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Abstract

With the purpose to prevent the dissemination and consequent metastasis of cancer cells at the time of operation we gave 10 mg of Mitomycin C per day for four consecutive days prior to surgical operation of gastric cancer (total of 322 patients), and this so-called adjuvant chemotherapy proved to be effective on the cases with serosal involvement and infiltrating type of cancer, irrespective of histological types. It also gave five-year survival rate of 35 per cent. However, to lymph nodes already metastasized, the adjuvant chemotherapy proved to be not effective.

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FOLLOW-UP STUDY ON GASTRIC CANCER TREATED WITH MITOMYCIN C PRIOR TO SURGICAL OPERATION

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Because of lack of subjective symptoms the treatment of gastric cancer may often start in its late stage and owing to the characteristics of rapid, disseminating metastases of the cancer cells to lymph nodes and subserosal tissue, the prognosis after the operation is much less favorable than that of cancers of other organs, even though the operation itself is radical and extensive. Actually most of the patients die from remote metastases than from local recurrence. For this reason chemotherapy combined with surgical operation has been increasingly employed to prevent the recurrence. In view of this we used Mitomycin C prior to the surgical operation with the purpose to check the dissemination of cancer cells freed at operation. The results of this study are briefly presented in the following.

MATERIALS AND METHODS

One of the features of the operation for gastric cancer performed in our clinic is to eradicate all the regional lymph nodes lying above the transverse colon as well as those communicating with these nodes. This includes not only the removal of greater omentum but of the anterior leaf of mesocolon, pancreatic capsule, lesser omentum and their adjacent tissues located along hepatic artery and bile duct.

As the antitumor agent, Mitomycin-C, was used in the dose of 10 mg per day for four consecutive days prior to the operation. The cases in which the administration of the agent had to be suspended because of its side-effects were excluded from this statistical study.

FOLLOW-UP STUDY OF PROGNOSIS

During January 1958 to July 1962, 322 patients were submitted to either radical or palliative operation for gastric cancer. These cases were divided at random into two groups; the chemotherapy and the non-chemotherapy groups.

The patients surviving more than five years were subjected to detailed analysis of the severity of cancer; serosal involvement, lymph-node metastasis, etc., by macroscopic and microscopic examinations.

Overall results are illustrated in Fig. 1. In those patients to whom radical operation with chemotherapy was performed, three-year survival rate proved to be 43 per cent (48 out of 111 cases) and five-year survival, 35 per cent (17 out of 47). This result is noteworthy in contrast to the result of patients receiving radical operation without chemotherapy in that 40 per cent of the patients (23 out of 57) survived three years and 26 per cent (7 out of 27) five years post-operatively. In those patients undergoing palliative operation combined with prior chemotherapy, only one of 62 patients survived three years after the operation, and none survived for five years. On the contrary, the excellent results were obtained in the patients undergoing palliative operation without chemotherapy; 12 per cent (5 out of 43) survived three years and 4 per cent (1 out of 26) five years.

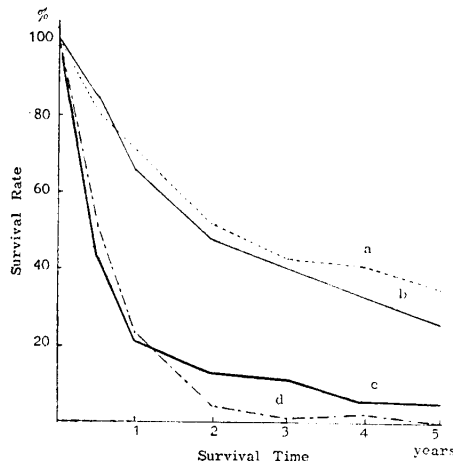


Fig. 1 Survival curve of surgical adjuvant chemotherapy for gastric cancer
 a: Radical operation + chemotherapy, b: Radical operation, c: Palliative resection, d: Palliative resection + chemotherapy

Of the patients in Stage I on which no macroscopic metastases nor infiltration was observed in liver, peritoneum, lymph nodes or serosal membrane, there was no death from recurrent cancer within five years after the operation in both the chemotherapy and non-chemotherapy groups. Of the patients in Stage II, showing no peritoneal dissemination nor liver metastasis by having slight metastasis in the primary and secondary lymph nodes and serosal infiltration, the five-year survival was better for the chemotherapy group than for the non-chemotherapy one; 27 per cent (3 out of 11) and 14 per cent (1 out of 7),

respectively. In Stage III with severe serosal invasion and metastases to the third group of lymph nodes, 38 per cent (13 out of 34) of patients with chemotherapy survived five years after the operation, but the five-year survival rate declined to 13 per cent (2 out of 16) in the non-chemotherapy group.

In the cases without serosal involvement, the five-year survival was 42 per cent (5 out of 12) in the chemotherapy group and this is slightly worse than in the non-chemotherapy group of 60 per cent. In the chemotherapy group the five-year survival was 47 per cent (6 out of 13) in the cases with a slight serosal involvement, and 29 per cent (6 out of 21) in the cases with severe serosal invasion. In contrast, in the non-chemotherapy group with slight serosal involvement none survived five years while those with severe serosal involvement 11 per cent did survive five years.

In those without lymph-node metastasis, long-term prognosis was a little better in the non-chemotherapy group than in the chemotherapy group. On the other hand, chemotherapy contributes significantly to the five-year survival in those with metastasis to the primary and tertiary nodes.

On the localized type of Borrmann, 10 out of 20 cases (50%) with chemotherapy survived more than five years while 4 out of 10 cases without chemotherapy. In the infiltrating type of Borrmann, the five-year survival was 24 per cent (7 out of 27) in the chemotherapy group, and 18 per cent (3 out of 17) in the non-chemotherapy. Chemotherapy seems to have improved the survival rate in both types, especially in the latter.

The five-year survival was 38 per cent of those with adenocarcinoma and 29 per cent of these with carcinoma solidum simplex in the chemotherapy group, which is significantly better than that in the non-chemotherapy group of 19 per cent and of 14 per cent respectively.

DISCUSSION

The objective of the chemotherapy adjuvant to surgery is to improve the therapeutic effects in combination with radical operation. MARTIN⁴ emphasized that for human cancer the anticancer agent is only significant as an adjuvant therapy and stated that cancer cells freed during surgical procedure are the most suitable target of chemotherapy. The clinical evaluation of chemotherapeutic effects is usually difficult. MOORE⁵ suggested that a long-term follow-up of five and ten years must be obtained before any conclusive statement can be made. The effect of chemotherapy must be evaluated not on the basis of transient improvement or symptomatic remission, but on the basis of follow-up study. It must be postulated that the follow-up should include patients treated during an identical period with and without chemotherapy.

Under such conditions, MOORE⁵ concluded that chemotherapy did not produce a significant difference in the four-year survival rate. In our series, chemotherapy as an adjuvant to radical surgery indicated better prognosis than when an anticancer drug was not used. The present results suggest that the anticancer drug inhibits free cancer cells to disseminate and metastasize, when the main tumor tissues are removed by radical surgery.

In those patients undergoing palliative surgery, better prognosis is obtained by surgical operation alone than by operation with chemotherapy. This result is in agreement with that of OHARA⁶ who suggested that chemotherapy may be insignificant to surgically inoperable cancer of the stomach. This may be due to the adverse effect of anticancer agent but further study seems to be necessary. In relation to the advancement of the grade of cancer, adjuvant chemotherapy did not produce any better results in those patients in Stage I than radical surgery alone. For patients in more advanced Stages II and III, chemotherapy significantly improved the long-term prognosis. This agreed with the experimental observation⁷ using MH-134 ascitic hepatoma with Nitromin that surgical adjuvant chemotherapy produced more significant effect on advanced cancer.

When the cancer had invaded the serosa, prognosis of the patients without chemotherapy is much worse than those with chemotherapy. The risk of polluting the operative field by cancer cells abraded during the surgical procedure had been suggested^{1,2,8}. Chemotherapy may prevent the dissemination of exfoliated cancer cells.

Cases with lymph-node metastasis are not influenced by chemotherapy. This may be due to adequate lymph-node extirpation performed during operation on the cases which was reported in this study, while the effect of an anticancer agent on metastasized lymph nodes, especially on microsolitary metastatic focus was previously reported by the present author³. It is generally believed that an antitumor agent can be effective on such a small metastatic focus but not on extended metastases. It is assumed that chemotherapy without surgical removal of lymph nodes shows no clinical result.

Chemotherapy appears to be more effective to the cancer of infiltrating type than to localized type. This may be explained similarly to its effect on cases with serosal involvement.

In summary, adjuvant chemotherapy appears to be effective to prevent the contamination of the operative field by exfoliating cancer cells freed during surgery. Some limitation of anticancer therapy is noted to lymph nodes already metastasized.

Adjuvant chemotherapy obtained better prognosis irrespective of the histological type of the cancer. So far chemotherapy appears to improve the prognosis

when used in combination with radical surgery for cancer, and further study is necessary to evaluate the methods of administration of the anticancer agent.

CONCLUSION

With the purpose to prevent the dissemination and consequent metastasis of cancer cells at the time of operation we gave 10 mg of Mitomycin C per day for four consecutive days prior to surgical operation of gastric cancer (total of 322 patients), and this so-called adjuvant chemotherapy proved to be effective on the cases with serosal involvement and infiltrating type of cancer, irrespective of histological types. It also gave five-year survival rate of 35 per cent. However, to lymph nodes already metastasized, the adjuvant chemotherapy proved to be not effective.

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REFERENCES

1. FORTHER, J.G. *et al.*: *Ann. Surg.* 132, 789, 1960
2. HARRIS, A.H.: *ibid.* 151, 330, 1960
3. JINNAI, D. *et al.*: *Gann no Rinsho* 8, 533, 1162
4. MARTIN, D.S.: *Am. J. Surh.* 94, 685, 1959
5. MOORE, G.E. *et al.*: *Ann. Rev. Med.* 14, 141, 1963
6. OHARA, T. *et al.*: *Gann no Rinsho* 3, 554, 1957
7. SAKAKIBARA, N.: *Okayama Igakkai Zasshi* 73, 475, 1961 (in Japanese)
8. THOMAS, G.G.: *Ann Surg.* 153, 697, 1961