three Ukrain therapy series the patient quickly developed strong subjective sensations, pain in the tumour area, paraesthesia, nausea and vomiting; these decreased steadily and were not recorded in the last series. During intervals in therapy the patient experienced no such symptoms. During and after Ukrain monotherapy the haematological status, enzymes, electrolytes, sero-proteins, urine and CEA titres were tested and showed values within normal limits. A vitiligo which the patient already had for many years seemed to have increased during the first year of therapy.

The area of the primary tumour, right shoulder dorsal-parasternal, showed a diffuse fluorescence of about 8 cm x 5 cm with spot-like appearances of undefined margin shortly after Ukrain administration. A strong fluorescence could be demonstrated 5 cm medial from the right posterior axillary sulcus. Within two days a 1.3 cm x 1 cm pustule developed, filled with clear amber-like liquid that was fluorescent, but healed without complication after punction. During the following weeks of therapy the fluorescent areas became smaller and were more concentrated around the dorsal shoulder and arm regions. In particular, a 1.5 cm x 1.5 cm fluorescent area was recognized at the posterior segment of the right deltoid muscle with a centrally-situated small brown-black point, about 6 cm from the suspected primary tumour, which was also fluorescent. All fluorescent phenomena disappeared after 2 1/2 months of Ukrain therapy. No further recurrences developed and the patient has remained in excellent health all this time. At last control in December 1995 no signs of recurrence were detected clinically.

Discussion

According to the diagnosis and prognosis of a stage III malignant melanoma with melanin excretion, this success could not be expected at onset of therapy, even though a few cases of spontaneous regression have been reported in malignant melanoma. Because of the personal wish of this patient, only Ukrain monotherapy was carried out. The kinetics of Ukrain, subjectively and objectively demonstrated, were the patient's sensations of pain and a feeling of warmth in the tumour area, paraesthesia, nausea and vomiting: phenomena that are thought to represent side effects of Ukrain therapy marking the degradation of tumour cells by the action of Ukrain. Such symptoms are not seen in healthy volunteers when treated with Ukrain. The objective phenomena could be demonstrated by ultraviolet light radiation on those areas which were near to the primary tumour. Varying in intensity and shape, these areas showed a tendency to decrease after Ukrain therapy, indicating that the malignant activity had disappeared from this region after the third course. As this area could not be examined histologically for malignancy, it must be pointed out that the accumulation of Ukrain could be demonstrated in operations and animal experiment specimens where the fluorescent locus was identical with the existence of malignant cells in

this very area. The strong subjective response at the onset and height of Ukrain therapy and its decline and total disappearance seems to correlate with the partial and later total eradication of the malignant melanoma cells by Ukrain.

References

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Note: The patient was treated with Ukrain in Vienna, Austria, by a physician. Full information was given about the kind of treatment and it was carried out with the patient's consent. The ethical rules were followed in accordance with the Helsinki Declaration.