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The Efficacy of Radiation Therapy in the Treatment of Pituitary Adenoma

Heung Lae Cho, M.D., Kwang Mo Yang, M.D.
Seung Chang Shon, M.D. and Hyun Suk Suh, M.D.

Department of Radiation Therapy, Inje University, Seoul Korea Seoul and Pusan Paik Hospital

Between 1984 and 1989, 22 patients with pituitary adenomas were treated with radiation therapy. The tumor was controlled in 18 of 22 (81.8%) patients for an observed period of II to 98 months. Eleven of 12 (92%) patients with visual field defect experienced normalization or improvement, and 3 of 5 evaluable patients with hyperprolactinemia achieved normalization in one and decrement in two patients. We concluded that: (a) postoperative radiotherapy is clearly effective in the controlling of clinical symptoms and signs resulting from pituitary adenoma: (b) In the macroadenoma, the difference of control rate between suprasellar, <2 cm. and suprasellar,> 2 cm. was not significant.

Key Words: Pituitary adenoma, Radiotherapy

INTRODUCTION

Pituitary adenomas represent approximately 10% of all intracranial tumors. Pituitary adenomas represent pathologically benign tumors but because of their tendency to invade adjacent structures and to cause hormonal imbalance, their growth can result in multiple medical problems and even death.

Transphenoidal surgery is generally regarded as the primary modality of therapy for pituitary macroadenomas. Radiation therapy has been used as an adjunct to decrease the recurrence rate from up to 86% to 10~25%[1~3].

This report details the result of treatment on 22 patients treated by a surgery and radiotherapy or radiotherapy alone as measured by visual improvement, response of hyperprolactinemia, and the improvement of galactorrhea-amenorrhea.

METHODS AND MATERIALS

1. Patient Charateristics

Between May 1984 and March 1989, 22 patients with pituitary adenomas were treated at the Department of Radiation Therapy at Pusan and Seoul Paik Hospital. There were 13 males and 9 females. The median age at initial presentation was 32 years old. Of the 22 patients, 17 patients (77%) were hormone producing pituitary adenonmas and 5 patients (23%) were nonfunctioning pituitary adenomas (Table 1). Presenting signs and symptoms are summarized in table 2. Thirteen patients had visual problems. Visual field defet were found in twelve patients, decreased visual acuity in ten and diplopia in two (Table 3).

Table 1. Patient Characteristics

Age	
median	32 years
range	13 – 63 years
Sex	
male	13 (59%)
female	9 (41%)
Functioning tumor	17 (77%)
PRL secreting	9 (53%)
GH secreting	6 (35%)
ACTH secreting	2 (12%)
Nonfunctioning tumor	5 (23%)

Table 2. Signs and Symptoms at Presentation

Headache	13
Visual field defect	12
Decreased visual acuity	11
Acromegaly	5
Galactorrhea / amenorrhea	4
Amenorrhea	3
Oligomenorrhea	2
Cranial nerve palsy	2
Cushing's syndrome	2

Table 3. Incidence of Visual Disturbance

Tumor size	Number of patients	↓VA	VFD
Microadenoma	4	0/4	0/4
Macroadenoma			
suprasellar < 2cm	7	2/7*	4/7**
suprasellar > 2cm	11	9/11*	8/11**
Total	22	11/22	12/22

↓VA denotes decreased visual acuity
VFD denotes visual field defect
* $P < 0.05$ ** $P > 0.5$

Table 4. Surgery

Method	Macroadenoma	
	Suprasellar < 2cm	Suprasellar > 2cm
TSA	5	2
F.C	1	8

TSA denotes Transphenoidal adenectomy
F.C denotes Frontal Craniotomy

2. Tumor Characteristics

To compare the difference of control rate between microadenomas and macroadenomas we classified the tumors into microadenomas with tumor sizes less than one centimeter or macroadenomas with sizes greater than one centimeter. The latter group was subdivided into (a) tumors with suprasellar extension of less than 2 cm, and (b) those with suprasellar extension of greater than 2 cm. Measurement of tumor extent was determined by the CT scan.

3. Treatment

Of the 22 patients, 15 patients received surgery and irradiation, 6 patients reveived radiation alone, and one patient was treated with radiation therapy for salvage treatment after surgical failure. Of the 16 patients in the postoperative group, 9 patients had transfrontal craniotomy and7 had transphenoidal adenomectomy (Table 4). Radiotherapy was given using CO-60 in 9, 4 MV Linear accelerator in 13. 16 patients received radiotherapy using one anterior and two lateral fields. Parallel opposed fields with paired 30 degree wedge. Parallel opposed fields were used in 6 patients. Tumor dose ranged from 5000 to 5580 cGy in 5.5~6 weeks. Field sizes were determined according to tumor volume as assessed by CT scan, ranging from 4×4 cm to 7×7 cm. The daily fraction sizes were 180~200 cGy with five fractions per week.

Table 5. Improvement of Vision

Tumor size	VA	VFD
Microadenoma	0/0	0/0
Macroadenoma		
suprasellar < 2cm	2/2	4/4
suprasellar > 2cm	8/9	7/8
Total	10/11 (91%)	11/12 (92%)

VA ; Visual Acuity
VFD ; Visual Field Defect

Table 6. Decrease of Hormone Level in Seven Evaluable Patients

Tumor size	PRL	GH	ACTH
Microadenoma	0/1	1/1	
Macroadenoma			
suprasellar < 2cm	2/2		1/1
suprasellar > 2cm	1/2		
Total	3/5 (60%)	1/1 (100%)	1/1 (100%)

PRL = prolactin
GH = growth Hormon
ACTH = adrenocorticotropic Hormon

Table 7. Improvement of Galactonnea/Amenorrhea Syndome

Tumor size	G	A	O
Microadenoma	0/0	1/2	0/0
Macroadenoma			
suprasellar < 2cm	2/3	0/2	2/2
suprasellar > 2cm	1/1	1/1	0/0
Total	3/4 (75%)	2/5 (40%)	2/2 (100%)

G denotes galactorrhea
A denotes amenorrhea
O denotes oligomenorrhea

4. Follow Up

Follow up was obtained from radiotherapy records, hospital charts, interviewing by telephone. Mean follow up time was 43.6 months (ranges from 11 to 98 months).

Tumor was considered "locally controlled" by one or more of the following criteria: (a) remission of clinical signs and symptoms, (b) decrease of hormone levels, and/or (c) stabilizaton or regression of tumor. Patients were considered to have tumor progression by one or more of the following criteria: (a) worsening of clinical signs and symptoms (b) rising hormone levels and/or (c) increasing tumor size by radiographic examination.

RESULTS

1. Tumor Control

Eighteen patients (81.8%) are free of tumor related symptoms with local control of disease (Table 8) Four (18.2%) tumors recurred with a mean time to recurrence of 22 months. Of these 4 tumors, 2 were classified as suprasellar extension,> 2 cm., 1 was suprasellar extension,<2 cm., remained 1 was microadenoma.

Salvage treatment consisted of radiotherapy was done in 1 patient who showed progress of symptoms after surgery alone. Remained 3 patients with tumor progression were received no salvage treatment. Overall of the control rate was 81.8% (18/22).

2. Visual Response

Ten of 11 (91%) patients with decreased visual acuity experienced improvement of visual acuity after therapy. Eleven of 12 (92%) patients with visual field defect experienced improvement of visual field after therapy (Table 5). Two patients had 3rd and 6th cranial nerve palsies. Both of the two patients were corrected without recurrence (Table 5).

2. Hyperprolactinemia

Nine patients had hyperprolactinemia. Patients who did not have both pre- and post-treatment prolactin determinations are excluded from this analysis. Five of 9 patients could be evaluable. Prolactin returned to normal level in one patient with resumption of menstruation who received radiotherapy alone. Follow up period of this patient was 66 months. Two patient achieved decreased level of prolactin when compared pretreatment prolactin level. One patient had a relapse of hyperprolactinemia after 10 months of radiotherapy (Table 6).

Menstrual disturbance was present in seven of 9 (78%) women with pituitary adenomas. In 57% of women with amenorrhea, the galacgtorrhea was noticed simultaneously. Galactorrhea was ceased in three of 4 patients. Amenorrhea was resolved in two of 5 patients and oligomenorrhea resolved in two of 2 patients (Table 7).

DISCUSSION

Recurrence rate with surgery alone has been shown in several studies as 50~60 percent[4], whereas for those treated with surgery and postoperative irradiation, the recurrence rate decrease to 10 ~20 percent. Ciric reviewed 108 pituitary adenomas treated by transphenoidal adenomectomy with and without postoperative irradiation and noted the close relationship between the residual tumor after surgery and the chance of recurrence[4].

In our study, local control rate of microadenomas was 3/4 (75%). This control rate was

Table 8. Tumor Control Rate

Tumor size	Number of patients	Tumor control	Tx Method		Control rate
			RT	S+RT	
Microadenoma	4	3	4		75.0%*
Macroadenoma	18	15	2	16	83.3%
suprasellar < 2cm	7	6	1	6	85.7%*
suprasellar > 2cm	11	9	1	10	81.8%*
Total	22	18	6	16	81.8%

S = Craniotomy or Transphenoidal Adenectomy RT = External Radiotherapy * P > 0.5

lower than that of other studies[5,6], possibly because of small numbers of patients in this group. In the macroadenoma, the control rate of suprasellar, <2 cm. and suprasellar,> 2 cm. was 85 percent and 82 percent respectively with no statistical difference ($p<0.05$). Similar results are well documented by Grigsby[7].

The improvement of visual fields in 92 percent of our patients having postoperative irradiation is comparable to that reported by Rush[6] and Pistenma[2]. Table 3 exhibits the relationship between tumor size and the presence of visual problems. None of the four patients with microadenomas had visual problems. However 50 percent of patients with macroadenomas had decreased visual acuity and 55 percent had visual field defect. Decreased visual acuity in suprasellar, >2 cm. was more frequent than in suprasellar,< 2 cm. with statistical significance ($p<0.05$). On the contrary our data failed to demonstrate a statistically significant difference of visual field defect in these two groups ($p<0.5$). We think that visual field defect can be exist whenever tumor grows above sellar regardless of extent.

Until recently, the role of radiotherapy in decreasing hyperprolactinemia appeared limited to reducing the serum value witout normalization[8]. However Mehta et al[9] reported long course toward normal prolactin values in 6 of 9 patients following radiotherapy. Our study, followed up for 15~66 months, showed decrease of prolactin values in three of 5 evaluable patients with hyperprolactinemia. Surgery lowers prolactin values to normal immeditely in more than 75 to 80 percent of patients with microadenomas and in approximately 30 to 50 percent of patients with macroadenomas[3,10]. On the other hand radiotherapy takes a much longer time to reach full therapeutic effect up to 14 years[9]. In our case, longer follow up time is necessary to evaluate the full therapeutic effect of radiation.

CONCLUSION

1) Postoperative irradiation was clearly effective in the controlling of clinical symptoms and singns resulting from pituitary adenomas.

2) Surgery lowered prolactin values immediately but radiotherapy took a much longer time to reach full therapeutic effect.

3) In the macroadenoma, the difference of control rate between suprasellar, <2 cm. and suprasellar,> 2 cm was not significant.

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국문초록 =

뇌하수체 선종의 방사선치료 효과 및 결과

인제의대 서울·부산백병원 치료방사선과학교실

조홍래 · 양광도 · 손승창 · 서현숙

1984년 부터 1989년까지 뇌하수체 선종환자 22명이 수술 및 방사선 치료를 받았다. 11개월에서 98개월간에 걸친 추적관찰 기간동안 22명중 18명(81.8%)의 환자에서 증상의 호전, 호르몬 감소, 또는 종양크기의 감소를 보였다.

시력감소를 보였던 환자 11명중 10명(91%)이 시력회복을 보였고 시야결손을 보인 12명의 환자에서 11명(92%)의 시야가 회복 또는 정상화 되었다. 이상에서 우리는 다음과 같은 결론을 얻었다. (1) 수술후 뇌하수체선종에 의한 증상 및 징후의 조절에 방사선치료가 유효하다. (2) 거대선종에 있어서 터어키안 위로 2 cm 이상인것과 2 cm 이하인 것의 치료효과에 있어서 통계학적 의의는 없었다.