

ADJUVANT THERAPY IN EARLY PROSTATIC CANCER

Summary of the discussion

P. L. ESPOSTI

The scope of adjuvant chemotherapy is eradication of micrometastases after radical surgery or radiotherapy. As it is practically impossible with the present diagnostic methods to detect micrometastases, various prognostic factors are of importance in selection of patients.

One rationale for early chemotherapy is that any tumor may by growth acquire resistance to drugs, mainly correlated to increased heterogeneity of the cell population.

The experience obtained in treating macroscopic disease is of importance in choice of drugs and selection of patients. An objective response rate of around 50% would be a sufficient reason to test the same drug in adjuvant chemotherapy trials.

Dose reduction, especially in view of avoiding acute toxicity, is as a rule not recommended: studies on dose intensity in other malignant tumors than prostatic cancer have shown that reduced doses are usually linked to decreased effect of treatment.

Different techniques have been developed for testing sensitivity to cytostatic drugs, such as evaluation of colony formation. The understanding of molecular mechanisms responsible for drug resistance is also of importance in improving results of therapy in patients with micrometastases of solid tumors.

The effects of endocrine treatment in early prostatic cancer are not clearly established. From studies on the possible mechanisms of action of endocrine therapy and from clinical experience, one would draw the conclusion that complete remission of prostatic malignancy is not to be expected. In fact the exact mechanisms of response to endocrine treatment are not clearly understood. Experiments on animals suggest that part of the tumor cells disappear after castration, while other remain in a dormant state.

Several investigations have shown that endocrine therapy usually is more effective against the primary tumor as compared to distant metastases. There is, however, no evidence that inoperable tumors may become operable after endocrine therapy.

With regard to choice of adjuvant chemotherapy in early prostatic cancer, different drugs and combination of drugs have been tried. The series reported are few and the number of patients small. Few agents have been tested, such as cyclophosphamide and doxorubicin compared to no treatment, estramustine compared to cyclophosphamide. At present there is no evidence of an efficacy of any adjuvant chemotherapy after radical prostatectomy or definitive radiotherapy.

The efficacy of adjuvant irradiation or androgen deprivation after radical prostatectomy, in cases with positive margins, has been studied: it has been shown that both postoperative irradiation and androgen deprivation reduce local recurrence rates in patients with residual disease. Survival rates, however, have not been altered.

In conclusion, further research is mandatory to increase the possibilities to cure patients with micrometastases of carcinoma of the prostate.

Corresponding author: Dr Luigi Esposti, Department of Oncology, Radiumhemmet, Karolinska Hospital, S-104 01 Stockholm, Sweden.

Presented at the Conference on Early Prostatic Cancer. The WHO Collaborating Centre for Urological Tumours, Karolinska Hospital, Stockholm, March 21–23, 1990.

Accepted for publication 30 September 1990.