Radiation Therapy for Pituitary Adenoma#

—Changes in Endocrine Function after Treatment—

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Seventy four patients with pituitary adenoma received radiation therapy (RT) on the pituitary area using 6 MV linear accelerator during the past 7 years at the Division of Radiation Therapy, Kangnam St. Mary's Hospital, Catholic University Medical College.

Thirty nine were men and 35 were women. The age ranged from 7 to 65 years with the mean being 37 years. Sixty five (88%) patients were treated postoperatively and 9 (12%) primary RT.

To evaluate the effects of RT, we analyzed the series of endocrinologic studies with prolactin (PRL), growth hormone (GH), adrenocorticotrophic hormone (ACTH), leuteinizing hormone (LH), follicular stimulating hormone (FSH) and thyroid stimulating hormone (TSH) etc after RT. All but one with Nelson's syndrome showed abnormal neuroradiologic changes in the sella turcica with invasive tumor mass around supra- and/or parasella area.

The patients were classified as 23 (29%) prolactinomas and 20 (26%) growth hormone (GH) secreting tumors, and 6 (8%) ACTH secreting ones consisting of 4 Cushing's disease and 2 Nelson's syndrome. Twentynine (37%) had nonfunctioning tumor and four (5%) of those secreting pituitary tumors were mixed PRL-GH secreting tumors. The hormonal level in 15 (65%) of 23 PRL and 3 (15%) of 20 GH secreting tumors returned to normal by 2 to 3 years after RT, but five PRL and five GH secreting tumors showed high hormonal level requiring bromocriptine medication.

Endocrinologic insufficiency developed by 3 years after RT in 5 of 7 panhypopituitarisms, 4 of seven hypothyroidisms and one of two hypogonadisms, respectively. Fifteen (20%) patients were lost to follow up after RT.

Key Words: Pituitary adenoma, Radiation therapy, Endocrinologic study, Functioning tumor, Non-functioning tumor

INTRODUCTION

Pituitary tumors are almost always benign. The rare malignant form accounts for less than 1% of the total[1~8,11,12,15~18].

Major advances have occured during the past decades in the diagnosis and management of patients with pituitary tumors.

Pituitary tumors can be classified into two broad categories, hormone producing and non-hormone producing[1~8,11,12,15].

Secreting tumors produce symptomes mainly due to the excess of particular hormones and also some mass effect depending on their size, but nonsecreting tumors only do by the mass effect[1~8,21~26].

The principal goal of therapy of pituitary tumor is decompression of the optic chiasm and hypothalamus by surgery and/or radiation therapy with recovery of normal hormonal status[3~5,8~11,15,18].

Radiation therapy for the management of pituitary tumor has been carried out either postoperatively or as a primary modality by the many institutions. On the other hand, progress in pituitary endocrinology and some recent tissue culture studies enabled us endocrinologic classification now used[3,4,8,11].

This is a retrospective review of the irradiated 74

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patients with pituitary adenoma to investigate the endocrinologic changes following irradiation.

MATERIALS AND METHODS

Seventy four patients with pitutiary adenomas received radiation therapy on the pituitary area using 6 MV linear accelerator (Nelac-6, Japan) from March 1983 to Apr. 1990 for over 7 years at the Division of Radiation Therapy, Kangnam St. Mary's Hospital, Catholic University Medical College.

1. Patients Characteristics

Thirty nine were men and 35 were women. The age ranged from 7 to 65 years with the mean being 37 years. Sixty five (87.8%) patients were treated postoperatively and 9 (12.2%) were primary RT (Table 1).

All but one in Nelson's syndrome showed abnormal neuroradiologic changes in the sella turcica with invasive tumor mass around supra and/or parasella area. Patients who received radiation doses below 20 Gy were excluded in this paper.

2. Radiation Methods

RT was given by conventional fractionation and dose schemes; daily 180 cGy, 5 fractionations per week, totally up to 45~65 Gy during 5 to 8 weeks with SAD 80 cm. Radiation ports were used parallel two opposing and Town's (coronal) projections generously encompassing the tumor including sella and sphenoid sinus, varying the fields size $4\times4\times4$ cm^3 to $8\times8\times8$ cm^3 [18].

Radiosurgery (RS) was also performed in 5 patients with single doses of 15~25 Gy using 6 to 7 arcs as described elsewhere[19,20](Table 1).

3. Pituitary Function Test and Follow Up

Every patient diagnosed as pituitary tumors was tested for hormonal level (so called Cocktail test) routinely before and after surgery and/or RT (Table 2).

To evaluate the hormonal influences after RT, we retrospectively analyzed the series of each patients' data of pituitary function test, eg, prolactin (PRL), growth hormone (GH), TSH, ACTH etc.

Follow up durations ranged from 1 to 7 years (mean 4.1 years).

Fifteen (4 PRLs + 11 GHs) were lost to follow up in this study.

RESULTS

Endocrinologic classification of the irradiated 74 patients were 23 (29%) prolactinomas, 20 (26%) growth hormone secreting tumors and 6 (8%)

Table 1. Endocrinologic Classifications and Treated Modalities in Irradiated 74 Pituitary Adenomas (%)

Hormonal Excess	Male (n=40)	Female (n=38)	Total (n=78)
PRL*	10*	13	23 (29)
GH*	9	11*	20 (26)
ACTH			6 (8)
Cushing's disease	1	3	4
Nelson's syndrome	1	1	2
Nonfunctioning	19	10	29 (37)
Modalities	**Male (n=39)**	**Female (n=35)**	**Total (n=74)**
S + RT	24	18	42 (57)
	8+3.	11+1.	23 (31)
RT	3	3+1.	7 (9)
	1	1	2 (3)

* One male and 3 females were dual hormonal mixed secreting pituitary adenomas.
S : surgery upper, pterion approach
lower, transsphenoid approach
RT : radiation therapy upper, primary RT
lower, adrenalectomy
. : radiosurgery

Table 2. Pituitary Function Test (Precocktail Test Orders)

1. NPO from midnight
2. Prepare
   LRH 1 ample (100ug)
   TRH 1 ample (200ug)
   RI 2 Unit (0.1 U/kg, 0.05 U/kg in child)
   50% glucose 50 ml 2 amples
   0.9% NaCl 500 ml
3. Blood Sampling
   1) Basal 8:00 AM 12 ml
      (glucose, TSH, GH, LH, FSH, PRL, cortisol)
   2) IV injection of above 2
   3) 8 : 30 AM 12 ml (" " ")
   4) 9 : 00 AM 12 ml (" " ")
   5) 9 : 30 AM 12 ml (" " ")

Table 3. Treated Modalities Related to Radiation Doses in 23 PRL's

Modality	SURGERY		RT
Dose (Gy)	Pterion	Transsphenoid	
20		1	
45	1		
50–51	9	1	
54–56	6		
60	1		
64–65			2
20&25		2*	
Total (n)	17	4	2

* : Radiosurgery

ACTH secreting ones (4 Cushing's disease and 2 Nelson's syndromes). Four (5%) of these functioning tumors showed mixed prolactin-growth hormone secreting tumors. Twenty nine (37%) were nonfunctioning ones (Table 1).

Sixty five (87.8%) patients were irradiated postoperatively and 9 (12.2%) were primary RT.

1. Prolactin (PRL) Secreting Tumors

Treated modalities related to radiation doses in 23 PRL showed in Table 3. Plasma PRL before and at intervals after RT in Fig. 1 A & B showed 15 (65.2%) normal hormone levels by 2 years after RT (Table 4). These 15 patients with normal PRL level were treated with doses of 50~65 Gy/6~8 weeks (Table 5). Five patients who showed high hormonal level were accompanied with bromocriptine

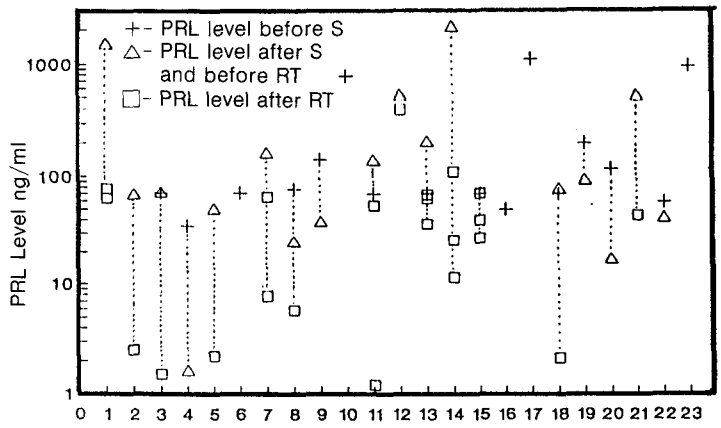

Fig. 1 A. Plasma prolactine levels before and after therapy (n=23).

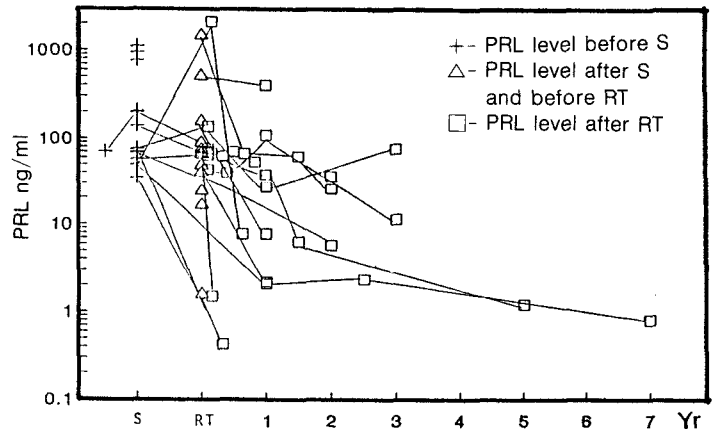

Fig. 1 B. Changes in PRL at intervals after therapy.

(BMCP) treatment.

2. Growth Hormone (GH) Secreting Tumor

In view of the relations between lapsed times and GH levels, three (15%) were returned to normal by 5 years after RT (Fig. 2 A & B, Table 6). Eleven (55%) patients were lost to follow up. Five patients who showed high GH level were treated with BMCP.

Table 4. Hormonal Response of 23 PRL's After RT

Hormone level / Lapsed years after RT	Normal	Sub-normal	Un-changed	Lost
7	4			
6	5			
5	1			1
4	2		2	
3	1	1		2
2	2			
1		1		1
Total (n)	15	2	2	4

Table 5. Relations Between Post RT Time and Doses in 15 Normal PRL's

Lapsed years / Dose(Gy)	–7–	–6–	–5–	–4–	–3–	–2–	–1
50 – 54	1	4	1	2	1	2*	
55 – 60	2						
61 – 65	1	1					
Total (n)	4	5	1	2	1	2	0

* : One of two was treated by radiosurgery (25Gy)

3. ACTH Secreting Tumors

The treatment course and follow up in 4 Cushing's disease and 2 Nelsone's syndrome showed in Table 7 and 8. Three of four Cushing's disease were turned out to be normal clinically (Table 7) and two Nelsone's syndromes were also normal in both clinically and hormonally after RT (Table 8).

4. Mixed PRL-GH Secreting Tumors

Four (5%) mixed PRL-GH secreting cases showed complete normalization of the hormone in one, normal PRL with high GH level in two and one lost to follow up (Table 9).

Table 6. Hormonal Levels of 20 GH–Secreting Pituitary Adenomas After RT

Hormone level / Lapsed years after RT	Normal	Sub-normal	Un-changed	Lost
7	1			
6	2		1	1
5				
4				2
3		2	1	3
2			1	4
1			1	1
Total (n)	3	2	4	11

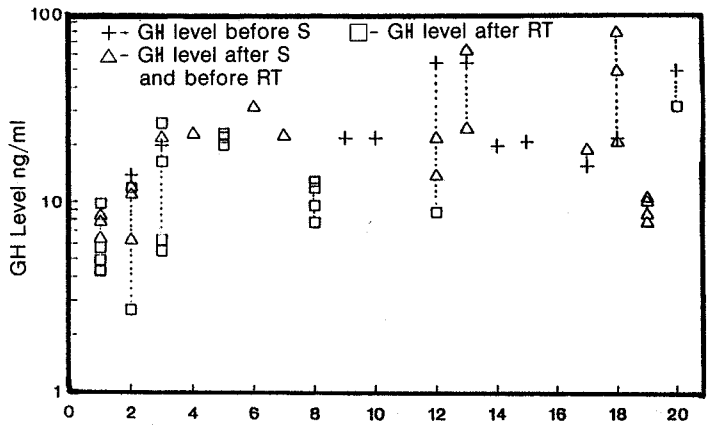

Fig. 2 A. Plasma GH levels before and after therapy (n=20).

5. Complications and Follow Up

Endocrine insufficiency related treatment showed 7 (9%) panhypopituitarisms, 2 (3%) hypogonadisms and 7 (9%) hypothyroidisms (Table 10). Five of seven panhypopituitarisms, 4 of 7 hypothyroidisms and one of two hypogonadisms were developed by 3 years after RT.

Majority of patients noted small square shaped hair loss at the temples only to regrowth within half a year. No problems on visual fields following RT were observed.

DISCUSSION

The diagnosis of pituitary adenomas is based appropriate endocrine and neuroradiologic find-

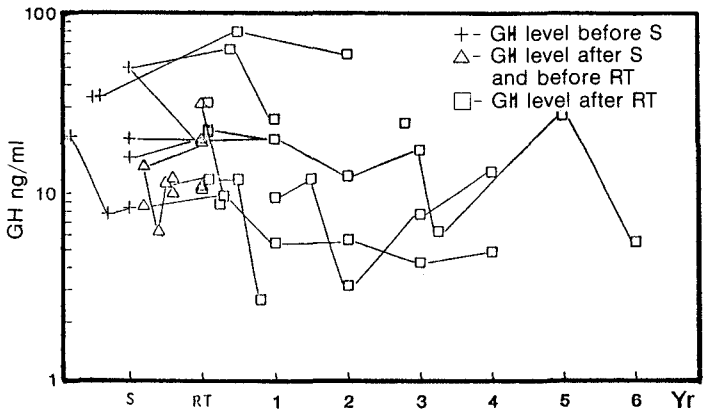

Fig. 2 B. Changes in GH at intervals after therapy.

Table 7. Treatment of 4 Cushing's Diseases

Case	Age/Sex	Symptoms (Sx)	Treatment Course & Follow up
1	17/M	cushingoid Pituitary Sx	Spt – PRT – 20 – 10.5 – 14 – 7.6 – (50.4Gy) (1yr) (2yr) (3yr) (7yr)
2	30/F	cushingoid Pituitary Sx	Sph – 43.4 – PRT – 21.3 – 11.6 – 6.5 – (50.4Gy) (1.5yr) (2yr) (6yr)
3	38/F	cushingoid Pituitary Sx	Sph – 38 – PRT – normal FBS – 6.8 (48.4Gy) (1yr) (4yr)
4	34/F	cushingoid Pituitary Sx	RS — 20 — not suppressed (15Gy) (1yr) (2yr)

Spt : Surgery, pterion
Sph : Surgery, transsphenoid
PRT : Pituitary radiation therapy
FBS : Fasting blood sugar
RS : Radiosurgery

Table 8. Treatment of 2 Nelson's Syndromes

Case	Age/Sex	Treatment for Nelson's syndrome & Follow up
1	19/F	A —— PRT ——— 1192 — 546 — 179 — 80 (50.4Gy) ACTH (22mo) (3yr) (6yr) (7yr)
2	22/M	A — 612 — PRT — 240 — 250 stable ACTH (50.4Gy) (22mo)

A : Adrenalectomy, Normal ACTH level 0–80 pg/ml
PRT : Pituitary Radiation Therapy

Table 9. Treatment of 4 Mixed PRL–GH Secreting Adenomas

Case	Age/Sex	Treatment & Follow Up
1	40/F	PRL 67.7 — RT (61.2Gy) ——— 2.2 (2yr) — 2.35 (2.5yr) — 0.8 (7yr) GH 8.39 — BMCP — 1.5 (1yr) — stop BMCP — 4.3 (2yr) — 4.1 (3yr) — 4.9 (7yr)
2	42/M	PRL, GH — S — 60 — RT (50.4Gy) — 65.1 (6mo) BMCP ——— 7.8 (1yr) — 5 yr ? GH — S — ——— 20↑ (6mo) ——— 20↑ (1yr)
3	38/F	PRL 50.5, GH 20 — S — RT (19.8Gy) — interrupted RT — 3 yr ?
4	37/F	PRL 76.9 ↑, GH 20 ↑ — S — 16.8 — RT (54Gy) — 2 yr ?

Table 10. Endocrine Insufficiency Related Treatment of 74 Pituitary Adenomas

Lapsed years	Insufficiency	Panhypopituitarism	Hypogonadism	Hypothyroidism
7		2	0	1
6		1	0	0
5		1	0	0
4		0	1	2
3		2	0	1
2		0	1	3
1		1	0	0
Total (n)		7	2	7

ings. Those were previously classified according to their tinctorial properties into eosiophilic, basophilic and chromophobe adenomas[3~5,8,11,15~17]. Today, detection of secretory granules of various types with the use of immunoperoxidase techniques has helped establish the secretory nature of various tumors[3~8,11,15,17]. Thus one distinguishes between PRL, GH, ACTH, TSH, FSH and LH-secreting tumors. Landolt and Wilson estimated the following frequencies in their review of tumors of the sella and parasella area[9]: 1) endocrine inactive tumors 20%; 2) growth hormone-secreting adenoma (acromegaly, gigantism), 25%; 3) prolactinomas, 35%; 4) corticotropic adenomas (Cushing's, Nelson's syndromes), 5%; and adenomas producing more than one hormone, 10%. In our seriers, hormonaly inactive tumors in 39%, GH secreting ones in 22%, prolactinomas in 26%, ACTH secreting ones in 8% and pleurisecreting ones in 5%, respectively, were observed.

Transsphenoidal surgery is generally regarded as the primary modality of therapy for pituitary macroadenomas[10]. Radiation therapy has been used as an adjunct to decrease the recurrence rate from up to 86% to 10~25%[3~5,11,15~17]. Primary radiation therapy has generally been reserved for one of the following reasons such as refused surgery, advanced age, inoperable for medical reasons and reservation of surgery as salvage for a macroadenoma requiring planned post operative RT [6,11]. In our series, RS was performed in 5 patients considered poor candidates to tolerate the conventionally protracted RT durations or inoperable for medical reasons etc, eventhough there were no available other data for the hormonal influences by RS.

Correa and Lampe reported 44% control with doses of 20 to 25 Gy, 60.6% with doses ranging from 29 to 35 Gy and 79.3% for doses greater than 40 Gy[3]. Increasing the dose over 50 Gy and be considered for massive tumors but a greater chance of local control along with high risk of radiation complications such as damage to the optic nerves and chiasm and hypopituitarism[3,8,11]. We observed 15 normal PRL level by 2 years after RT with the doses range of 50~65 Gy for 6 to 8 weeks (Table 5).

1. PRL-Secreting Tumors (Prolactinomas)

The endocrine diagnosis of PRL seceting pitui-

tary adenoma rest on the detection of hyperprolactinoma. It is believed that a serum PRL level of over 200 mg per ml constitutes the strong endocrine proof of a PRL secreting pituitay (micro) adenoma[4,5,8,11,15,17,18]. With PRL elevations below 100 ng per ml, the differential diagnosis includes a number of other possibilities. For examples, physiologic status such as pregnancy or excess of physical exercise may be associated with hyperprolactinemia. Ingestion of phenothiazide, tricyclic antidepressant theapy, hypothyroidism and estrogen containing contraceptives are the most common cause of iatrogenic hyperprolactinemia [4,5,8,11,15]. Furthermore moderate hyperprolactinemia can occur in patients with disturbed portal circulation with the stalk, interferring with the transmission of the PRL-inhibitory factor[4].

Prior to the introduction of PRL assay, these tumors were usually termed nonfunctioning chromophobe or mixed adenomas. Treatment with resection alone, results in a return of the serum PRL level to the normal range, however, later recurrence occurs, in 25 to 80% of the patients depending on its size, and degree of extension into suprasella or parasella region[3~11].

Gomez et al reported the PRL levels droped in 62% after RT, initially relatively rapidly within one month, but then slowly over a period of 3 to 4 years [3,11]. In our cases, 15 (65.2%) of 23 were returned to normal PRL level by 2 years after RT (Fig. 1A & B, Table 4).

Bromocriptine (BMCP), a dopamine agonist, is frequently successful in reducing circulating PRL to normal, restoring menses and fertility in over 80% and also in reducing tumor size[3~5,8,11,15,18,23,24]. However, current evidence indicates that, although BMCP can reduce the tumor size and slow the rate of secretion, it can not reach a cure. It has been known rapid reurrence of prolactinoma volume, elevated PRL levels and visual decompression within days of discontinuing prolonged therapy with BMCP.

Combination of surgery, BMCP and RT may be required to improve the therapy of this tumors, especially macroadenomas and tumors associated with serum PRL levels exceeding 200 ng/ml [3~5,8,11,15,18].

2. GH-Secreting Tumors

The endocrine diagnosis of GH-secreting pituitary adenomas is based on a detection of elevated baseline serum GH levels above 5 ng per ml, on an abnormal dynamic response to glucose stimulation and on a determination of the serum somatomedin-c levels[1~5,7,8,10,11]. The presence of very low (less than 2 ng per ml) or a very high (greater than 25 ng per ml) baseline serum GH level is probably the most reliable endocrine proof as to the abscence or presence of a GH elevation (5 to 25 ng per ml). Glucose tolerance test is an added diagnostic tool. In normal individuals, oral glucose tolerance test will effect a fall in the serum GH level to below 2 ng per ml 60 minutes after administration of glucose. A failure to do so is indicative of GH secreting pituitary adenoma[3~5,8].

Two of the widely used modalities for the treatment of GH secreting tumors of the pituitary include surgery and irradiation[1~5].

In more than three fourths of patients undergoing transsphenoidal operations for acromegaly[10], GH levels revert to normal within 24 hours. Clinical improvement is often striking and prompt with disappearance of arthritic pain, early regression of soft tissue changes and weight loss. About 5 to 10% of patients lose some degree of pituitary function and require hormonal replacement[4]. Incomplete responses and therapeutic failures are more frequent with suprasella extension of tumor, preoperative GH greater than 40 ng per ml, or diffuse destruction of the sella floor[4,5~8].

In general, these tumors grow very slowly. If a permanent cure is to be proven, the observation period must be adequately long. Sheline reported the mean time to recurrence for patients who failed to respond to surgery alone, was 4 years and 9 years for those who developed recurrent disease after combination of surgery and postoperative RT [12]. Erlichman et al found a median time to recurrence of 2.4 years for patients treated by surgery alone and of 3.5 years for those treated by surgery and postoperative RT[8].

Conventional irradiation with 40~60 Gy delivered during a period of 5 to 7.5 weeks has been an accepted treatment for many years. It makes alone lower GH levels in patients treated primarily by operation, and in whom significant extrasellar extension is noted or in whom GH levels remain elevated postoperatively[3~5,8]. Eastman et al reported 80% fall in normal GH levels in patients with elevated levels postoperatively[7]. Baskin et al reported remission of GH levels less than 10 ng per ml in 16 (73%) of 22 patients not controlled by transsphenoidal surgery[3,10,11]. Such reductions can be extreamely and unacceptably delayed, sometimes requiring 4 to 6 years to accomplish[3~5]. Partial or complete hypopituitarism induced by

therapy is frequently seen. With proton beam therapy, a focused beam of 120 to 150 Gy can be delivered to the pituitary tumor. The beam is aligned so that Bragg peak is centered in the anterior portion of the sella. Under this conditions, 75 to 90% of the anterior lobe will be destroyed by radionecrosis[3,8,11]. The fall in GH occured slowly. GH levels in 30% of patients falling to less than 5 ng/ml within two years and 68% within 6 years of treatment[3]. There are considerable numbers of patients with hypopituitarism (20 to 35%), visual field defect and extraocular nerve palsies (up to 20%)[25,26]. Furthermore patients with extrasellar extension of tumor can not be treated. When both transphenoidal excision and RT are required for remission, the incidence of hypopituitarism exceeds 50% (Baskin et al)[10].

3. ACTH Secreting Tumors

The endocrine diagnosis of an ACTH secreting pituitary adenoma rests on the detection of hypercortisolism that is not suppressible by dexamethasone in low dosages[3~5,8~11]. A 24-hour urine collection for urinary free cortisol is the single most reliable test for hypercortisolism. In patients with Cushing's disease, the value for urinary free cortisol is usually greater than 100 mg per 24 hour volume of urinary excertion. A good screening test is the overnight 1 mg dexamethasone test, which in normal subjects suppresses the morning plasma cortisol to below 5 mcg per ml[4,17]. Then, hypercortisolism may be associated with such chronic illness as cardiac disease, renal disease depression or alcoholism. In addition, the low dosage dexamethasone suppression test may give false negative results due to a delayed clearance of dexamethasone with higher than usual plasma levels. Anticonvulsants accelerate the metabolism of dexamethasone and thus cause a false positive dexamethasone suppression test[3~5,8].

Since most of this tumors are too small to cause sella changes or to be detected by special radiographic procedures, the clinician reaches the diagnosis by the previously dscribed laboratory test (Table 2). When the diagnosis of a pituitary tumor as the cause of hypercortisolism can be made, transsphenoidal operation is the treatment of choice[8,11]. More than 90% of patients with intrasella tumors reverse the clinical manifestations of hypercortisolism. ACTH and cortisol levels return to normal.

Orth and Liddle reported pituitary irradiation with the doses of 40~50 Gy[13]. Although such treatment did not result in restoration of normal diurnal rhythm in plasma cortisol or normal responses to dexamethasone suppression test in patients considered cured. 23 (45%) of 51 patients improved enough to require no further therapy. The available data on the value of RT in Cushing's disease are, at present, very incomplete[11]. The effect of postoperative irradiation after primary microsurgical adenomectomy should be investigated. Kjellberg and Kliman effected total remissions in 63% of patients treated with proton beam irradiation[3,11].

The role of RT in the treatment of Nelson's syndrome is uncertain. Possibly, prophylactic irradiation of the region of the pituitary may lower the incidence of Nelson's syndrome, which occurs in about 10~15% of patients submitted to bilateral adrenalectomy[8,11,15]. Moore et al reported that 6 out of 7 patients who received RT alone (the one death was not due to the underlying disease) are still alive and well after a mean observation period of 9.4 years[14].

Despite the paucity of data in the literature on RT of Cushing's disease and Nelson's syndrome, we are of the option that present standard treatment comprise surgical removal of the tumor followed by routine postoperative RT[3]. We have experienced 3 of four Cushing's disease and two Nelson's syndromes were normal in both clinically and hormonally after RT (Table 7 & 8).

4. Pleurihormonal and Hormonally Inactive Adenomas

Pleurihormonal pituitary tumors are relatively frequent. The most common association in that between GH and PRL secretion[2~5,8]. Approximately 30 to 40% of acromegalic patients have a simultaneous elevation of serum PRL level[3,11]. Then, in our cases, 5% incidence of mixed PRL-GH secreting tumors were observed. The serum PRL elevation may be consequence of secretion by the adenoma or may be caused by the stalk effect[4]

Hormonally inactive tumors are diagnosed only when they have already expended intracranially, and have compressed the optic nerve and given rise to the symptomes of a space occupying process[3~6,8,11,17]. Erlangen demonstrated the efficacy of RT in large pituitary tumors[11]. In the UCSF reports [11], those who had been given RT alone and those in whom only partial tumor resection had been followed with postoperative RT, recurrent free survival was identical. But only 49% of the patients treated by surgery alone still alive and recurrence-free after 2 years, while no patients survived for 15 years or

longer. And in patients who had received postoperative RT of at least 45 Gy, recurrent lesions were extreamly rare and the control rate was estimated to be about 95%. Large space-consuming pituitary tumors, in particular the hormonally inactive tumors, should receive postoperative conventional RT. Although RT alone, particularly in small tumors, is effective, in general, surgical debulking of the tumor mass should be undertaken. This rapidly relieves the pressure on the neighbouring tissue[3~6,8,11,1,17].

5. Complications of RT

With doses in the 40 to 50 Gy range delivered at 180 to 200 cGy per day fractions, acute reactions are limited to slight fatigue and small areas of temporary epilation within the radiation portals. The most frequent long term complications now appear to a slowly developing but definite incidence of hypopituitarism secondary to radiation[3~5,8,11,15,17]. Samaan et al reported on 15 young adults who had been treated with radiation doses of 50 to 85 Gy for nasopharyngeal carcinoma [22]. These patients showed more global deficiencies involving hypothalamic and pituitary dysfunction. Pistenmaa et al reported 1 (9%) of 11 patients of developing hypothyroidism and a 60% (4 of 6 pattients) incidence of decreased libido in his series of acromegalics[11,12]. Feek et al, Aloia et al and Eastman et al have reported similar but varied incidences of anterior pituitary failure in acromegalics treated with conventional radiation[7,11]. From these series, it would appear the 1) pituiary function is affected by radiation doses in the therapeutic range greater than or equal to 40 Gy, 2) children appears to be more susceptible to the side effects of radiation with lower doses greater than or equal to 20 Gy, 3) GH deficiency is the most prevalent defect and clinically most apparent in children, 4) evidence suggest that both hypothalamic and pituitary sites are responsible for the defects seen after radiation[8,11]. The overall incidence of hypopituitarism expected after conventional radiation doses of 40 to 50 Gy is in the range of 10 to 25%[3~5,8,11,15,17].

The long term complications of radiation other than hypopituitarism are rare. Injury to optic nerves and chiasm have been reported by several authors [3,8,11]. Harris and Levene reported 5 cases of visual loss among 55 patients treated with radiation fractions greater than 250 cGy per days part of the treatment for pituitary adenoma and craniopharyngioma[3]. No patients receiving less than 250 cGy per day exhibited visual loss. Atkinson et al also reported visual loss in 4 of 23 acromegalics treated with fractions of 280 to 300 cGy per day[3,11]. It would thus appear that visual loss can be avoided by utilizing conventional radiation fraction of 180 to 200 cGy per day.

Rare cases of induction of malignancy in patients treated with conventional radiation have been reported. These are usually sarcomas and present after a long latent period of 10 to 20 years [3~5,8,11,15,17].

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국문초록 =

뇌하수체선종의 방사선치료후 혈중 호르몬치의 변화

가톨릭의대 강남성모병원 방사선과학교실, 내과학교실* 및 신경외과학교실**

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가톨릭의대 강남성모병원 방사선치료실에서는 1983년 3월부터 1990년 4월 사이 7년여 동안에 뇌하수체선종으로 확진되었던 74명의 환자(7~65세, 평균 37세, 남 : 여=39:35)에 대하여 뇌하수체 부위에 외부방사선치료를 하였다.

방사선치료는 6 MV 선형가속기를 사용하여 선원중심축거리 80 cm, 4×4×4~8×8×8 cm^3 조사야로 3문조사하였다(180cGy/일, 5회/주, 20~65Gy). 5예에서는 정위다방향고선량단일조사(15~25 Gy/1회)를 실시하였다.

이 환자들의 수술전후 및 방사선치료 후에 복합뇌하수체자극검사를 실시하여 종양의 호르몬분비에 따른 분류와 방사선치료가 호르몬분비에 미치는 영향을 추적조사하였다.

호르몬분비에 따른 뇌하수체선종의 분류는 프로랙틴종 23예(29%), 성장호르몬분비종 20예(26%), 부신피질자극호르몬분비종 6예(8%)(쿠싱병 4예와 넬슨증후군 2예)였으며 4예(5%)에서는 프로랙틴과 성장호르몬을 동시에 분비하였다. 한편, 호르몬분비기능없는 종양이 29예(37%)였다.

23예의 프로랙틴종 중 15예(65%)와 20예의 성장호르몬분비종 중 3예(15%)에서는 방사선치료 2~3년 후 정상 호르몬 수치로 전환되었다. 부신피질자극호르몬분비종은 6예 중 1예를 제외한 전예에서 치료 후 모두 정상이되었다.

방사선치료에 따른 부작용으로서 범하수체기능저하증 및 갑상선기능저하증이 각각 7예(9%)씩 그리고 성선기능저하증 2예(3%) 등이 관찰되었다.

전예 중 15예(20%)에서는 정기적인 호르몬 추적검사를 실시하지 못하였다.