MANAGEMENT OF CUSHING'S DISEASE: SINGLE CENTER EXPERIENCE

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INTRODUCTION

Cushing's disease (CD) is an uncommon condition of excess endogenous glucocorticoids caused by ACTH secreting pituitary corticotroph adenoma.

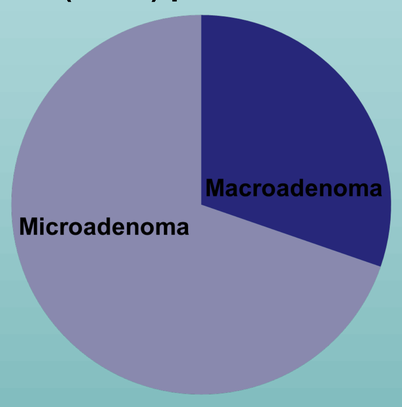
The purpose of this study is to review therapeutic outcomes and comorbidity of patients with CD in a single center.

METHODS

We conducted a retrospective study of 33 patients with CD undergoing transsphenoidal surgery from January 2007 to February 2014 (27 female and 6 male, median age 38 years, range 18-71 years). The median follow-up period was 28 months (range 1 - 122 months).

The diagnosis of Cushing's syndrome was established on the basis of the patient's history, characteristic clinical features and laboratory data, including elevated 24-h urinary free cortisol (UFC) level, lack of serum cortisol suppression after suppression tests (1-mg overnight dexamethasone suppression test and/or 2 mg-2 days dexamethasone suppression test) and elevated midnight cortisol level. In 28/33 patients tumor was visualized on MR of sellar region, while in 5 it was diagnosed using an inferior petrosal sinus sampling.

Figure 1. Macroadenoma (N=10) vs. micoradenoma (N=23) patients



RESULTS

Ten patients had macroadenoma, the remaining 23 had microadenoma (Figure 1). Transsphenodial surgery was applied as the first line treatment in all the patients after which 18/23 (78.3%) of the patients with a microadenoma and 8/10 (80%) of those with a macroadenoma achieved remission of the disease (Table 1).

Seven patients failed to achieve disease remission. They were treated with second-line treatment modalities (second operation, radiotherapy, bilateral adrenalectomy and/or ketoconazole). One patient rejected all treatment modalities after surgery.

Cumulative remission after all the treatment modalities was achieved in 90.9% of patients.

In the follow-up period one female patient with a macroadenoma and one with a microadenoma had recurrence of hypercortisolism (29 and 12 months after the initial remission, respectively). The first patient underwent another transsphenoidal surgery followed by ketoconazole treatment, after which temozolomide and conventional radiotherapy were employed. The other patient with the recurrence of Cushing's disease is taking ketoconazole.

Twenty-one patients (63.6%) had hypertension, 17 (51.5%) dyslipidemia, while 7 (21.2%) had type 2 diabetes or Impaired Glucose Tolerance. The postoperative frequencies of hypertension, dyslipidemia and type 2 diabetes mellitus or IGT were 30.3%, 24.2% and 12.1% respectively, which was statistically significantly lower compared to the preoperative frequencies (Table 2).

Table 1. Disease outcome in relation to tumor size in total cohort (N=33)

	Microadenoma (N=23)	Macroadenoma (N=10)
Remission after surgery	18/23 (78.3%)	8/10 (80%)
Remission after all treatment modalities	21/23 (91.3%)	9/10 (90%)

Table 2. Prevalence of the most frequent comorbidities in the total cohort (N=33)

Comorbidity	Before treatment N (%)	After treatment N (%)	p
Hypertension	21 (63.6)	10 (30.3)	0.007
Dyslipidemia	17 (51.5)	8 (24.2)	0.022
Diabetes mellitus or IGT	7 (21.2)	4 (12.1)	0.322

CONCLUSION

Cushing's disease is associated with multiple complications resulting in significant morbidity that severely impairs the quality of life and increases mortality when the disease is not controlled. Early diagnosis and treatment are important in terms of reducing such complications and cardiovascular risk. Cumulative remission after all treatment modalities in our study was achieved in 93.9% patients. The results are comparable to leading centers in the world and they demonstrate that, when combining all the available treatment modalities, remission rates can increase to almost 100%.

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