Endocrinologic Outcome Following Endonasal Transphenoidal Excision of Growth Hormone Secreting Pituitary Adenomas

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ABSTRACT

Background: Endonasal Transphenoidal Approach for excision of pituitary adenomas has been gaining popularity over the traditional microsurgical approach. The objective of this study is to assess the rate of hormonal recovery following endonasal transphenoidal excision of growth hormone secreting pituitary macroadenoma in out center.

Methods: In this prospective observational study all cases subjected to endonasal transphenoidal excision of growth hormone secreting pituitary adenoma, during the study period from January 2019 to December 2020 at National Neurosurgical Referral Center, Bir Hospital, Kathmandu were included in this study. Preoperative and postoperative patient characteristics were recorded. Hormonal remission was defined as normal insulin-like growth factor-1 level at 3 months follow-up.

Results: A total of 24 cases were included. The mean age of acromegaly cases was 39.42±10.41 years (24-56 years), with male to female ratio of 0.71:1. Majority (9) of cases had a Knosp grade 1.Thirteen cases had a Wilson-Hardy Extension Grade 0. Majority (11) of cases had a Wilson-Hardy Invasion Grade I. Three cases developed post-operative CSF leak, which recovered after lumbar drainage with no sequel. Five cases developed epistaxis which resolved with nasal packing. Sixty three percent (15 cases) had normal IGF-1 levels at 3 months follow up.

Conclusion: Endoscopic endonasal transphenoidal approach to excision of growth hormone secreting pituitary adenomas is a safe and effective modality at achieving hormonal control in our setting.

Keywords: Acromegaly, Endoscopy, Outcomes, Short-term, Transsphenoidal

INTRODUCTION

Acromegaly is a clinical syndrome that arises as a result of excessive Growth Hormone (GH) secretion from the pituitary gland.[1] GH itself and its stimulated hypersecretion of insulin-like growth factor-1 (IGF-1) from the liver causes the characteristic clinical features of acral and soft tissue overgrowth, jaw overbite, arthritis, respiratory obstruction and headache.[2] The associated metabolic dysfunction and cardiovascular disease are the main contributing factors to increased mortality in these patients.[3,4]

The treatment of choice for acromegaly is surgical excision of pituitary adenoma, with the goal of lowering IGF-1 concentration to within normal range.[2] The microsurgical transphenoidal approach has been the most frequently used approach.[5,6] More recently the fully endoscopic approach has gained popularity, having several advantages such as larger field of view, and has been found to be efficacious in the long term.[5]

The objective of this study is to assess the rate of short term hormonal recovery following endonasal transphenoidal excision of growth hormone secreting pituitary macroadenoma at our center. As secondary objective we evaluate the complications and morbidity following the procedure in the short term. Knowing the hormonal recovery rates and complications occurring at our center will allow optimization of care.

METHODS

A prospective analytical study was conducted over a duration of two years, from January 2019 to December 2020, at National Neurosurgical Referral Center, Bir Hospital, Kathmandu, Nepal. All patients undergoing endonasal transphenoidal excision of pituitary adenoma

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for acromegaly during the study period were included. Approval from the Institutional Review Board, National Academy of Medical Sciences, Bir Hospital was obtained (IRB Ref No. 871/2077/78).

Initial evaluation and optimization of all patients were done by endocrinologist before admission. Diagnosis of tumour was made following contrast enhanced MRI, and acromegaly was confirmed after measuring serum GH and IGF-1 levels. All the cases in our series were offered surgery as first line therapy, and no patients were placed on medical therapy initially. Preoperative visual field assessment was done by Ophthalmologist. Un-enhanced CT scan of head was done for neuronavigation purposes. Nasal swab was also taken for culture to rule out pathogenic organisms and to guide postoperative antibiotic use. Endonasal transphenoidal excision of the pituitary tumour was done with the use of a stereoscopic endoscope (VisionSense®) with guidance from neuronavigation (Medtronic Stealth Station®). Decision to place a lumbar drain was made if a CSF leak was identified intraoperatively. At the end of procedure, nasal packing was done using Merocel coated with soframycin cream. Patients were managed in ICU for the initial 48 hours. Nasal pack was removed after 48 hours and patients were transferred to ward and typically discharged within 7 days. Postoperative visual field assessment was done after discharge. Hormonal assessment was done 3 months after surgery.

Data were collected using standard proforma. Data entry and analysis was done using IBM SPSS® 22 software. The statistical tests used were student t-test for comparison of means and chi-square test for comparison of frequencies.

RESULTS

During the study period, 84 patients underwent Endonasal Transphenoidal Excision of Pituitary adenoma at the study site. Twenty seven patients had a diagnosis of acromegaly. Three of these patients were excluded from the study due to incomplete data. A total of 24 cases were included in this study. (**Figure 1**)

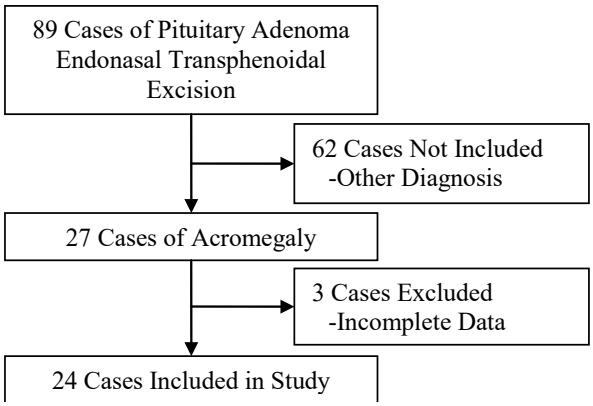

Figure 1: Case selection process

The mean age of cases was 39.42±10.41 years (24-56 years). The mean age was similar to that of other cases of pituitary adenoma that were operated in this center (40.35±12.32 years, p = 0.742). Females were more common in the acromegaly cases, with the male to female ratio being 0.71. The other cases of pituitary adenoma also had a similar male to female ratio (0.55, p = 0.595) (**Table 1**).

Table 1: Comparison of age and sex between cases of acromegaly and other cases of pituitary adenoma.

Variables	Cases of Acromegaly	Other cases of pituitary adenomas	p value
Age (years)	39.42±10.41	40.35±12.32	0.742[a]
Sex (M:F)	0.71:1	0.55:1	0.595[b]

[a]Student t-test, [b]Chi Square Test

The majority of cases had a Knosp Grade[7] of 1 (9 cases). Thirteen cases had a Wilson-Hardy[8,9] Extension Grade 0. Majority of cases had a Wilson-Hardy[8,9]8,9 Invasion Grade I (11 cases). (**Figure 2**).

At presentation, 6 patients had some visual field defects. Out of them, 4 had visual improvement after surgery, and none of the cases had deterioration of vision. The most common other hormonal imbalance in the series was hypothyroidism (6 cases), followed by hypocortisolism (3 cases). Five cases had diabetes mellitus type 2, and four had hypertension.

With regard to post operative complications, 3 cases developed CSF leak, which resolved after lumbar drainage with no sequel, except for a prolonged hospital stay. The 3 cases with CSF leak stayed in the hospital for an average duration of 10 days longer. Five of the cases developed epistaxis following removal of nasal pack. The bleeding resolved with re-packing of the nasal cavity. None of the cases developed postoperative meningitis. There were no mortalities in this series.

The mean preoperative IGF-1 level, relative to upper limit of normal for age and sex (ULN), was 4.03±1.65 times ULN. On assessment of IGF-1 levels at 3 months following surgery, 15 cases had normal levels. This is a hormonal control rate of 63%. All of the cases that did not achieve remission (9 cases) were started on cabergolin and placed on follow up.

DISCUSSION

The current recommendation of the Acromegaly Consensus Group is that all acromegaly cases undergo treatment by a multidisciplinary team.10 This is the standard of care provided to patients at our center, in which all cases undergo evaluation and optimization by endocrinologist before the first line surgical intervention.

The strategies that have been employed for first line management of acromgealy are surgery and use of somatostatin analogues (SRL).2 Out of these modalities, the most cost effective one has been found to be surgery.11This is the case in our setting also, and surgery is offered to all cases as first line therapy.

The remission rate following surgical excision of pituitary adenoma in acromegaly is around 65% in previous studies.5,12 Taghvaei et al. (2018) in their study of 68 cases, who underwent endonasal excision, had remission rate of 64.7%, while Aydin et al. (2020) studied 106 cases where the remission rate was 66.3%.13,14 Our result of 63% is similar to previous studies. The follow-up duration in our study is 3 months, therefore we were unable to assess long

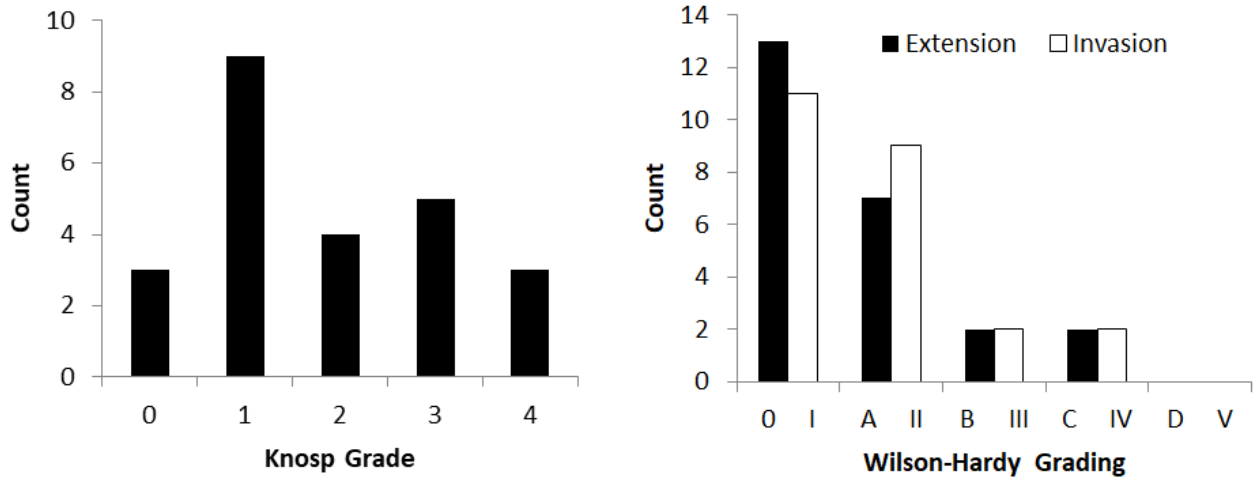

Figure 2: Knosp and Wilson-Hardy grading of tumours in cases of Acromegaly

term outcome with this data. A study with longer duration of follow-up will be helpful in making this assessment.

Previous studies have found the endonasal approach to be both safe and effective in management of acromegaly.5,14 In our case series there were no mortalities following surgery. All of the complications that occurred – CSF leak and epistaxis – were managed with no sequel except for a prolonged hospital stay. None of the cases developed post-operative meningitis or had increased visual deficit following surgery. The results from our study demonstrate the safety of the endonasal approach at this hospital. We were unable to compare the endonasal approach to the sublabial microsurgical approach in this study. A 2017 retrospective study by Phan et al. has demonstrated improved outcomes when compared to microsurgical approaches.15 To date there are no randomized trials comparing the two modalities.

According to the Acromegaly Consensus Group, hormonal assessment should be done at least 12 weeks after surgery.10 The current recommendations for first-line therapy in patients with persistent disease after surgery is either first-generation SRL (octreotid or lanreotide) or Cabergolin.10 Because of the high cost of SRLs, our patients are typically offered cabergolin, and followed-up by endocrinologist. Patients that have persistent disease even with cabergolin are offered re-surgery. Our study does not assess patients who undergo re-surgery at our center.

CONCLUSION

Endoscopic endonasal transphenoidal approach to excision of GH secreting pituitary adenoma is an effective modality at achieving hormonal control in our setting.

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