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Long-term remission and recurrence rate in a cohort of Cushing's disease: the need for long-term follow-up.*

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Background

Transsphenoidal surgery (TSS) is the procedure of choice in Cushing disease (CD), with inmediate post-operative remission rates ranging between 59 and 94% and recurrence rates between 3 – 46%, both depending upon the definition criteria and the durationt of the follow-up.

Our aim was to assess the rate of remission, recurrence and persistence of the disease after the first treatment and to identify predictors of remission in the CD population of our center during the last 40 years.

Methods

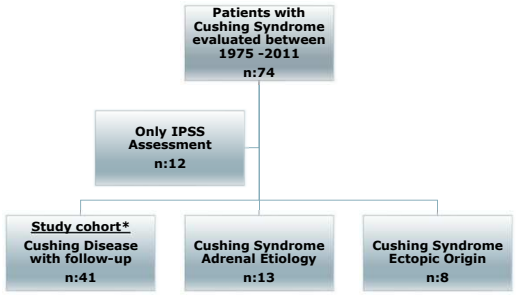
Retrospective cohort study of the patients diagnosed of CD and with complete follow-up in our center between 1974 and 2011.

We analyzed 41 patients (35 women and 6 men) with a mean age at diagnosis of 34±13 years. The mean follow-up was 14±10 years (1 – 37 years) and the median of follow-up period was 6.68 years.

p-value was considered significant when <0.05 (p**<0.05)

Results

Study cohort selected from the wole serie of Cushing Syndrome diagnosed between 1975 - 2011



•Our study cohort
IPSS: inferior petrosal sinus sampling

Preoperative data of Cushing's disease patients with remission and persistent disease after first treatment

	Remission (n:32)	Failure (n:9)	*p-value*
Gender ♀/♂	30/2	5/4	**0.015****
Age (years)	32±12	38±16	0.255
Durations of symptoms (yr)	2.0±1.2	2.3±1.4	0.527
24h-UFC (mcg/24hs)	347.03±152.5	292.8±58.9	0.212
Cortisol 8hs (mcg/dl)	25.9±8.0	28.8±7.28	0.403
Night Cortisol (mcg/dl)	23.6±11.3	22.7±5.8	0.828
Plasma ACTH (pg/ml)	60.9±32.3	89.0±49.8	0.092
1mg- overnight dexamethasone cortisol	14±5.16	15.09±7.43	0.685
Microadenoma	16	3	0.645
Macroadenoma	4	2	0.668
Normal pituitary image	8	2	0.703
Postoperative adrenal insufficiency*	12	0	**0.037****
Adenoma in histopathology*	14	3	0.772
Normal pituitary in histopathology*	9	2	0.671
Hypopituitarism	16	6	0.381
Panhypopituitarism	7	5	**0.033****
Mortality	2	1	0.535

Baseline differences between patients with persistent remission after the first treatment *vs.* after several treatments *vs.* persitent disease

	Remission after 1 treatment (n:10)	Remission after several treatments (n:23)	Persistent disease (n: 8)	*P* value
Age (years)	37±13	30±13	40±14	0.197
Gender ♀/♂	8/2	20/3	7/1	0.858
Durations of symptoms (yr)	1.8±1.3	1.8±0.8	3.6±1.6	**0.009****
24h-UFC (mcg/24hs)	322.1±120	352.2±158.7	317.07±147.09	0.851
Cortisol 8hs (mcg/dl)	21.2±3.4	29.9±8.5	25.06±4.5	**0.018****
Night Cortisol (mcg/dl)	14.7±5.4	28.01±8.9	14.9±1.03	**0.018****
Plasma ACTH (pg/ml)	72.3±35.8	72.8±40.9	36.7±15.5	0.224
1mg-overnight dexamethasone cortisol	12.5±5.52	15.0±6.22	15.9±4.06	0.558
Recurrence time (years)	0	2.2±1.5	3.0±1.9	0.333
Follow up time (years)	7.7±5.1	18.4±9.9	7.13±5.3	**0.001****
Time of disease activity (years)	2.5±3.6	5.5±4.5	6.6±3.9	0.103
Microadenoma	5	8	6	0.267
Macroadenoma	1	3	2	0.280
Normal pituitary image	2	8	0	0.242
Postoperative adrenal insufficiency*	6	4	2	0.054
Adenoma in histopathology*	6	8	3	0.634
Normal pituitary in histopathology*	3	6	2	0.640
Hypopituitarism	4	16	2	0.051
Panhypopituitarism	2	9	1	0.305

Treatment Outcomes

- Thirty-five (85.4%) patients underwent transsphenoidal surgery as first treatment option.
- Histopathological evidence of pituitary adenoma was registered in seventeen (48.5%) patients.
- Thirty-two **(78%)** patients achieved disease remission after the first treatment; 21 **(65.6%)** of them presented disease recurrence.
- Mean time to recurrence was 2.4±1.7 years (range 0.5 – 5yr).
- Pesistent disease was observed in 9 **(22%)** patients.
- Twelve (29.3%) subjects developed post-surgical adrenal insufficiency; seven of them (70%) achieved stable remission.
- Two parameters were found to be significant predictors of remission after the first treatment: age at CD diagnosis *(p:0.05)* and the development of adrenal insufficiency in the inmediate post-operative state *(p:0.03)*
- Overall lethality index was 7.3%; 75% (2/3) being females.

Conclusions

- The recurrence rate in our serie is higher than in many others probably due to the long follow-up time.
- Early post-surgery adrenal insufficiency predicts remission rate.
- Hypopituitarismo was also higher and strongly associated with radiotherapy
- This leads us the coclusions that CD needs a life-long close follow-up

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