

## BLEOCIN ALONG WITH RADIOTHERAPY AND METRONIDAZOL IN THE TREATMENT OF CERVICAL MALIGNANCY

by

M. B. DESHMUKH

P. GURTU

and

K. W. TAYADE

### SUMMARY

This study has evaluated the selective response of cervical cancers to Bleocin along with Radiotherapy and metronidazole in 25 patients of Carcinoma cervix.

Two cases of cancer cervix stage II B, who were treated, did not show any histopathological evidence of malignancy after Wertheim's Hysterectomies. Combined Chemotherapy and Radiotherapy offers a promising future for better results in the management of cervical cancers.

### Introduction

Cancer Cervix enjoys the reputation of being the leading cause of death in our country. It is the commonest type of malignancy in female as seen at Govt. Medical College, Nagpur. During 1980 there were 318 cases of cancer cervix admitted in the hospital while cancer breasts were only 162. Majority of cancer cervix patients have poor response when treated with conventional forms of radiotherapy. This study aims at the evaluation of the selective response of cervical cancer to Bleocin alongwith Radiotherapy and Metronidazol.

### Material and Methods

Twenty patients of carcinoma cervix stage IIIB and 5 patients of Carcinoma

Cervix stage IIB were included in this study. Twenty-three patients were between 40 to 60 years of age while 2 patients were below 35 years of age. These patients were given Bleocin I.V. 15 mg every week with total dose of 150 mg in 10 weeks. Patients received metronidazol 400 mg three times daily initially and after observing good tolerance the dose was increased to 800 mg three times daily and subsequently 2.4 gms was administered as a single dose, 4 hours before radiation treatment. All patients received Tab. Stemetil 10 mg half an hour before single dose of Metronidazol. The patients were started on external irradiation 200 rads/day, 5 days a week for 21 sittings. External irradiation was given in the form of low energy transfer Gamma rays. All patients received anabolic steroids and supportive therapy during treatment. Total dose of radiation varied between 4000-5000 rads. The response was assess-

From: Department of Obstetrics and Gynaecology, Government Medical College, Nagpur.

Accepted for publication on 27-2-86.

ed subjectively and objectively.

Subjective: Patients acceptability of the drugs and radiation.

Objective: Regression of tumour at the end of ten weeks which was graded as follows.

Excellent: Almost complete regression of tumour.

Good: 50-70% regression of tumour.

Fair: 30-50% regression of the tumour.

Nil: No response in regression of the tumour.

### Results

All patients accepted and tolerated Metronidazol during the therapy except for nausea. Twenty patients developed fever maximum up to 100.0°F about 3 to 5 hours after Bleocin injection. Sclerosis of the fingers and palms, pigmentation changes in the nails developed on reaching the total dose of 150 mg. Severe side effects like pulmonary fibrosis was not seen in any cases. Bleocin was tolerated by the patients but all these patients could not afford the cost of treatment for continued therapy.

All the 20 patients of stage IIIB and 3 cases of stage IIB showed excellent results at the end of 10 weeks. Two cases of cancer cervix stage IIB had complete regression of the local growth and parametrium. These 2 cases subsequently underwent extended wertheim's hysterectomy. The histopathology of the specimens did not reveal any malignancy in the exterpated tissues.

### Discussion

Bleocin is an anticancer antibiotic produced by streptomyes verticillus isolated from the soil in Japan. It has a synergism with radiation. DNA is divided by radiation and this broken DNA is normally completely repaired within 10 min. This repair

is inhibited by Bleocin, without bringing lucopenia.

The main targets of anticancer agent Bleocin in the treatment of cancer cervix are the destruction of undifferentiated carcinoma adjuscent to stroma by Bleocin and of the differentiated carcinoma in the central part of the tumour by Metronidazol and radiation. Chronically hypoxic cells are present in solid tumour in man and animals. The radioresistance of such cells is a limiting factor in the local control of the solid tumour, when treated with radiotherapy alone. There are two different techniques in radiotherapy currently under investigations that could potentially lead to improved results; one is high linear energy transfer irradiation which provides a lower oxygen enhancement ratio for cells irradiated *in vitro* and the other is the combination of chemical radiosensitizer which are selective for hypoxic cells with low linear energy transfer irradiation which might reduce the oxygen enhancement ratio of tumour cells to that observed with high LET irradiation. The classic work of Utrasum (1974, 1976); Mogre *et al* (1979) and Ayyagari (1979) demonstrated the importance of hypoxic cells in the radioresistance and the use of oxygen as radiosensitizer.

In the present study of 25 patients the combined use of these three brought about remarkable degeneration and necrosis of cancer cervix. Katokichi, Sekimoto Kezuyush and Takeda Sachiko from Japan studied the effect of several kinds of anticancer agents by the use of transplanted carcinoma of uterine cervix in nude mice. The combined use of Bleocin and Metronidazol brought about remarkable degeneration and necrosis of the cancer. They used combination of chemotherapy in 26 cancer cervix patients. In early cancer group many of their operated cases revealed no malignant foci while in advanced group of cases

there was considerable degeneration and necrosis in the tumour.

This combined chemotherapy and radiotherapy offers a good chance of cure of cancer cervix.

**Acknowledgement**

We wish to thank the Dean of the Govt. Medical College and Hospital, Nagpur for allowing this present study.

**References**

1. Abstracts FIGO 1979 IX World Congress of Gynaecology and Obstetrics No. 20

Katokichi, Sekimoto Kezuyushi, Takeda Sachiko.

2. Katokichi Sekimoto Kezuyushi, Takeda Sachiko: Abstracts of the papers from FIGO 1979; IX World Congress of Gynaecology and Obstetrics held at Tokyo, Japan, Cervical cancer 020.
3. Ayyagari, S.: quoted unique group of Phar. Personnel Communication 1979.
4. Mogre, K.: quoted by unique group of Phar. Personnel Communication 1980.
5. Mogre, K., Bhalavat, R. L. and Pinto J. M.: Ind. J. Cancer Chemotherapy, 1: Oct.-Dec. 1979.
6. Utrasum, R. C. and Strunwind, J. et al.: Brit. J. Radiology, 47: 297, 1974.
7. Utrasum, R. C.: New England J. Medicine, 294: 1364, 1976.