

## 성인 쿠싱병의 치료성적과 예후인자\*

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= Abstract =

### Treatment Outcome and Prognostic Factors of Cushing's Disease in Adults

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**Objectives** : The authors analyzed the surgical series of Cushing's disease to evaluate the proper treatment policy and to verify the possible prognostic factors.

**Material and Methods** : Of 50 patients diagnosed as Cushing's disease and operated at Department of Neurosurgery of our institute between 1988 and 1999, 48 patients with available medical records were analyzed retrospectively. Mean follow-up period was 48 months (3 to 109 months). Preoperative diagnosis was made after evaluating the patients with multiple-stage endocrinological studies and 31 selective patients were evaluated with inferior petrosal sinus sampling (IPSS). Magnetic resonance imaging (MRI) and/or high resolution computerized tomography (CT) was done in all patients. A total of 51 transsphenoidal adenomectomy (TSA) were performed including 3 revision for initial surgical failure cases. Remission was decided on the basis of both endocrinological criteria and clinical status. Radiation and/or ketoconazole therapy were applied to failed cases. For the verification of prognostic factors, the authors evaluated the statistical significance of multiple variables over remission rate by chi-square test.

**Result** : Sensitivity of IPSS for central localization was 93.5% which was better than that of MRI (87.5%). But for lateralization, it was 72.4% for IPSS versus MRI 90.5%. Success rate of TSA was 82% (42/51) and recurrence rate was 9% (4/48). When including adjuvant treatments for surgically failed cases, overall success rate was 89.6% and all of 3 reoperated cases (TSA) due to recurrence were successful. Significant complication occurred in 7.8% (4/51) after TSA including hypopituitarism, diabetes insipidus, and visual loss. Non-existence of tumor in MRI and prolonged symptom duration (> 3 years) were significant prognostic factors.

**Conclusion** : TSA can be considered as initial treatment for Cushing's disease. In surgically failed cases, multiple treatment modality may improve the overall outcome and repeated TSA for recurrent cases seem to provide similar success.

**KEY WORDS** : Cushing's disease · Transsphenoidal adenomectomy · Surgical outcome · Prognostic factor.

## 서론

(Adrenocorticotrophic hormone, A-CTH) (Cushing's disease) (cortisol) 가 1 (Cushing syndrome) 가 100 0.7 2.4 5 50% 9). (transsphenoidal adenomectomy, TSA) 1969 Hardy 가 TSA 63 83% (magnetic resonance imaging, MRI) TSA가 가 12-15) 48 10 가

(high dose dexamethasone suppression test, HDDST) 가 10mm (microadenoma), 10mm (macroadenoma) . MRI (dynamic MRI) , 31 (inferior petrosal sines sampling, IPSS) . IPSS ACTH ACTH 가 1.4 TSA 4 3 TSA 51 TSA (selective adenomectomy), (partial adenomectomy), (hemihypophysectomy) (total hypophysectomy)

## 대상 및 방법

1988 1997 10 ACTH 48 50 가 3 109 6.6% 48 24 cortisol 60pg/ml , 3 25g/dl, 30 130g 가 (low dose dexamethasone suppression test, LDDST)

1) , 2) , 3) LDDST 가 , MRI 가 chi-square test

## 결과

### 1. 역학적 분석

48 14 60 ( 32 ) 20 , 20 40 가 13 : 35 가 3

(Fig. 1).

### 2. 임상증상 및 징후

(Table 1).

30 (63%), 9 (24%)

40

(2 108 ) 가

가

3. 수술 전 내분비학적 검사

ACTH 65.9pg/ml

(10 201) cortisol 24 cortisol

32.4g/dl(13.1 59.8) 820 µg(106 4590)

. 40

LDDST HDDST LDDST

(2.5%) 가 39 (97.5%)

, HDDST 34 (85%)가

6 (15%)가

4. 신경방사선학적 검사

MRI

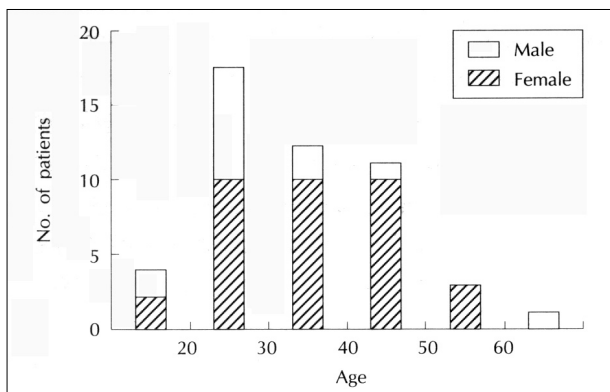


Fig. 1. Distribution of gender according to age.

Table 1. Presenting symptoms of Cushing's disease (N = 48)

Symptom	Patient	(%)
Obesity	40	(83%)
Hypertension	30	(63%)
Headache	21	(44%)
Easy bruise	17	(35%)
Fatigability	14	(29%)
Irregular menstruation	13	(27%)
Hirsutism	9	(19%)
Diabetes mellitus	9	(19%)
Visual acuity	8	(17%)
Palpitation	6	(13%)
Mental change	3	(6%)
Loss of libido	2	(4%)

42 (87.5%)

38 ( 18 , 20 )

, MRI 가

MRI 90.5%(38/42)

100% . MRI

6.9mm ,

. MRI 6 41

가 7 1cm

. 31 IPSS 가

29 (93.5%)

MRI

29 21 (72.4%)

MRI가 IPSS

5. 치료

51 TSA 가 42

82% . 34

32 가 , 4

4

12 9 가 ,

1 가 (Table 2).

가 9

1) 가 7 , 2) MRI

IPSS 가 가 6 , 3)

가 가 5 , 4)

4 가

42 4 (9%)가

8, 10, 28, 54 . 4

30 , MRI 가

가 가 2 .

9 ketoconazole 3 가

, 2 ketoconazole 1

1 가 .

4 3 TSA , 1

(Table 3).

Table 2. Outcome according to operation method

Operation	Remission (%)	Failure (%)
Selective adenomectomy	32( 94)	2( 6)
Partial adenomectomy	0( 0)	4(100)
Hemihypophysectomy	9( 75)	3( 25)
Total hypophysectomy	1(100)	0( 0)

**Table 3.** Treatment and its result after surgical failure

Treatment	Number of cases	Result
Initial failure(N = 9)		
Radiation + Ketoconazole	6	3 remission(50%)
Ketoconazole only	2	1 remission(50%)
Follow-up loss	1	?
Recurrence(N = 4)		
Revision TSA	3	3 remission(100%)
Radiation	1	1 remission(100%)

**Table 4.** Analysis of possible prognostic factors and outcome

Prognostic factors	Remission(%)	Failure(%)	Statistics*
MRI localization			
Localized	36(86)	6(14)	p = 0.036
Unlocalized	3(50)	3(50)	
Symptom duration			
Under 36months	28(90)	3(9)	p = 0.030
Over 36months	11(64)	6(35)	
Tumor size			
Microadenoma	35(85)	6(14)	p = 0.077
Macroadenoma	4(57)	3(43)	
Preop s-ACTH level			
Below 65.9pg/ml	22(82)	5(18)	p = 0.963
Above 65.9pg/ml	17(81)	4(19)	
Preop s-cortisol level			
Below 32.4ug/dl	13(81)	3(19)	p = 1.000
Above 32.4ug/dl	26(81)	6(19)	
Preop u-cortisol level			
Below 820ug	13(68)	6(32)	p = 0.065
Above 820ug	26(90)	3(10)	
HT or DM			
Present	23(74)	8(26)	p = 0.091
Absent	16(94)	1(6)	

\* : Chi-square test

48                      43  
89.6%

6. 합병증

2  
1                      4                      7.8%

7. 예후인자

(Table 4).

3

**Table 5.** Surgical outcome of TSA in literature

Authors(year)	Success rate(%)	Recurrence rate(%)	Follow up (months)
Salassa, et al. (1978)	16/18(89)	0/16(0)	18
Hardy(1982)	63/75(84)	0/63(0)	21
Semple, et al.(1984)	17/19(89)	1/17(6)	40
Tagliaferri, et al.(1986)	19/23(76)	2/19(11)	39
Chandler, et al.(1987)	24/34(71)	-	-
Nakane, et al.(1987)	86/100(86)	8/86(9)	38
Guihaume, et al.(1988)	42/61(69)	6/42(14)	24
Mampalam, et al.(1988)	171/216(79)	9/171(5)	46
Arnott, et al.(1990)	24/28(86)	3/24(13)	22
Burke, et al.(1990)	44/54(82)	2/44(5)	56
Tindall, et al.(1990)	46/53(87)	1/46(2)	57
Robert, et al.(1991)	60/78(77)	5/60(8)	77
Tahir, et al.(1992)	34/45(76)	7/34(21)	69
Trainer, et al.(1993)	39/48(81)	3/39(8)	-
Ram, et al.(1994)	205/222(92)	-	-
Bochicchio, et al(1995)	510/668(76)	65/510(13)	-
Present series(2000)	42/51(82)	4/42(10)	48
Total	1418/1759(80.6)	116/1213(9.6)	

, MRI 가  
cortisol 820g 가  
ACTH cortisol ,  
가 .  
7 가 1  
가 4  
2 가 가 .  
고 찰

TSA가  
가 20

(Table 5)<sup>1)2)5)11)12)17)18)20-23)25)26)28)29)</sup>

82%  
. MRI

, (1)

가 , (2) 1 13 가  
, (3) , (4) 가  
corticotropin , (5) TSA 가  
, (6) 2 가  
, (7) 50%, 85% 가  
4)7)8)11)18)25)28). 8)16)20).  
ketoconazole  
가 , MRI 가  
가 가 20). TSA  
MRI 가 가 71% , Friedman 10) 73%  
26% Nel -  
son 가  
1 TSA  
가  
IPSS 가 93.5% 가 가  
MRI IPSS 가  
가 가  
5 20% 2)18)24)28).  
, MRI  
가 2 4 2)11)15). Bo -  
chicchio 2) 104 ,  
(1) cor - 3)8)24). MRI 가  
tisol , (2) 가  
, (3) cortisol 가  
, (4) 가  
2)18)24)28). 9% 가 24 cortisol 가  
54 가  
30  
결 론  
가 , 1 48  
2 TSA가  
, (82%) 1  
가

TSA

MRI IPSS  
MRI가 100%

MRI 가  
( > 3 )

- : 2000 3 9
- : 2000 7 25
- :

110 - 744 28

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