Urological Research 6, 263-264 (1978)

Urological Research

Chemotherapy in Bladder Carcinoma

F. Edsmyr and L. Andersson

The Radiumhemmet and Department of Urology, Karolinska Sjukhuset, Stockholm, Sweden

Summary. In a series of patients with recurrent bladder carcinoma, treatment with various cytostatic drugs was generally unsatisfactory in cases of infiltrating carcinoma. Better results were achieved using instillation of Thiotepa for bladder papillomatosis and by instillation of Adriamycin for carcinoma in situ.

Key words: Bladder carcinoma - Chemotherapy - Carcinoma in situ - Papillomatosis.

Since 1970 a systematic programme has been undertaken to investigate the effects of various cytostatic drugs on carcinoma of the bladder. The majority of patients had persisting or recurring tumour following radiotherapy but in a few cases it was the primary treatment for carcinoma in situ or extensive papillomatosis. The tumours were categorised according to the TNM system and the histo-pathological grading recommended by the WHO. Cytological investigation of bladder irrigation fluid was performed in all cases.

Criteria of Tumour Regression

a) reduction of tumour size as recorded by cystoscopy and/or bimanual palpation.
b) disappearance of malignant cells in bladder irrigation fluid.

TREATMENT SCHEDULES AND RESULTS

a) Drugs Given Systemically

Bleomycin

This was introduced in our centre in 1970 (2). The first series comprised 9 patients with recurrent bladder carcinoma following full irradiation. Bleomycin 30 mg intramuscularly was given three times weekly to a total dose of 300 mg. One patient had a complete remission of the exophytic tumour. He is alive and tumour free 5 1/2 years later.

5-Fluorouracil (5-Fu)

This drug is one of those most studied in bladder carcinoma (1). In many of the reports, however, definitions of patient categories and criteria of tumour regression are lacking.

In a series of 30 patients with recurrent carcinoma following radiotherapy, 5-Fu was given in a daily dose of 500 mg for 10 days. In 15 patients the drug was given orally, in the remaining 15 intravenously. This treatment was repeated once per month for 4 months. After 5 months cystoscopy and cytological investigation of bladder irrigation fluid were performed.

One patient in each group had complete tumour regression lasting over 6 months. In these two patients the same treatment was continued once monthly but the tumours later recurred. In the other 28 patients no effect of the drug was observed. They were later given the treatment described below.

No serious side-effect of 5-Fu occurred in this series.

Combination Chemotherapy

α 5-Fluorouracil 1000 mg, Adriamycin 50 mg and Vincristine 2 mg, given by intravenous

0300-5623/78/0006/0263/$01.00

injections immediately following one another, were administered to those patients where 5-Fu alone had no effect. The treatment was given 4 times at monthly intervals. If no significant effect on the tumour was observed after 5 months, the therapy was changed for the following combination.

β Bleomycin 7.5 mg, Adriamycin 30 mg and Vincristine 2 mg. Bleomycin was given intramuscularly, the other drugs intravenously. The treatment was given every two weeks. In addition these patients were given 80 mg CCNU once per month. The treatment was given for a period of 4 months. It was discontinued if no significant effect was observed after 5 months.

Several patients in each of these 2 groups had complete remission for over 10 months.

ϑ Ftorafur

Ftorafur is a pyrimidine antimetabolite first synthesised in 1966 in the USSR. It is a derivative of 5-Fu which gradually dissociates in the tissues forming free 5-Fu (4).

Ftorafur alone or in combination with Adriamycin 1000 mg and Vincristine 2 mg was investigated in the last 6 months in a randomised series with three arms. Ftorafur was given as an intravenous daily dose of 2.4 g for 10 days, once per month. Cystoscopy was done after 5 months.

Twelve patients, given Ftorafur alone, have been observed for at least 4 months. In one there was partial tumour regression, in one increase of the tumour, and in the remaining ten no change of the tumour was observed.

b) Intravesical Chemotherapy

Thiotepa

Bladder instillation of 50 mg Thiotepa in 50 ml solution was given to 29 patients (3) with extensive papillomatosis. The solution remained in the bladder for 60 minutes with the patient in varying positions. The treatment was given, every second day, six times. These patients had small, slender papillomas over large areas of the bladder mucosa rendering effective electrofulguration difficult. Complete or almost complete regression occurred in 23 cases (80 %). In patients with partial regression later fulguration was facilitated.

Adriamycin

Instillation of 80 mg Adriamycin in 100 ml solution was given once monthly, four times, in 20 patients. Six of them had carcinoma in situ, previously untreated, i.e. malignant cells in the irrigation fluid and positive bladder biopsies but no exophytic tumour and only minute mucosal lesions on cystoscopy. The remaining 14 patients had had previous full irradiation or chemotherapy for infiltrating carcinoma.

Cytological investigation of irrigation fluid was performed before every instillation and cystoscopy after 5 months. The longest observation period is 24 months.

All 6 patients with carcinoma in situ had complete tumour regression resulting in normal cytology and normal cystoscopic appearances. Half of the patients with infiltrating carcinoma had partial regression, in the remaining half the tumour was not influenced.

In the patients with carcinoma in situ no side-effects were observed. Some of the other patients experienced a decreased bladder volume.

DISCUSSION

In this series like in others reported (1) the effect of chemotherapy was as a rule unsatisfactory in cases of infiltrating carcinoma, irrespective of their previous treatment. The result of instillation treatment in bladder papillomatosis was much more encouraging. In our opinion, however, chemotherapy is indicated only in cases where the extent of the papillomatosis or urethral lesions render transurethral surgery impossible.

Of particular interest is the good effect in patients with carcinoma in situ, since this type of bladder tumour is usually not influenced by radiotherapy.

REFERENCES

1. Carter, S.K., Wasserman, T.H.: The chemotherapy or urologic cancer. Cancer 36, 729 (1975)
2. Edsmyr, F., Almgård, L.-E., Lagergren, C., Ljungkvist, A., Stjernswärd, J., Unsgaard, B.: Study of the clinical efficiency of Bleomycin in human cancer. In: Bleomycin in the treatment of malignant disease. London: Lundbeck 1972
3. Edsmyr, F., Boman, J.: Instillation of Thio-Tepa (Tifosyl) in vesical papillomatosis. Acta Radiologica (Therapy, Physics, Biology) 9, 395 (1970)
4. Smolyanskaya, A.Z., Tugarinov, O.A.: The biological activity of antitumor antimetabolite "Ftorafur". Neoplasma 19, 341 (1972)

Dr. F. Edsmyr
Karolinska Sjukhuset
S-10401 Stockholm 60
Sweden