The results revealed PR in 1 case, MR in 2, NC in 1 and PD in 3 in 1) group; PR in 2, MR in 4 cases, NC in 1 case and PD in 1 case in 2) group; PR in 1, MR in 1 and PD in 1 in 3) group; and PR in 4, NC in 1, and PD in 1 in 4) group.

352. Effect of Each Combination Chemotherapy for Malignant Ovarian Tumors

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The prognosis of malignant ovarian tumors were extremely poor among gynecological malignancies. We made several trials to improve the prognosis of ovarian malignancies.

At present, we have been used several combinations of chemotherapy for screening the most effective drug or combination to treat ovarian malignancies.

In the retrospective study, we reviewed 460 cases of malignant ovarian tumors from 1970 to 1978, with a number of combination chemotherapies freely chosen, such as VEM, MFC, FAMT, METT, METVFC, QFC, etc.

We used accumulative survival rate as the parameter to evaluate effectiveness. In patients with Stage III, VEM combination showed statistically significant, and better survival rate than the other combinations but had strong side effects. However, therapy of MFC combination seems next effective and relatively has small side effects, so widely used in retrospective studies.

From 1979, we treated prospectively 397 patients using 3 protocols: these were MFC, MFCP, CAP combinations. Judging from accumulated survival rate concerns, CAP showed the better anticancer effect and followed by MFCP and MFC combinations. When the accomplishment of surgery was taken note, CAP combination was found any difference between complete and incomplete surgery with Stage III patients. Therefore, CAP combination seemed to be the most effective among three, judging from present studies.

353. Direct Effect of Tranexamic Acid and Retinoic Acid on Proliferation of Cell Line Established from Human Ovarian Cancer Tissues

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Thirteen patients with advanced ovarian carcinoma who had a marked amount of ascites during the course of previous chemotherapy were treated with intraperitoneal injections of tranexamic acid, followed by combination chemotherapy. Four gram of tranexamic acid was intraperitoneally administered every day for two weeks. Nine out of 13 patients (69.2%) had benignant channges in view of Papanicolaou smear in the ascitic fluid after treatment with tranexamic acid. Complete disappearance of ascitic fluids was observed in 6 of 13 patients (46.2%). If 2 cases with partial reduction of ascites were included, the response rate increased to 61.5%. Median length of survival after start of treatment with tranexamic acid was significantly longer in patients with good response in view of decrease of ascites (13 months) than in patients with poor response (5 months). Proliferation of cells (HR) established from ovarian cancer tissue of a patient with good response to tranexamic acid was inhibited at all concentrations of tranexamic acid used in this study without any effect on thymidine uptake by the cells, while proliferation of cells (KK) established from ovarian cancer tissue of a patient with poor response was not inhibited at any concentration of tranexamic acid. Retinoic acid stimulated the ability of cells (YK) derived from human immature teratoma of the ovary to secrete AFP into the medium, while inhibiting the cell proliferation.

354. Evaluation of Cancer Chemotherapy Using Rat Ovarian Cancer Induced by DMBA

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Rats with primary autochthonous ovarian cancer induced by DMBA confirmed by biopsy received the chemotherapy (Cis-DDP or Ifosfamide). Four to five weeks after the administration, they were killed and lightmicroscopically, the histologic effects of the anticancer agents were evaluated. Microangiography was also performed to study vascular changes in the tumor.

Vessels were damaged all together at a certain point of the internal part of the tumor. In this area, microscopically, the boundary between cancer tissues and necrotic ones were clearly observed. Location of the survived neoplastic tissues at the periphery of the tumors with various degrees of histologic effects was typical for the post-treated tumors. 1) Proliferation of connective tissues. 2) Both cytoplasm and nucleus were changed to small and narrow in shape. 3) Pyknosis. 4) Necrosis. 5) Many cystic spaces contained histiocytes (Phagocytosis).

Although not a exact replica of human counterpart, DMBA-induced cancer in rat ovary was regarded as a promissing model of the common epithelial tumor.

355. Second-look Operations in Malignant Ovarian Tumors

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Approximately ten years after it was first incorporated into the treatment of malignant ovarian tumors, the second-look operation (SLO) is today coming to be accepted as an indispensable procedure. However, many problems remain to be solved, including the selection of cases and the timing of the operation. The indications for second-look operations have conventionally been categorized as 1) excision of a residual tumor, 2) evaluation of the effectiveness of treatment, or 3) other reasons. Because the number of cases has risen steadily since 1973 and has reached 133, we have regrouped them by indication into 9 categories and have examined each category in detail.

Whereas many of the second-look operations were conducted to evaluate the effectiveness of therapy, those conducted for the purpose of excising residual tumors are decreasing in number, due to the wide use of reduction surgery in recent years. There were 20 cases in which residual tumors were successfully excised by a second-look operation after the initial laparotomy. The prognoses for these cases were excellent, compared to those of the controls. Among those cases in which the second-look operation was performed to evaluate the effectiveness of the initial palliative or complete excision of the tumor, abnormalities were revealed in 33.3% of the former and in 17.6% of the latter. In four of the cases, abnormalities were found simply by cytological examination of the irrigation fluid, thus indicating the effectiveness of this method. In addition, the second-look operation was aimed at restaging the tumor in 7 cases, resulting in the restaging of one case. In all 11 cases in which the purpose was to treat complications, the complication involved was ileus.

356. Distribution of a Newly Developed Anticancer Agent KM 2210 in the Malignant Ovarian Tumor

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Concentrations of a newly developed anticancer agent KM 2210 and its metabolites in various tissue of the female reproductive organs, including malignant ovarian tumor were measured with liquid chlomatography. The agent KM 2210 was a conjugate of estradiol and chlorambucil, developed based on an idea of acumulating the anticancer agent in the tissue with estrogen-receptor. After oral administration of 100 mg of KM 2210, the concentration of KM 2210 and its metabolites in blood were measured at 1, 3, 6, and 24 hours. The concentration in the malignant ovarian tumor in six cases and in the normal ovaries in five cases were also determined. KM 2210 in the blood showed no marked change for 24 hours after the oral administration, there was no significant difference of blood concentration between malignant cases (8.43 ± 1.88 ng/ml) and the control (7.95 ± 3.07 ng/ml). The concentrations of KM 2210 and its metabolites were eight times higher (829 ± 435 ng/g-wet tissue) in malignant ovarian tissue as compared to the normal ovarian tissue (111 ± 18.8 ng/g-wet tissue). The low concentration of KM 2210 in the normal endometrial tissue suggests that the agent is acumulated in the malignant tissue not because of the presence of estrogen-receptor but through some other unknown