Special article

Thirty-four-year experience of immunochemosurgery for gastric cancer in 14033 cases

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First of all, I, the third president of the International Gastric Cancer Association, would like to offer sincere congratulations on the 10th anniversary of the Association. In this special congratulatory issue of *Gastric Cancer*, I would like to present a summary of my lifelong study of gastric cancer surgery in 14033 cases from 1971 to 2004 [1]. I will continue my study on gastric cancer up to 15000 cases, then will retire, probably in 2007. I

also hope that the Jin-Pok Kim lecture at the biennial congress will continue forever, and I will continuously support it.

Introduction

Gastric cancer is the second most common cancer in the world after lung cancer, and is still the most common cancer in developing countries; it is the number one cause of cancer death in Korea. The outcomes of gastric cancer treatment have markedly improved as a result of early detection and radical surgery. Until now the only potentially curative treatment modality of gastric cancer has been radical surgery. As yet, the majority of gastric cancer patients are first diagnosed in the advanced stage, and even with grossly curative surgery, recurrences do occur in about 60% of patients within 2 to 3 years after surgery. Therefore, to improve the prognosis of advanced gastric cancer, systemic treatment such as chemotherapy and immunotherapy to kill the micrometastatic or remaining cancer cells after curative resection is required. There are many controversies about the role of adjuvant therapy, however.

Immunochemosurgery

I have already reported the effectiveness of early post-operative immunochemotherapy in the first randomized trial in 1983. Then to compare the effectiveness of immunochemosurgery, surgery plus chemotherapy, and surgery alone, a second randomized trial was also carried out and reported. The 5-year survival rate of the immunochemosurgery group was 45.3%, that of the surgery plus chemotherapy group was 29.8%, and the surgery alone group was 24.4%. The difference between the immunochemosurgery group and the other two groups was statistically significant. The postopera-

tive T-cell percentage was increased in the immunochemosurgery group after immunochemotherapy, but was decreased in both the postoperative chemotherapy and surgery alone groups. Other immune status data also showed improved reactivity in the immunochemotherapy group. The superior effectiveness of immunochemosurgery over postoperative chemotherapy or surgery alone was also proved by retrospective study.

Prognostic factors

The clinicopathologic characteristics were analyzed for 14033 consecutive patients who underwent operation for gastric cancer from 1970 to 2004. We also evaluated the survival and prognostic factors for 9262 consecutive patients from 1981 to 1996. The prognostic significance of treatment modality was evaluated in stage III gastric cancer. The incidences of these cases in accordance with UICC TNM classification were 19.2% for stage Ia, 11.9% for stage Ib, 13.6% for stage II, 17.7% for stage IIIa, 22.3% for stage IIIb, and 15.2% for stage IV. The 5-year survival rates according to TNM stage were 92.9% for Ia, 84.2% for Ib, 69.3% for II, 45.8% for IIIa, 29.6% for IIIb, and 9.2% for IV. Regarding adjuvant treatment modality, significant survival difference was observed in stage III patients. The 5-year survival rates were 44.8% for the immunochemosurgery group, 36.8% for the surgery plus chemotherapy group, and 27.2% for the surgery alone group. Curative resection, depth of invasion, and lymph node metastasis were the most significant prognostic factors in gastric cancer. With regard to the status of lymph node metastasis, the

ratio of involved lymph nodes to resected lymph nodes has a more precise and comprehensive prognostic value. Our recent study on long-term survival patients also showed that the ratio of involved lymph nodes to resected lymph nodes has a precise and comprehensive prognostic value even in patients with far-advanced disease. Besides clinical and pathologic prognostic factors in gastric cancer, recent biological molecular level studies on new prognostic factors showed some significant results and now are being extensively investigated for further evaluation. Those are growth factors and receptors (EGF and receptors, TGF- β 1 receptor, etc.); oncogenes, and suppressor genes (*c-erbB2*, *ras*, *HST-1*, *K-sam*, *c-met*, *p53*, *DCC*, *Rb P21*, *nm23*, etc.); cell adhesion molecules (integrins, cadherin, immunoglobulin superfamily, CD44); chromosome deletion of 1q, 5q, 7p, 17p; and TIMP, MMPs, uPA, microsatellite instability, and so on. We are also investigating some of these factors and expect to find new prognostic factors.

Conclusion

Early detection and curative resection with radical lymph node dissection followed by immunochemotherapy, especially in patients with stage III gastric cancer, should be recommended as a standard treatment principle for patients with gastric cancer.

References

1. Kim JP, Lee JH, Kim SJ, Yu HJ, Yang HK. Clinicopathologic characteristics and prognostic factors in 10783 patients with gastric cancer. *Gastric Cancer* 1998;2:125–133.