INOPERABLE CARCINOMA OVARY—TREATED WITH MITOMYCIN-C

(A case Report)

by

S. R. HARIDAS, M.D. (Bom.), D.G.O. (Bom.)

Methothrexate, among the chemotharapeutic agents, has given very encouraging results in cases of chorio-carcinoma. In Japan, they hav discovered the most suitable method of administration for such excellent drugs as Mitomycin-C(MMC), 5-Fluoro-Uracil (5FU) or Cyclophosphamide (Endoxan), drastically improving the effects of these drugs by means of combined therapy or adjuvant-therapy with operation and radio-therapy. MMC in particular has been in use for a period long enough for them to obtain the results of 5 years and more. The results indicate: (a) a remarkable improvement in the 5 years survival rate for those with stomach and lung cancers, for which MMC has been used adjuvantly with operation, (b) an improvement in the remission rate for those with lymphoma and cancer of cervix, for which MMC has been used in combination with radio-therapy and (c) increase in responsiveness to drugs and improvement in subjective symptoms among those with various terminal stage cancers, for which large dose intermittent administration or multi-agent administration has been carried out.

In ovarian carcinoma, Kumabe (1969) has reported efficacy rate of 2 out of 7 with MMC alone and 4 out of 8 with combined chemotherapy. Kyowa (1970) has reported various changes in the results of clinical examination and changes in the subjective and objective symptoms in 17 cases out of 22, and such improvements as recession of tumour and softening in 32.2% of the cases.

Four cases of advanced carcinoma ovary were treated by the author with Mitomycin-C. First one survived 1 year after the initial treatment and the case report is given below. Second one, Mrs. N. is still alive and well after 9 months of operation for bilateral papillary adenocarcinoma, with subsequent development of secondaries in the lungs. She had 2 courses of Mitomycin-C 60 mgs. each. Last two, which were far too advanced and with too poor general condition, died during the course of therapy. Initially, in the first case, a smaller dose of 4 mg. twice weekly was given, but subsequently, in the same case and others, larger dose of 10 mg. of MMC was administered in one dose, twice weekly, followed by coenzymatic Vitamin B_6, 200 mgs., given as antidote.

The principles of the method lie in elevation of the blood level of MMC by giving large dose so that there is increase in cancer uptake of MMC, in as large amount as possible in a short period, with resultant beneficial results. The antagonistic substance, vitamin B_6, which is harmless to living organs, should be administered while MMC concentration is still low in normal organs, so that it can

Assistant Associate Professor (Resigned), Bangalore Medical College and Vani-Vilas Hospital, Bangalore.

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break this drug remaining in the blood and thus prevent the side-effects of MMC. Moreover, MMC was administered once every 3 days, in accordance with the intermittant tumour multiplication, as pointed out by Skipper (1962), to destroy cancer effectively.

Case Report

Mrs. K. S., aged 43 years, married and with four children, came on 9-12-1968, with complaints of weakness, loss of appetite, vomiting and pain in left iliac fossa. Actually, her complaints started way back in November, 1967, when she had a profuse bout of bleeding per vaginam followed by pain in lower abdomen, during the period. This recurred in December and so she went for a check-up to St. Martha's Hospital, Bangalore, where a surgeon detected a mass in the lower abdomen and admitted her for further investigations. A laparotomy was done in February, 1968 and left sided overian tumour, with intestinal adhesions all round, and with extensive secondaries all over the peritoneum, intestines and liver, were detected. As it was considered inoperable, a biopsy from the tumour was taken and abdomen closed. Histopathological report was papillary adenocarcinoma.

In May, 1968, she went to CMC Hospital, Vellore, where she had a full course of radio-therapy with Cobalt 60, followed by 5 doses of 5-Fluoro-Uracil (5 FU), 500 mgs each, once a week, and then discharged. She was re-admitted in August, 1968, for incisional hernia and ascites. Endoxan 200 mgs. was introduced intraperitoneally daily for nearly a week and then herniorrhaphy was done. During the operation, secondaries were detected all over. Later, Endoxan was continued and she had a total of 2200 mgs. of Endoxan parentarily, followed by 50 mgs. tablet twice daily, which she continued till November and then stopped because of toxic effects. Thus, she had a full course of Radio-therapy with Cobalt 60, 2500 mgs. of 5 Fu. and more than 5000 mgs. of Endoxan, before she came to me.

She was emaciated and anaemic when she came. She had oedema feet, ascites, with no palpable liver or spleen. There was a hard, irregular mass 2" x 1 " x 1", adherent to abdominal wall in left hypochondrium. There was another hard, irregular, tender mass, almost 16 weeks' pregnancy size in the hypogastrium and it was extending into right and left iliac fossae and left lumbar region. On pelvic and rectal examinations, it was found that the mass occupied the whole of pelvis and uterus could not be made out separately. X-ray chest showed no secondaries in the lungs. Haemoglobin was 10 Gms., R.B.C. count 4.1 millions/Cu. M.M., with total W.B.C. count of 8200/ Cu.m.m. A diagnosis of inoperable carcinoma ovary with secondaries and ascites was made. It was decided to try Mitomycin-C on her and got her admitted to Vani-Vilas Hospital, Bangalore. On admission, she was started on liver extract and B complex injections on alternate days. Durabolin 25 mgs. twice weekly and a pint of blood was given. Then she was given Mitomycin-C 4 mgs. in 250 c.c. of 5% glucose in half an hour, twice weekly. From the second week onwards, she had 100 mgs. of Vitamin B6 after each Mitomycin-C drip and a pint of blood every week. At first, there was increase in abdominal girth, but nausea and vomiting disappeared and her appetite improved. After 40 mgs. of MMC and 5 pints of blood, it was found that ascites had disappeared, omental and pelvic masses had become very much smaller and softer, her general condition had improved, Hb had gone upto 12 Gms%, and total W.B.C. count was 8000/ Cu.m.m. At this stage, it was decided to operate on her and remove as much of the tumour mass as possible. During the laparotomy on 14-1-1969, there were no secondaries over the peritoneum, intestines or liver and there was minimal fluid. Omental mass was adherent to the abdominal wall and was easily removed. Intestines, the tumour and the uterus had formed one mass. Intestines were carefully separated from the mass and the tumour along with the uterus was removed. Only subtotal hysterectomy could be done as cervix was badly adherent to the rectum. She had 2 pints of blood during the operation. Abdomen was closed with tension sutures. Postoperatively, 4 mgs. of MMC was given and then continued twice weekly. She had a total of 60 mgs. of MMC.

Abdominal wound healed with primary intention. There was slight induration in the pelvis at the time of discharge on 10-2-1969. The histopathological report, once again, was papillary adenocarcinoma. She had very much improved in her health, when she joined her duties at the end of February as Sister in-charge of the Lepresorium. During the second post-operative check up on 12-4-1969, there was slight suspicion of free fluid in the peritoneal cavity, even though there was no other evidence of cancer in the abdomen or pelvis. She was re-admitted, and this time, she was given 10 mgs. of MMC in a pint of 5% glucose, run in one hour, followed by Vitamin B6 200 mgs, repeated twice weekly. At the end of 3 weeks, after 60 mgs. of MMC, she was discharged. She remained healthy and well till the end of June, 1969.

She came back in the second week of August, with complaints of loss of appetite and slight pain in right hypochondrium. There was evidence of moderate ascites and enlarged, tender liver but pelvis was free. She was readmitted for a third course of MMC. But this time it was decided to give her combined therapy of 10 mgs. MMC twice weekly and Endoxan 200 mgs. I.V. four times a week, even though the patient said she could not tolerate Endoxan, because of the better results reported with combined therapy. But unfortunately, at the end of first week's treatment, she suddenly lost all her hair and became bald; and her condition became bad, Chemotherapy was stopped for two weeks, and she was given 2 pints of blood and large doses of vitamin B complex. Subsequently she was given only MMC 10 mgs. twice weekly. There was slight improvement in her general condition, appetite improved and ascites decreased. When she had finished 40 mgs. of MMC, it was thought that the response was not as good as in the past and it was decided to stop MMC and put her on Leukeran 5 mg. tablet daily, which she had till the end of October and then 2.5 mgs. daily. Her condition improved very much, ascites almost disappeared, liver was not palpable, and appetite improved considerably. But in the third week of November, her condition suddenly deteriorated, she could not take anything but fluids by mouth, could not tolerate any drug and started getting reactions to blood transfusions. She suddenly collapsed in the evening of 28th and died in the early hours of 29th November 1969.

Thus, here is a case of advanced ovarian cancer, which survived for 2 years after the initial onset of symptoms. She probably survived 1 year longer due to chemotherapy with MMC and it is possible that she would have survived for some more time, if Endoxan was not combined with MMC.

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