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UKRAIN THERAPY OF STAGE T1N0M0 BLADDER CANCER PATIENTS

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Summary: *The aim of the present study was to evaluate the efficacy of Ukrain as a new treatment modality in 28 patients with stage T1N0M0 bladder cancer. The tumor dimensions varied from 0.5 x 0.5 cm to 3 x 4 cm. The first group (nine patients) was treated with a total dose of 100 mg Ukrain, the second group (10 patients) received 200 mg Ukrain, and the third group (nine patients) was treated with 300 mg Ukrain. In all patients Ukrain was administered i.v. at a dose of 10 mg per day. In the patients from the second and third group each course of treatment, consisting of 10 injections, was followed by 14 days of no treatment. Ukrain, at a total dose from 100-300 mg as neoadjuvant therapy in patients with T1N0M0 bladder cancer, resulted in either complete or partial regression of tumors in 60.7±9.2% of cases. The best treatment regime included three courses of Ukrain at 2-week intervals.*

Introduction

In recent years Ukrain has attracted the attention of several researchers. Its efficacy in the treatment of oncological diseases has been investigated in a number of experimental and clinical studies (1-4). Ukrain has been found to bring about a selective cytostatic and/or cytotoxic effect on malignant but not normal cells, and its antitumor effect has been accompanied with decreased oxygen (O_2) consumption and inhibited synthesis of RNA, DNA and proteins in tumor cells (4-8). Numerous clinical and experimental studies indicate that it has an immunopotentiating effect (3, 7, 9, 10).

Over 2,000 patients, aged from 9-85 years, with stage I-III of malignant tumors, have been treated with Ukrain in different clinics. The areas of its application have been different: after surgery as multi- chemo- and/or radiation therapy, or as neoadjuvant monotherapies. Nearly all solid tumor types have been represented in the various investigations.

The patient response rate to Ukrain was 93% at stage I, 72% at stage II, and 30% at stage III of cancer. On the whole, objective tumor regression was observed in 40-75% of the patients treated with the drug. Some patients had a remission of 6-10 years (4, 6, 10-12).

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The aim of the present study was to evaluate the efficacy of Ukrain in patients with superficial bladder cancer (BC).

Methods

Twenty-two men and six women with BC at stage T1N0M0 were included in this study. The age of patients ranged from 42-77 years. Single tumors were found in 19 subjects and multiple tumors in nine. In all the cases the tumors had a villous structure and a fungoid form. According to the cystoscopy and ultrasound data, the tumor dimensions varied from 0.5 x 0.5 to 3 x 4 cm. Before treatment patients underwent tumor biopsy. Sixteen tumors were histologically classified as highly differentiated transitional cell carcinoma, 10 as moderately differentiated transitional cell carcinoma, one as adenocarcinoma, and one as nondifferentiated cancer. Ukrain was administered i.v. at a dose of 10 mg per day. Nine patients received one course of treatment (100 mg), 10 patients received two courses at 2-week intervals, and nine patients received three courses. Two weeks following the treatment a cystoscopy and an ultrasound examination of the bladder were performed to monitor tumor growth. The efficacy of treatment was evaluated according to World Health Organization (WHO) solid tumor classification adapted to BC. Grade 1 consisted of complete tumor regression, *i.e.,* disappearance of all the intrabladder components of the tumors; grade 2 consisted of partial regression >50%, regression of the tumor with no growth of other foci being observed; grade 3 consisted of stable disease, *i.e.,* less than 50% tumor regression with no fresh damage to the bladder mucosa, or no more than 25% tumor growth; and grade 4 consisted of progression >25%, increase in the dimension of one or more tumors, or appearance of new foci of the tumor tissue.

Results and discussion

Clinically, Ukrain was well tolerated by the patients. No negative side effects or complications were noted. On the contrary, as early as after the first course of treatment (10 injections) patients noted an improvement in their general condition, namely a cessation of hematuria and improved appetite.

In group I, consisting of nine patients receiving one course of treatment (100 mg), in four patients cystoscopy revealed partial tumor regression, in the other five the disease was classified as stabilized. In the patients with partial regression, the tumors had smaller dimensions, were found covered with necrotic foci and fibrin deposits, and the tumor villi shortened and were more defined than at the initial diagnosis. Patients with partial tumor regression easily underwent transurethral resection (TUR) of the remaining tumor tissue. Among the patients with stabilized tumor growth, two patients underwent bladder resection and two underwent TUR.

In patients from group II, 2 weeks after discontinuation of treatment with Ukrain, a followup cystoscopy disclosed one patient with complete tumor regression. Before treatment the patient had a tumor of 2 x 2 cm in size which was histologically classified as moderately differentiated bladder carcinoma. In the next four patients the tumors were found in partial regression, and in the remaining patients the disease was evaluated as stabilized. As in group I patients, in group II, a followup cystoscopy revealed several changes in the tumor tissue, including necrosis, fibrin deposition, deformation of villi, and their local destruction. After the second course of treatment eight patients underwent TUR of the tumor remnants, and due to tumor localization in a vicinity of the *ostium uretheri*, one was subjected to resection of the urinary bladder with uretheroneocystoanastomosis.

Table I *Ukrain in treatment of T1N0M0 cancer of the urinary bladder*

Number of courses	Number of patients	Total dose of the drug (mg)	Complete tumor regression	Partial tumor regression	Stable disease
1	9	100	–	4	5
2	10	200	1	4	5
3	9	300	2	6	1
Total:	28	100-300	3	14	11

From group III, patients treated with 300 mg Ukrain, two demonstrated complete tumor regression. Partial tumor regression was observed in six patients and stable disease was observed in one patient. Six patients from this group underwent TUR of the tumor remnants, whereas one patient, in whom the tumor showed no regression after treatment, was subjected to chemo- and/or radiation therapy.

Table I summarizes the results obtained after Ukrain treatment in patients with T1N0M0 bladder cancer. Three patients in whom a total tumor regression was observed had no signs of relapse during 5-6 months of followup. Patients subjected to TUR and treated with 200 mg and 300 mg of Ukrain showed no relapses during 8-12 months of followup. After TUR and after 100 mg Ukrain two patients had recurrences in new localizations which were diagnosed 4-6 months after discontinuation of the treatment.

Thus, the application of Ukrain at a total dose of 100-300 mg as systemic chemotherapy in patients with T1N0M0 BC resulted in complete tumor regression in 15.8% of cases, a partial regression in 52.6%, and a stabilization of the process in 31.6% of cases. The best regimen of therapy consisted of three courses of treatment carried out at 2-week intervals. According to data presented elsewhere, using larger doses of Ukrain in patients with carcinoma of urinary bladder, complete regression of the tumor may be obtained in almost all patients.

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