Radiation Therapy in Malignant Tumors of the Parotid Gland

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From 1970 to 1982, thirty one patients with malignant tumors of the parotid gland were treated with radiation therapy at department of Radiation Oncology, Yonsei University College of Medicine, Yonsei Cancer Center. Indication for radiotherapy were as follows: 1) when there were microscopic or gross residual diseases (6 patients), 2) when the patients considered to have high risk factors (15 patients), 3) when the tumor found to be inoperable (6 patients), 4) when there was recurrence after surgery (4 patients). Most patients were treated with a total of 5,000 to 6,500 cGy in 5 to 6 weeks except when there were gross diseases, in which patients received slightly higher dose up to 7,000 cGy in 7 weeks. Locoregional failure rate was 43% in patients with microscopic or gross residual disease and high risk factors (postoperative radiotherapy group) and 20% in patients with inoperable tumor and recurrence after surgery (primary radiotherapy group). There was no difference in the failure rates among the various histological types. Eight patients failed distantly. Severe complications appeared only in 2 patients irradiated for inoperable advanced diseases.

Key words: Parotid cancer, Radiation therapy.

INTRODUCTION

Surgery is an essential part of treatment for most malignant tumors of the parotid. Local recurrences following surgery remain frequently, particularly in patients with unfavorable prognostic signs such as high histologic grade, those in whom known microscopic disease was left at or near the surgical margin, or the presence of lymph node metatasis.[5] Even the most extensive radical surgery yield high local recurrence rates in patients with the poor prognostic variables.[4, 12, 13, 15, 22, 26, 30]

In spite of high local recurrence rate following surgical treatment of malignant parotid tumors, postoperative irradiation was not used because these tumors were once thought to be radioresistant.[8] Recently have data supporting improved local control rate with the use of postoperative radiotherapy begun to appear in many literatures. And there are increasing evidences in the literature supporting the necessity of adjuvant radiotherapy.[5, 9, 10, 11, 14, 17, 23, 28] Radiotherapy, therefore, might have a very definite role in the management of parotid tumor and the combined use of surgery and radiotherapy could prove to be the optimum treatment policy.

The purpose of present study is to evaluate the results in patients who received radiotherapy at the department of Radiation Oncology, Yonsei University College of Medicine, Yonsei Cancer Center and

to attempt to formulate guidelines for the management of parotid tumors.

MATERIALS AND METHODS

From January, 1970 to December, 1982, thirty one patients with malignant parotid tumors were treated with radiotherapy at the department of Radiation Oncology, Yonsei Cancer Center.

The chart review took place in September, 1985.

Of the thirty one patients seen at our institution, 13 underwent either surgical resection or biopsy only at another hospital and were referred to our department. Remaining 18 patients underwent surgery at our institution.

Of 31 patients twenty three patients were followed 1 to 5 years, five patients were followed 5 to 10 years, and three patients were followed more than 10 years.

The median age was 55 years with a range of 25 to 74 years. There were 5 females and 26 males.

Disease was retrospectively restaged based on AJC staging system as shown in table 1. Five were stage I, five, stage II, nine, stage III, ten, stage IV, and two, unknown stage.

Distribution of various histological types is shown in table 2. The common types were mucoepidermoid carcinoma, adenocarcinoma, and adenoid cystic carcinoma.

Postoperative radiotherapy was administered when there were gross and microscopic residual diseases left behind after surgery (6 patients) and when there were high risk factors such as cervical lymph node met-astasis, high grade histology, facial nerve involvement, and close surgical margin (15 patients) in 21 patients (postoperative radiotherapy group). Radiotherapy alone was used in 10 patients because of either inoperable stage (6 patients), or recurrence (4 patients).

In postoperative radiotherapy group (21 patients), fice in 10 patients (Table 3). Radical neck dissection patients and for recurrent tumor in 15 patients. Surgery consisted of wide excision in 5 patients, subtotal parotidectomy sparing facial nerve in 4 patients, total parotidectomy sparing facial nerve in 2 patients, and total parotidectomy with nerve sacrifice in 10 patients(Table 3). Radical neck dissection was performed in three of seven patients who presented with cervical lymph node metastasis at the time of initial presentation.

Radiotherpy was administered employing Co-60 wedge pair technique or mixed beam with 10 or 12 MeV electron and Co-60 photon in an attempt to concentrate the dose on the ipsilateral side and

Table 1. Distribution of Patients by TNM Stage (AJCC)

	Tx	T1	T2	T3	T4a	T4b
NO	1	1	4	5	1	7
N1	1	0	1	2	0	8*

* Included one case of M1

Table 2. Histologic Types (1970-1982, YCC)

Histology	No. of patients
Acinic cell	1
Mucoepidermoid	8
Low Grade	3
High Grade	3
Unknown	2
Adenocarcinoma	6
Malignant mixed	3
Adenoid cystic	5
Squamous cell	5
Undifferentiated	3
Total	31

Table 3. Types of Operation for Primary Lesion (Postopeerative Radiotherapy Group)

Type of operation for primary lesion	No. of pts
Wide excision	5
Subtotal parotidectomy sparing facial nerve	4
Total, parotidectomy sparing facial nerve	2
Total parotidectomy with nerve sacrifice	10

Table 4. Pattern of Failures

Treatment	No. of pt.	Persistence after Tx.	Local recurrence	Distant metastasis
Postop. RT Group	21	3	9	7
Primary RT Group	10	8	0	1
Total	31	11	9	8

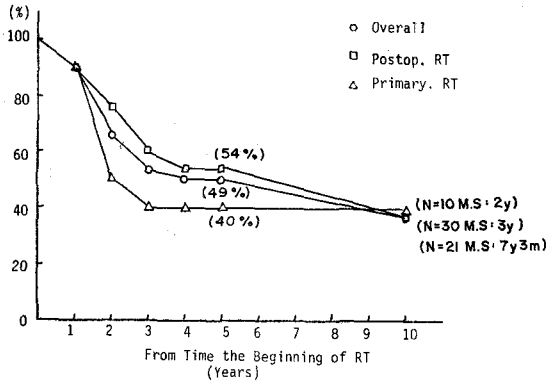

Fig. 1. Actuarial survival curve.

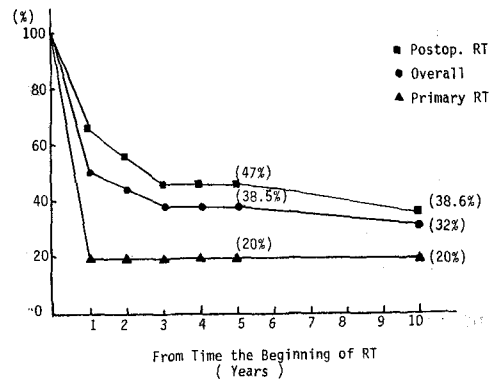

Fig. 2. Actuarial disease free survival curve.

Table 5. Pattern of Loco-regional Failures

Treatment	Failure	Salvage (OP. or RT)	Control	Ultimate failure (%)
Postop. RT (21)	12	5 (OP. 1, RT4)	0	12/21 (57%)
Primary RT (10)	8	2 (OP. 1, RT1)	1	7/10 (70%)
Overall (31)	20	7	1	19/31 (61%)

sparing the opposite salivary gland. Total doses ranged from 2,600 to 7,000 cGy. Twenty nine of thirty one patients received a total of 5,000 cGy or more.

The main bulk of the gross tumor bearing tissue received a significantly higher dose up to 7,000 cGy. Radiation was delivered at 180-200 cGy per fraction, five times per week. The neck node were treated with Co-60 using an anterior single field. The total doses to the neck node ranged from 4,000 cGy in 4 weeks to 6,000 cGy in 6 weeks. The ipsilateral lower neck was treated in 14 patients with cervical lymph nodes and 4 patients with negative neck nodes.

RESULTS

The 5 year actuarial survival and 5 year actuarial disease free survival for overall was 49% and 38.5%, respectively. For postoperative radiotherapy group, the 5 year actuarial survival and 5 year actuarial disease free survival was 54% and 47%, respectively, and for primary radiotherapy group, 40% and 20%, respectively.

Table 4 shows the pattern of failures.

Of thirty one patients irradiated for malignant parotid tumors, locoregional failure occurred in 20 patients and distant metastasis developed in 8 patients.

Table 5 shows the pattern of locoregional failure in postoperative radiotherapy group and primary radiotherapy group. The locol control rate for radiotherapy was 43% in postoperative radiotherapy group and 20% in primary radiotherapy group.

Of twenty one patients who received postoperative radiotherapy, locoregional failures developed in 12 patients; three at primary site, six at cervical lymph node, another three at both sites. Of six patients showed primary site failure, two were infield failures and other four patients had marginal failures. All primary failures were in advanced stage (stage III or IV) except one (stage II). Neck node failures noted in 9 patients. Three patients of them had cervical lymph node metastasis at the time of diagnosis and they received irradiation to ipsilateral lower neck. The remaining six patients who did not have cervical lymph node metastasis at the time of diagnosis did not receive prophylactic low neck irradiation except only one who received 3,000 cGy. All the neck node failures were found in either margin or outside of the field of radiotherapy.

Table 6 demonstrates failures according the histological types and there was no relationship between them.

The incidence of locoregional failure according to

the stage is shown in table 7. There was no significant difference in postoperative radiotherapy group.

Of ten patients with primary radiotherapy group, inoperable cases were six. Five of them showed partial or minimal responses and expired within 10 months to 24 months of completing treatment. The remaining one had complete response at the primary site and minimal response at neck node (Only 2,500 cGy to neck nodes was given in this patient). This patient survived with the disease for 6 year and 6 months. The follow up was lost afterwards in this patient. Of four patients with gross recurrence after surgery, two patients had complete response at the primary site as well as neck nodes. One had minimal response at the primary site and died at 3 years following treatment. And another one had no response at the primary site and local control was ultimately achieved by excion.

Distant metastsis occurred in eight patients mostly in the lung, bone and brain. Seven patients of them were postoperative radiotherapy group and one was primary radiotherapy group (Table 8). Five of eight patients with distant metastasis had persistant local and/or regional diseases. All the patients with distant metastasis expired within ten months to six years and five months of completing treatment.

All the patients developed acute skin or mucosal reactions. Long-term minor complications are listed in table 9. In two patients who developed major long-term complications such as trismus and serous otitis with hearing difficulty, the diseases were locally far advanced and inoperable.

DISCUSSION

Malignant tumor of the parotid gland is rare, presenting less than 0.3% of all malignancies.[27] The average age is 55 years with a peak incidence in the six decade.[5, 18] The sex incidence is about equal in most series. In our study, median age was 55 years. Nineteen patients (63%) were 6th and 7th decades. Twenty six were males and five were females: male to female ratio was 5:1.

Proper performance of surgery of the parotid gland requires a therough understanding of the anatomy and its variations. The intimate relationship between the facial nerve and its branches and the parotid gland makes difficult adequate resection of the gland with preservation of the nerve.[6, 11, 20, 21, 29]

The anatomical concept of the facial nerve sandwiched between two lobes forms the basis for the

Table 6. Local-regional Failure by Histological Type

Histology	No. of fail./No. of pt.
Acinic cell	1/1
Mucoepidermoid	4/8
Low Grade	1/3
High grade	2/3
Unkown grade	1/2
Adenocarcinoma	5/6
Malignant mixed	2/3
Adenoid cystic	2/5
Squamous cell	4/5
Undifferentiated	2/3
Total	20/31

Table 7. Loco-regional Failure Rate by Stage (Postoperative Radiotherapy Group)

Stage (No. of Patients)	No. of Failures
I (2)	2
II (4)	1
III (8)	5
IV (5)	3
Unknown (2)	0

Table 8. Distant Metastasis

Treatment	Time (M)	Histology	Site of Failure	Locoregional Failure	Follow up
Primary RT	0	Adenocarcinoma	C-Spine	Yes	Dead 10M
Postop. RT	1	Epidermoid	Brain	No	Dead 1Y11M
	12	Adenoid Cystic	C-Spine & Lung	No	Dead 6Y5M
	13	Malignant Mixed	Axillary L/N	Yes	Dead 2Y6M
	13	Undifferentiated	Lung	Yes	Dead 1Y1M
	16	Adenocarcinoma	Brain	Yes	Dead 1Y4M
	20	Adenocarcinoma	Brain	No	Dead 2Y1M
	39	Acinic Cell	Lung	Yes	Dead 3Y4M

Table 9. Minor Radiation Complications

Complication	No. of Patients
Xerostomia	9
Trismus	4
Serous otitis	6
Hearing difficulty	1
Dental caries	1
Others	4

* One patient may have several complications.

operative procedures, subtotal superficial parotidectomy and total parotidectomy. The malignant neoplasms infiltrate the parotid gland, invade the facial nerve or the auriculotemporal nerve, and spread along nerve sheaths. Tumor may invade the adjacent skin, muscle, and bone, depanding on the site of origin. Adenoid cystic carcinoma, in particular, infiltrates widely all adjacent tissues without respect for anatomical planes.[3, 25]

Surgical resection is the main stay of treatment for major salivary gland. However, radical surgery, which is limited by the proximity of vital structures dose not prevent high local recurrent rates.[1, 4, 7, 13, 15, 22] Hodgkinson showed a 38% local recurrent rate at 5 years occurred despite aggressive surgery that included the sacrifice of the facial nerve in 64% of the patients.[12] Woods et al. showed a 28% recurrent rate for radical surgical procedures in management of aggressive parotid tumors.[30] Spiro et al. reported a local recurrent rate of 58% for more advanced lesions (stage III by Spiro staging system) in their series.[26]

No evidence was seen to suggest that more radical surgery would have produced better results.[9, 26] On the other hand, postoperative radiotherapy appeared to improve the local control rate.[7, 9, 11, 14, 23, 28] King and Fletcher reviewed 93 cases of parotid tumors of which 46 received postoperative radiotherapy either electively or because of microscopic residual left at the time of surgery.[16] Employing doses of 6,000 cGy, they were able to obtain local control in 93.5% of the irradiated cases. FU et al. stated that the incidence of local recurrence was 14% for patients who received a adjuvant radiotherapy as compared with 54% who were treated by surgery alone.[9] McNaney reported 87% in locoregional control with postoperative radiotherapy.[17]

In our study, the locoregional control rate were only 43% in postoperative radiotherapy group. Significant number of our patients were referred from various outside hospital and received inappropriate treatment such as unnecessary biopsies or inadequate surgery prior to referral which might result in contaminating tumor cell to surrounding structures. This might be the main factor contributing to poor clinical result as compare to other reports. According to the results of our study, cancer surgery performed by skillful and well experienced surgical team who has sound knowledge on anatomy is essential for malignant parotid tumor. High grade malignancy should be managed with total parotidectomy and postoperative radiotherapy. Subtotal parotidectomy can be a adequate treatment for lower to moderate grade malignancy. Postoperative irradiation may be used in the case of close or positive margins, invasion of extraparotid tissues, tumor involving the deep lobe, recurrent tumors, regional node metastasis, and microscopic and gross residual tumor.

All the patients with the primary site failures were in advanced stage except one and estimation of the irradiation field were too narrow in all of them. Eight of fourteen patients who had neck node failures did not received the lower neck irradiation. Neck failures were probably a result of lack of elective irradiation of the lower neck. Our result, therefore, suggest that the margin of radiation field should be generous, the minimum treatment volume includes the parotid bed and upper neck nodes, and ipsilateral lower neck is electively irradiated for high grade lesions or for clinically positive nodes. Since there was enough evidences that contralateral neck node metastasis is very rare, we did not treat opposite site of the neck. The tumor dose to the primary area was 5,000 cGy in 5 weeks or 6,000 cGy in 6 weeks if there is microscopic residual disease and higher doses for gross disease.

Radiotherapy seems to be effective in all histological types.[9, 16] Our results as well as those of Fu et al, King and Fletcher, and McNaney however do not suggest any significant difference in radiation response among the different histological types of malignant parotid tumors.

Spiro et al found close correlation between stage of disease at initial presentation and prognosis in 288 patients with previously untreated cancer of the parotid gland with local control rates of 93% for stage I, 78% stage II, and 42% for stage III. Fu et al in view of 61 patients reported 100% local control for stage I and II and 75% for stage III.[26] They also showed that initial stage rather than extent of surgery was the most important factor in local con-

trol. Our results do not support the prognostic value of staging system probably because the number of study group is small and most patients were advanced disease.

The local control rate for patients with radiotherapy alone was 20% in our study and this figure was very much compatible to Fu's study, although there has been a report as high as 81% by King and Fletcher.[9, 16]

Distant metastasis was the major cause of failure, alone or in associated with active disease above clavicle in the series reported by King and Fletcher, and Hollander and Cunningham.[13, 16] Fu et al suggest that distant metastasis correlated to the amount of residual disease and structures invaded by tumor and frequently associated with locoregional failures.[16] The major metastatic site: lung, brain, and bone were same in our study and others (Table 8).[9, 14]

Some authors suggest that surgery and radiotherapy are limited only to local and regional disease, further improvement in survival will probably be dependent upon adjuvant systemic forms of therapy using chemotherapy and/or immunotherapy.[9]

Complication of radiotherapy could have been minimized by better oral hygiene and prophylactic dental care. Improved radiotherapy techniques using a combination of high energy photons and electrons or Co-wedge pair technique would also have helped.

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=국문초록=

이하선암의 방사선 치료

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박 정 수 · 민 진 식

이하선 악성종양의 치료는 근치적 수술이 주된 치료법으로 알려져 왔으나 이하선이 해부학적으로 주위의 근육, 골조직, 혈관, 신경등과 밀접하게 부착되어 있어 피막 및 주위 조직의 침윤이 있거나 조직학적으로 high grade tumor, 임파절 전이가 있는 경우등에서 광범위한 근치적 수술로도 종양을 완전히 제거하기가 어렵고 수술후 국소재발이 빈번한 것으로 알려져 있다. 수술만으로는 국소재발율이 상당히 높은 데도 불구하고 이 종양이 방사선치료에 반응하지 않는 것으로 잘못 인식되어져 와서 수술후 방사선치료를 시행해 오지 않다가 근래에 와서 수술후 방사선치료가 실시되었고 수술만 시행한 경우에서보다 국소재발율이 현저히 감소한 것으로 보고되고 있어 현재는 방사선치료가 치료결과를 향상시키는 중요한 치료방법으로 인식되고 있다.

이에 저자들은 1970년 1월부터 1982년 12월사이 연세대학교 의과대학 연세암센터, 치료방사선과에서 이하선암으로 치료를 받은 31예를 대상으로 후향적 추적조사를 통하여 치료방법과 치료실패 양상을 분석하여 향후 치료방법의 설정과 치료 결과의 향상을 위하여 본 연구를 실시하였다.