

# TREATMENT BY COMBINED CHEMOTHERAPY FOR RECURRENT OVARIAN CANCER

Pages with reference to book, From 340 To 343

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## Abstract

Neoplasms of the ovary are the cause of more deaths than any other female cancer. Approximately 23% of all gynaecological cancer are of ovarian origin, but 47% of all deaths from cancer of the female genital tract are due to ovarian carcinoma<sup>1</sup>. Combination systemic chemotherapy frequently produces startling remissions and yet the overall five year survival rate remains 25%, the lowest survival statistic for any major pelvic malignancy<sup>2</sup>. This report describes the recurrence of a tumour nine years after extensive surgery and radiotherapy and emphasises the importance of prolonged follow up as well as described treatment by combined chemotherapy after debulking of tumour (JPMA 35: 341 ,1985).

## CASE REPORT

This 59 year old lady para 12<sup>+2</sup> first presented in March 1973 with a prolapsed uterus. It was decided to perform a vaginal hysterectomy but the patient postponed operation until November 1974. When the patient was examined under general anaesthesia, two masses were palpable in her pelvis which had not been noted in 1973. A laparotomy was decided upon and hysterectomy with bilateral salpingo.oophrectomy was performed because of tumours present in both ovaries. No secondaries were noted in the pelvis, abdomen or diaphragm. Histology confirmed bilateral ovarian mucinous cystadeno carcinoma. The patient was sent for radiotherapy in the form of a course of Cobalt 60 Teletherapy to the whole pelvis. She attended the Gynae Clinic for five years and was well at each visit.

The patient again presented in September 1983 with a mass in the left iliac fossa. She was admitted for laparotomy, which was performed with the help of General Surgeon after routine investigations. A large mass of malignant tissue was removed from the left iliac fossa. A very large para aortic gland and a large nodule on the anterior abdominal wall were noted. There was very fine granular deposition present on the lower surface of the diaphragm. The patient was treated with Cisplatinum and Treosulphan monthly for 8 months. C.A.T. scan was then performed which revealed no evidence of residual growth in either the pelvis or the abdomen.

After consultation with the General Surgeon a second look operation was performed in May 1984. In contrast to the findings of the C.A.T. scan, two masses were present, one in the lesser curve of the stomach and the other in the left iliac fossa. Both the masses were mobilised and removed. There were no other obvious secondary deposits seen or felt. The liver and diaphragm were clear.

After discussing with the Oncologist, further treatment with Cisplatinum and Treosulphan was given monthly from June to December 1984. She attended the Gynae clinic in the last week of December 1984 and clinically there was no evidence of any mass in the abdomen and she remained well up to April 1985.

## DISCUSSION

No organ in the body gives rise to as many different histologic types of neoplasm as the ovary. Cancer of the ovary is frequently symptom-less in its early stages and indeed is widely disseminated throughout the peritoneal cavity in 70% of patient when the diagnosis is first made.<sup>2</sup>

Surgery, Radiotherapy and Chemotherapy are the modern methods of treating ovarian cancer, depending upon staging, type and age of the patient. The present review of selected clinical trials of the use of radiotherapy in ovarian cancer indicates that radiotherapy has a curative role in post operative treatment<sup>3</sup>. There is a continuing effort to improve the survival of patients with abdominal cancer by the use of a variety of combinations of Cytotoxic agents<sup>4</sup>. The importance of surgery is increasing in the management of ovarian tumours<sup>5</sup>. Second look laparotomy to determine the response to chemotherapy is generally considered to be the appropriate management of ovarian cancer<sup>6-8</sup>. The patient described here is an interesting example of treatment by various methods including surgery, radiotherapy, chemotherapy and second look laparotomy followed by further chemotherapy. Failure to follow up the patient beyond 5 years, delayed diagnosis and may have increased the morbidity, thus showing the importance of prolonged routine review after treatment of cancer. Surgery was the main treatment initially, and after recurrence the combined efforts of the General Surgeon and Gynaecologist were necessary for a better result. Radiotherapy was given after the initial laparotomy for recurrence, chemotherapy caused sufficient regression to allow complete clearance at the second look laparotomy. The dose of anti cancer drugs was reduced according to the blood picture and the complaint of nausea or vomiting. Modern methods of investigation were helpful but total body scan didn't pick up the metastases and the ultimate decision was dependent upon clinical observation and judgement. After the diagnosis and staging of ovarian tumour, there are different methods of treating the disease. Initial surgery remains a basic method of reducing the bulk of the tumour<sup>9</sup>. Radiotherapy and Chemotherapy are widely applied in centres all over the world. Although radiotherapy has a curative role in post operative patients, progress is proportional to the volume of remaining tumour. Its pathology, sub-type, grade and the presenting stage each independently influence the outcome of the therapy<sup>3</sup>. Some of the trials showed that the role of radiotherapy is limited in the case of epithelial tumours.<sup>5</sup> There are different regimes of chemotherapy available at the moment. Adriamycin, Ifosfamide, cyclophosphamide and cisplatin are the main drugs for chemotherapy today. A study with Ifosfamide showed that it is an effective drug in the treatment of patients with ovarian cancer but that it is not superior to the traditional single alkylating agent<sup>10</sup>. Combine therapy with cyclophosphamide and cisplatin showed an excellent result. A study by Decker<sup>4</sup> demonstrates a definite superiority of combination therapy with cyclophosphamide and a moderate amount of Cisplatin over treatment with cyclophosphamide alone in patients with ovarian carcinoma. In another study with cyclophosphamide, Daunorubicin and Cisplatin the results showed that despite the side effect of nausea, vomiting, hematological, renal and cardiac toxicity, that 52% of the patients showed a response after the first course, an additional 6% after the second course and an additional 19% after the third course<sup>11</sup>. Indiana University experience showed that the use of Cisplatin, Adriamycin and Cyclophosphamide is an active chemotherapeutic drug combination for the treatment of advanced epithelial ovarian cancer, achieving an 81.5% response rate<sup>12</sup>. In all studies on chemotherapy, second look surgery is advised. Computerized axial tomography and ultra sound techniques are relatively accurate where large tumour masses are present but are less sensitive than pelvic examination by an experienced Gynaecologist in determining the early recurrence of gynaecological malignancies<sup>13</sup>. The most effective and accurate way to determine the presence of persistent ovarian epithelial cancer is to perform a second look operation<sup>8</sup>. In different studies it was shown by others that a satisfactory definition of second look laparotomy is needed before we can evaluate the real result of its findings.<sup>14</sup> At the same time in another study it was shown that timing of second look laparotomy also influenced the result of treatment.<sup>15</sup>

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## REFERENCES

1. DiSaia, P.J. Foreword. *Clin. Obstet. Gynaecol.*, 1983; 10 : 153.
2. Benigno, B.B. Management of advanced ovarian cancer. *Prog. Obstet. Gynaecol.*, 1982; 2:123.
3. Dembo, A.J. Radiation therapy in the management of ovarian cancer. *Clin. Obstet. Gynaecol.*, 1983; 10 :261.
4. Decker, u.u., Fleming, LK., Mailcasian, (G.D). Jr., Webb, M.J., Jaffries, J.A. and Edmonson, J.H. Cyclophosphamide plus Cisplatin in combination; treatment program for Stage III or IV ovarian carcinoma. *Obstet. Gynaecol.*, 1982; 60 : 481.
5. Decker, D.G. Mayo clinic experience with epithelial ovarian cancer. *Clin. Obstet. Gynaecol.*, 1983; 10 : 337.
6. Smith, J.P., Delgado, G. and Rutledge, F. Second-look operation in ovarian cancer. *Cancer*, 1976; 38 : 1438.
7. Roberts, W.S., Hodel, K., Rich, W. M. and Disaia, P.I. Second-look laparotomy in the management of gynaecologic malignancy. *Gynaecol. Oncol.*, 1982; 13 : 345.
8. Schwartz, P.E. Current status of the second-look operation in ovarian cancer. *Clin. Obstet. Gynaecol.*, 1983;10 :245.
9. Cohen, C.J., Bruckner, H.W., Goldberg, J.D. and Holland, J.F. Improved therapy with cisplatin regimens for patients with ovarian carcinoma (FIGO III and IV) as measured by surgical end-staging (second-look surgery) the mount sinai experience. *Clin. Obstet. Gynaecol.*, 1983; 10 307.
10. Yazigi, R., Wild, R., Madrid, J. and Arraztoa, J. Ifosfamide treatment of advanced ovarian cancer. *Obstet. Gynaecol.*, 1984;63 : 163.
11. Belinson, J.L. McClure, M., Ashikaga, T. and Krakoff, I. H. Treatment of advanced and recurrent ovarian carcinoma with cyclophosphamide, doxorubicin and cisplatin. *Cancer*, 1984; 54 1983.
12. Enruch, C.E. et al. Treatment of advanced epithelial ovarian cancer using cisplatin, Adriamycin and Cyteran The Indiana Experience. *Clin. Obstet. Gynaecol.*, 1983; 10 : 325.
13. Sommer, R.F., Walsh J.W. et al. Evaluation of gynaecologic pelvis masses by ultrasound and computed tomography. *Reprod. Med.*, 1983; 27 : 45.
14. Berek, J.S., Hacker, N.F. Lagasse, L.D., Poth, T., Resnick, B. and Nieberg, R.K. Second-look laparotomy in stage III epithelial ovarian cancer; clinical variables associated with disease status. *Obstet. Gynaecol.*, 1984; 64 : 207.
15. Vogl, S.E., Seltzer, V., Calanog, A., Moukhtar, M., Camacho, F., Kaplan, B.H. and Greenwald, E. "Second-effect" surgical resection of bulky ovarian cancer. *Cancer*, 1984; 54 : 2220.