Efficacy of Repeat Transsphenoidal Surgery for Recurrent Cushing's Disease

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Introduction

To systemically review indications and outcomes in patients undergoing repeat transsphenoidal surgery (TSS) for recurrent Cushing's disease (CD).

Methods

Retrospective analysis and a literature review was performed. The retrospective analysis was conducted on the 'Current Cohort,' occurring between 2008 - 2016, which consists of patients who have at least 24 months of post-op follow up after undergoing repeat transsphenoidal surgery (TSS) with senior author (ERL) for recurrent CD, performed at Brigham and Women's Hospital (BWH).

Patients were included for retrospective analysis if they underwent repeat TSS for clinical and/or biochemically recurrent CD with follow up at least 24 months post-operatively. Immediate post-operative remission was defined biochemically as serum cortisol < 5 microgram/dl or clinical adrenal insufficiency and remission on follow up was defined as normal 24-hour urine free cortisol or need for glucocorticoid replacement.

A 'Combined Cohort' was created which includes the Current Cohort pooled with a group of patients who underwent repeat TSS with senior author for recurrent CD at a different institution, obtained from prior publication, between 1992 – 2006. (1)

Results

Potential Predictors	Current: Total Patients (12)	Current: Immediate Remission (11)	Combined: Total Patients (48)	Combined: Immediate Remission (33)
MRI Presence				
Positive	7	7 (100%)	33	20 (60.6%)
Negative	5	4 (80%)	15	13 (86.7%)
Final Pathology				
Positive	7	6 (85.7%)	31	18 (58.1%)
Negative	5	5 (100%)	17	16 (94.1%)
Extent of Resection				
Lesionectomy	3	3 (100%)	27	17 (63.0%)
Hemi-Hypophysectomy	2	2 (100%)	3	2 (66.7%)
Subtotal Hypophysectomy	6	5 (83.3%)	12	9 (75.0%)
Total Hypophysectomy	1	1 (100%)	6	5 (83.3%)

Results

Current Cohort

The current cohort included 12 patients. Pre-operative MRI showed evidence for tumor recurrence in 7/12 (58.3%) patients, and following TSS 5/12 (41.7%) patients had a pathology report that was negative for ACTH secreting tumor. Operations performed included: lesionectomy 3/12 (25.0%), hemi-hypophysectomy 2/12 (16.7%), subtotal hypophysectomy 6/12 (50.0%), and total hypophysectomy 1/12 (8.3%).

Remission was achieved immediately post-operatively in 11/12 (91.7%). Over an average follow up of 51.7 months (range: 24 – 96), 9/12 (75.0%) achieved continued remission. Two patients with initial remission had recurrence of CD at 24 and 50 months postoperatively.

Combined Cohort

When combined with the historical cohort, 33/48 (68.8%) had evidence of recurrent disease on pre-operative MRI and 17/48 (35.4%) patients had a pathology report that was negative for ACTH secreting adenoma. Operations performed included: 27/48 (56.3%) lesionectomy, 3/48 (6.25%) hemi-hypophysectomy, 12/48 (25.0%) subtotal hypophysectomy, and 6/48 (12.5%) total hypophysectomy.

Thirty-three (68.8%) patients went into remission immediately post-operatively and 29/48 (60.4%) had continued remission at most recent follow up averaging 40.1 months (range 2 – 126). Four patients had recurrence of CD after initial remission at 6, 11, 24, and 50 months postoperatively.

Endoscope vs. Microscope

All patients in the Current Cohort (n=12) underwent operations using endoscopy, while all patients from the previously published study (n=36) underwent operations with microscopy. Operations using endoscopy were significantly more likely to achieve immediate remission (11/12 vs. 22/36; p=0.047).

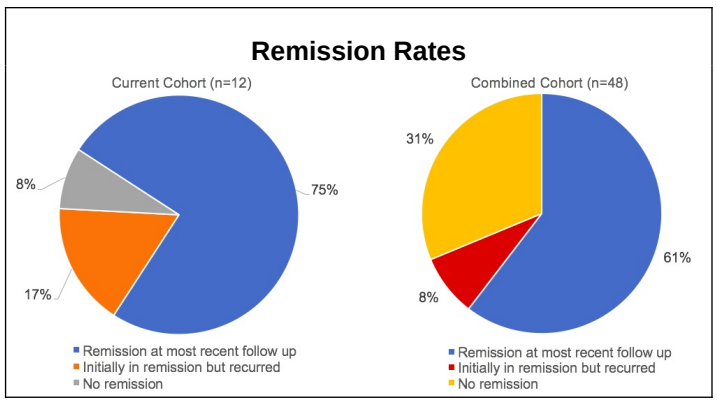
Conclusions

Recurrent CD recurrence can be a therapeutic challenge; however, these data demonstrate repeat surgery is an effective and safe next step prior to radiation or medical therapy.

The predictive value of tumor presence on pre-op MRI may be overstated, with 80% and 86.7% of patients with no identifiable tumors achieving immediate remission.

The predictive significance of ACTH tumor on patholgy report folowing TSS may be overstated, with 100% and 94.1% of patients with a negative pathology report achieving immediate remission.

Endoscopy use results in a more likely chance of immediate remission in this single surgeon study.



References

(1) Patil CG, et al., Outcomes After Repeat Transsphenoidal Surgery for Recurent Cushing's Disease. Neurosurgery. 2008 63:226-270.