

성장호르몬분비 뇌하수체 선종 80예의 수술성적 및 예후 인자의 분석*

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= Abstract =

Surgical Results of 80 Patients with Growth Hormone-Producing Pituitary Adenomas : Analysis of Outcome and Prognostic Factors

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Objectives : The surgical results of 80 patients with growth hormone (GH) - producing pituitary adenoma were analyzed retrospectively to evaluate the clinical manifestations and to determine which preoperative factors significantly influenced the surgical outcome.

Patients and Methods : The patients consisted of 39 men and 41 women and the age of patients at the time of initial operation ranged from 17 to 67 years (mean age, 40.5 years) Between January 1990 and June 1996, 77 patients underwent transsphenoidal surgery and 3 patients underwent craniotomy for GH - producing pituitary adenoma at our institution. Preoperative administration of octreotide was performed in 18 patients. Surgical control was defined as a postoperative serum basal level of GH less than 5ng/ml. A logistic regression model was used for univariate and multivariate analysis. Probability value of less than 0.05 was considered as statistically significant.

Results : The most common presenting symptom was acromegaly, followed by headache, visual disturbance, and fatigability. Visual symptoms were present in 39% of the patients. Diabetes mellitus was associated in 24 patients and hypertension in 12. Preoperative mean basal level of GH was 93.2ng/ml (range 72 - 500ng/ml) which was closely related with tumor size ($p < 0.05$). Grade II by Hardy's classification was the most common radiological type. Preoperative octreotide treatment significantly reduced the level of GH ($p < 0.05$), but not enough to induce endocrinological remission. One patient died of cerebral infarction after craniotomy. The most common surgical complication was transient diabetes insipidus. The symptom of the earliest improvement after surgery was paresthesia and tightness of the hand and foot, followed by headache and easy fatigability. The preoperative visual symptom was improved in all patients. The patients who had hypertension or DM experienced alleviated symptoms in 67% and 92%, respectively. The overall rate of endocrinological remission was 44%. By multivariate logistic regression analysis, the size of tumor, extrasellar extension, and extent of removal were significant prognostic factors for endocrinological remission.

Conclusion : Early detection of a small tumor without extrasellar extension followed by a complete resection is highly recommended in order to achieve endocrinological cure of GH - producing pituitary adenomas.

KEY WORDS : Clinical manifestation · Endocrinological remission · Growth hormone - producing pituitary adenoma · Prognostic factor · Surgical outcome.

서론		(CT)	(MRI)	(seller MRI)
1886	Pierre Marie		가 10mm	
1967	Guiot	(microadenoma), 10mm	30mm	
1969	Hardy	(giant adenoma)	(macroadenoma), 30mm	
		(grade) Hardy가	가	1
		36%		
87%	64.9% ⁷⁾	가	(no evidence of disease),	가
		가	5mm	
1990	1996 6	6 6	(no evidence of regrowth), 5mm	
80			가 (regrowth), 5mm	(de-
			creased size) 가	
			3) 병리학적 자료	
			80 H & E	
			33	
			4) 내분비학적 자료	
			가	
			가 5ng/ml	(remission)
			5) 치료방법	
			77	3
			sublabial	transcollumellar - transseptal ap-
			proach	2
			roach	1 pterional app-
			subfrontal approach	95%
			(gross total removal), 50%	95%
			(subtotal removal), 50%	
			(partial removal)	
			octreotide(somatostatin analog)	18
			100 300 µg	3
			21 240	80
			41	
			2) 방사선학적 자료	

대상 및 방법

1. 연구대상

1990 1 1996 6 6 6

80 0

78 30.3 가

75 3 78

32.2 44

0 65 15.7

2. 연구방법

1) 임상자료

2) 방사선학적 자료

61 (3.3), 1445 5.5%, 282
 28.4% 39 : 41
 720cGy 1 40
 4500cGy 5580cGy (whole 30 , 50 가 40.5
 brain irradiation) (Fig. 1).

6) 통계학적 분석

linear regression
 , octreotide
 paired t - test , octreotide
 Fisher's exact test
 가 75
 (extrasellar extension), (extent of re-
 moval), (postoperative irradiat -
 ion) 5가 chi -
 square test

logistic regression
 5%(p<0.05)

결 과

1. 개 요

1990 1 1996 6
 80

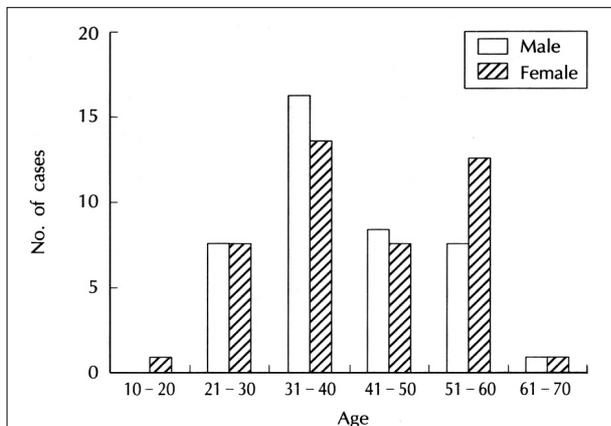


Fig. 1. Age and sex distribution in 80 patients with GH-producing pituitary adenomas.

2. 임상증상

24 (30%), 12 (15%)
 (Table 1), 9 420
 82 0.0
 1.5(0.66), 0.0 1.5(0.68) ,
 21 (26%)
 11 (52%) 가

Table 1. Clinical symptoms and signs in 80 patients with GH-producing pituitary adenomas

Symptom & Sign	No. Cases (%)
Acromegalic feature	75(94%)
Headache	41(51%)
Diabetes mellitus	24(30%)
Decreased vision	23(29%)
Visual field defect	21(26%)
Easy fatigability	20(25%)
Amenorrhea	17(21%)
Hypertension	12(15%)
Decreased libido	12(15%)
Heat intolerance	8(10%)
Weight gain	7(8.8%)
Impotence	3(3.8%)
Weight loss	3(3.8%)
Diabetes insipidus	2(2.5%)
Cranial N. palsy	1(1.3%)

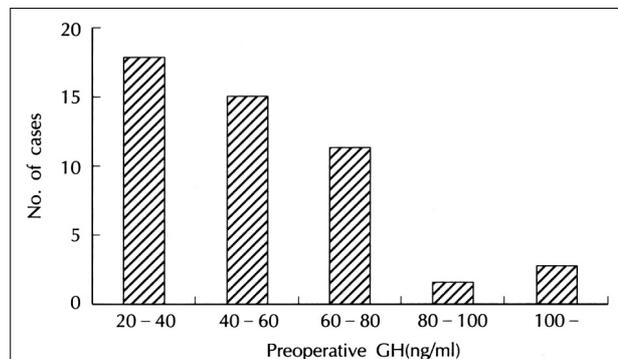


Fig. 2. Distribution of preoperative growth hormone level in 80 patients with GH-producing pituitary adenomas.

3. 수술 전 기저 성장호르몬 값

9.7ng/ml 425ng/ml
93.2ng/ml (Fig. 2).

p-value가 0.003(p<0.05)

가 0.327 (Fig. 3).

4. 방사선학적 소견

5mm 60mm
26.3mm 9, 50, Hardy
21 (Fig. 4).

Grade I 15, 1cm
Grade II가 32, 1cm
(localized erosion) Grade III
가 23, Grade IV
가 10 (Fig. 5).
가 17 가, 가 4,

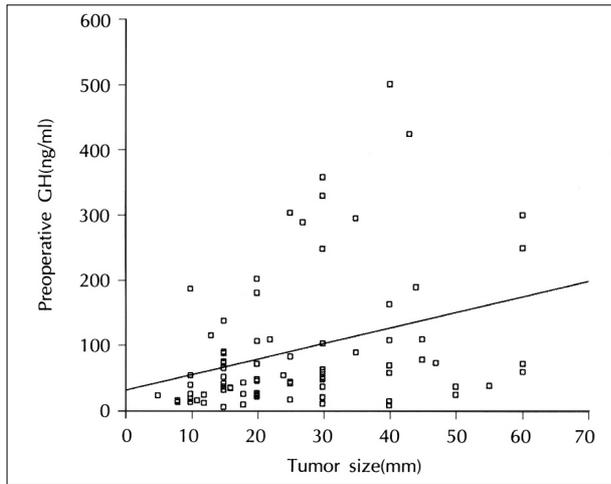


Fig. 3. Scatter diagram between preoperative growth hormone level and tumor size in 80 patients with GH-producing pituitary adenomas.

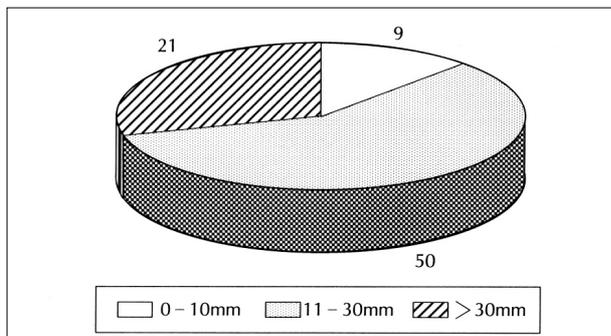


Fig. 4. Size distribution of adenoma in 80 patients with GH-producing pituitary adenomas.

1, (extension) 62

가 43 가, (Table 2).

5. 수술 전 octreotide(somatostatin analog) 치료성적

octreotide 18
22.9ng/ml 425.0ng/ml(153.
8ng/ml), 0.1ng/ml 161.
0ng/ml(27.7ng/ml)
(p<0.05).

octreotide (p>0.05)(Table 3). Octreo-
tide 가 가
5 27.8%, 가 (softening)
가 6 33.4%. Octreotide 3

6. 수술적 제거정도

77 3
가 44, 가 28,

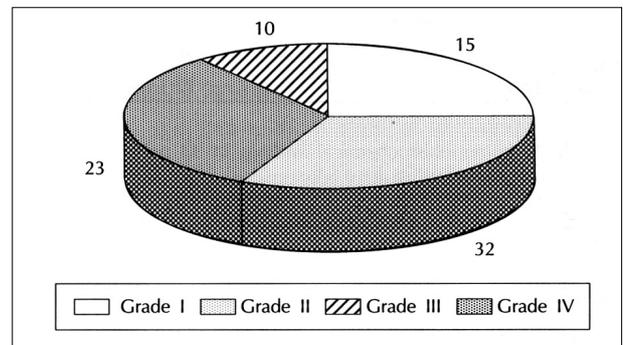


Fig. 5. Distribution of radiological grade in 80 patients with GH-producing pituitary adenomas.

Table 2. Radiological findings in 80 patients with GH-producing pituitary adenomas

Findings	No. Cases(%)
Extrasellar extension	62(78%)
Suprasellar	43
Cavernous sinus	18
Sphenoid sinus	15
Subfrontal	4
Clival	1
Cystic change	17(21%)
Necrosis	4(5%)
Hydrocephalus	1(1%)

가 8 . 7. H & E (chromo - (Table 6), 8 가 .
phobe) 38 , (acidophilic) 30 , 1
가 12 (Table 4).
33
20 가 , 7 ,
- - 3
(Table 5).

8. 합병증

13 가

9. 수술후 방사선학적 성적

가 44
22 , 16 , 가 5 ,
1 (Table 7).

(p=0.

001)

Table 3. Correlation between octreotide treatment and endocrin-ological remission in 75 patients with GH-producing pituitary adenomas

	Remission		p-value
	Yes	No	
Octreotide treatment			
Yes	5	13	0.093
No	28	29	

Table 4. Pathologic findings in 80 patients with GH-producing pituitary adenomas(H & E staining)

Findings	No. cases(%)
Chromophobe	38(48%)
Acidophilic	30(38%)
Unspecified	12(14%)

Table 5. Immunohistochemical findings in 33 patients with GH-producing pituitary adenomas

Findings	No. cases(%)
PRL + GH	20(61%)
GH only	7(21%)
PRL + GH + ACTH	3(9%)
GH + PRL + ACTH + FSH	1(3%)
LH	1(3%)
PRL	1(3%)

(abbreviations : PRL, prolactin, GH, growth hormone, ACTH, adrenocorticotrophic hormone, LH, luteinizing hormone, FSH, follicular stimulating hormone)

Table 7. Radiological outcome in 44 patients with GH – producing pituitary adenomas

Outcome	Extent of removal			Radiation		Total No. cases(%)
	PR	STR	GTR	(-)	(+)	
NED	1	5	13	12	10	22(50%)
NER	1	12	2	4	12	16(36%)
Decreased size	3	1	-	-	5	5(11%)
Regrowth	-	-	-	-	1	1(3%)
p – value		0.001			0.06	

(abbreviation : NED, no evidence of disease, NER, no evidence of regrowth, GTR, gross total removal, STR, subtotal removal, PR, partial removal)

10. 수술후 임상증상의 호전

, , , ,
75
, ,
71 (95%) , 20
15 (75%) , 41 30 (73%) ,
17 7 (41%) , 12 8 (67%)
, 24 22 (92%)
가 23 0.0
1.2 0.21
가 9 (39%), 가 2 (9%), 가
12 (52%) (Table 8).

0.1/0.02, 0.02/0.5 , 1 , 1

Table 6. Postoperative complications in 80 patients with GH-producing pituitary adenomas

Complications	No. cases(%)
Diabetes insipidus(permanent)	14(1)(18%)
CSF leakage	9(11%)
Hypopituitarism	1(1%)
Loss of vision	1(1%)
6th N. palsy	1(1%)
ICH	1(1%)
Cerebral infarction*	1(1%)

(* : Died due to ICA occlusion)

2 77 20

11. 수술후 내분비학적 성적

1) 내분비학적 관해율

Table 8. Clinical improvement of symptoms in 80 patients with GH-producing pituitary adenomas

Improved symptoms	No. Improved cases(%)
Acromegalic feature (tingling, tightness)	71(95%)
Headache	30(73%)
Diabetes mellitus	22(92%)
Decreased vision	9(39%)
Easy fatigability	15(75%)
Amenorrhea	7(41%)
Hypertension	8(67%)
Visual disturbance	
Improved	9(39%)
No change	12(52%)
Aggravated or lost	2(9%)

Table 9. Analysis of prognostic factors for endocrinological remission in 75 patients with GH-producing pituitary adenomas

Factors	Remission		p-value	
	Yes	No	Univariate [@]	Multivariate [#]
Size of tumor				
0 - 9	3	0	0.039*	0.0157*
10 - 29	20	20		
30 -	10	22		
Extrasellar extension				
Yes	15	35	0.001*	0.0232*
No	18	7		
Sex				
Male	15	24	0.315	0.1054
Female	18	18		
Extent of removal				
GTR	25	15	0.001*	0.0248*
STR	5	22		
PR	3	5		
Postoperative irradiation				
Yes	11	30	0.001*	0.2042
No	22	12		
Age	-	-	0.459	0.8004
Preoperative GH	-	-	0.001*	0.0688

(* : statistically significant, @ : chi-square test for size of tumor, extrasellar extension, sex, extent of removal, postoperative irradiation, and logistic regression analysis for age, preoperative GH, # : logistic regression analysis, abbreviations : GTR, gross total removal, STR, subtotal removal, PR, partial removal)

33 44% 가 75

2) 내분비학적 관해의 예후인자 분석

(1)

5가 (p<0.05)(Table 9).
가 , 가 ,
(2) 가
3가 가
(p<0.05).
(p>0.05)(Table 9).

고 찰

8 15%
26% 21)
2 4%
28.4% 5.5%, 20
40
15).
50 가

1. 수술 전 임상 양상

IGF - 1 93%
21), 75 94%
29%

가 4% 70% 2)13), 50% (parsely granulated adenoma) (densely granulated 100 250nm 가 adenoma) 가 21), 350 450 nm 가 , 21), 33 73% 24 가 (pituitary stalk) (plurihormonal) 21% 7 가 - (GH only - monohormonal) 21) 68%, 32% 1 16) IGF - 1 16) (antinatriuretic effect) 11)16)

4. 수술 후 합병증

가 가 21) 가 가 (16.3%), (11.3%), (7.5%) (0 8. 12) 가 82%), (0 3.12%), (0 25.7%) 10% 7) 가 , 1990 가 가 7) 18 가 7) 1990

2. 수술 전 octreotide 치료의 효과

octreotide 가 7) 18 octreotide 27.8%, octreotide 가 33.4% octreotide 87% 10), 가 가 6)18) 1987 Spinas 19) 2396 (0 5.88%) 0.71% 7) 1 octreotide . octreotide 1.25%) 2 3 7)

5. 치료 결과에 대한 분석

3. 조직 병리 및 면역조직화학 염색 소견

H & E 68 80 100% 38 : 30 1991 Giovanelli 7)

43 IGF - 1
 23 20.9%, 가 2.4% 76.7%, 가가
 39%, 52%, 가 9% IGF - 1 가 가
 0.21 5ng/ml 10ng/ml 가
 가 5ng/ml 36% 87%
 가 64.9% 7) 44%
 가 1987 Nabaro 15) 6
 4 (67%), 1980 Arafah 3) 4
 (100%)
 17 7 (41%)
 가 75 100% 80 45% 36 가
 22) 가 가 가
 73% 68 100% 2 17)20)
 4)22) 92% 18mm 13.6mm 26.3mm
 6 가
 7), 32 18 (56%) (giant adenoma) 가 33 41%
 15)
 가 12 8 (67%) 가
 가
 75 95% 가
 가
 7) 가 가
 가 가
 (cure) 가 가
 가
 (cure) 가
 (remission) 가 4가 **결 론**
 가
 IGF - 1 , TRH, GnRH 6 6 80
 (paradoxical response)
 가
 가 가

가

• : 1999 9 8
 • : 1999 12 9
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