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Incidence of headache as a presenting complaint in over 1000 patients with sellar lesions and factors predicting postoperative improvement

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ABSTRACT

Introduction: Due to the high incidence of headaches and pituitary tumors, neurosurgeons often evaluate patients with benign-appearing sellar lesions and headaches without insight into whether the headache is attributable to the lesion. We sought to evaluate the incidence of headache as a presenting complaint in patients undergoing transsphenoidal surgery for various pathologies and to identify factors predicting postoperative improvement.

Methods: We conducted a 5-year retrospective review of our first 1015 transsphenoidal surgeries since establishing a dedicated pituitary center.

Results: Of 1015 patients, 329 (32%) presented with headache. Of these 329 patients, 241 (73)% had headache as their chief complaint. Headache was most common in patients with apoplexy (84%), followed by Rathke's cleft cysts (RCCs) (60%). Multivariate analyses revealed diagnosis ($P = 0.001$), younger age ($P = 0.001$), and female gender ($P = 0.006$) to be associated with headache. Of patients presenting with headaches, 11% reported improvement at 6-week follow-up and 53% improved at 6-month follow-up. Multivariate analyses revealed gross total resection (GTR; $P = 0.04$) and decreased duration of headache ($P = 0.04$) to be associated with improvement, while diagnosis, age, gender, lesion size, whether headache was a chief complaint, and location of headache were not associated with improvement ($P > 0.05$).

Conclusion: In analyzing over 1000 consecutive patients undergoing transsphenoidal surgery, younger patients, females, and patients with RCCs and apoplexy were more likely to present with headache. Patients who underwent GTR and had shorter duration of headache were more likely to experience headache improvement. This information can be used to counsel patients preoperatively.

1. Introduction

Lesions of the sellar and parasellar region are a common finding in the general population. In fact, the prevalence of these lesions discovered incidentally ranges anywhere from 1.7% to as high as 27% based on cadaveric and healthy volunteer imaging studies [1–3]. Despite their high prevalence, these lesions become symptomatic less frequently, with registry-based epidemiologic studies reporting incidences of 8 per 100,000 person-years [4], leading to an estimated prevalence of symptomatic adenomas in the range of 1:1000–1:1300 based on recently published work from well-defined populations [5,6]. While these ranges are far more frequent than previous reports, which were limited to patient populations from tertiary centers [5–7], their continued contrast with cadaveric and healthy volunteer imaging studies still suggests that at most 5% of adenomas that are present are symptomatic. Symptoms arise from the narrowed confined space of the sella and parasellar region, in which expanding masses can lead to clinical symptoms such as visual abnormalities or endocrine deficits [8,9]. The transsphenoidal approach for surgical resection of sellar and parasellar lesions has proven to be a safe and effective method for improving and eradicating presenting complaints of vision loss and hypopituitarism, as reported by our group as well as others [10–12].

While anatomy, preoperative testing, and surgical results make it clear that hypopituitarism and vision loss are attributable to these lesions, in the case of headache in patients with sellar lesions, the

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evaluation is considerably more complicated. This is because, just as sellar pathology is quite common on volunteer imaging studies as described above, headaches are quite common in the general population with a point prevalence of 22% in women and 11% in men, either arising from different underlying pathologies or of unclear etiology [13]. Headache as a presenting complaint among patients with pituitary lesions has been reported to have a wide range, ranging from 33% to as high as 72%, but consistently higher than the prevalence of headaches in the general population, meaning that sellar lesions do cause headaches beyond the high basal level of headaches seen in the general population [11,14–18]. In fact, headache is often the primary reason for pituitary patients seeing a physician, which leads to the discovery of the tumor on imaging studies [11,14–18]. These numbers render the decision whether to resect sellar and parasellar lesions in patients with headaches who lack other indications for surgery challenging. While it is reasonable to hypothesize that mass effect on the innervated dura from a lesion that has yet to self-decompress by breaking through anatomic constraints such as the sellar bone preventing erosion into the sphenoid sinus or the diaphragma preventing suprasellar extension, deciding which patients are exhibiting headache from this mass effect and which have headache not attributable to their sellar lesion is challenging. Unfortunately, rates of headache improvement after transsphenoidal surgery have not been evaluated in a large cohort, rendering it difficult to identify preoperative factors associated with improvement.

In this study, we sought to evaluate headache as a presenting symptom to determine variables related to its improvement in patients harboring pituitary lesions. We investigated the prevalence and rate of headache and its improvement in transsphenoidal surgery in a comprehensive series of 916 consecutive patients with representative pathologies of the wide spectrum seen in practice and who were operated on during the past 5 years at our institution.

2. Methods

2.1. Study design, setting, and participants

Our study retrospectively reviewed the first 1015 transsphenodial surgeries in the 5-year time period since establishing a pituitary center of expertise. This study was reviewed and approved by our institution's Committee on Human Research.

2.2. Variables recorded pre-operatively

After carefully reviewing medical records of the patients in this study, we collected information on each patient's age at time of the operation, gender, size of the lesion (average of the maximal anteroposterior, left-right, and superoinferior dimensions on preoperative MRI), lesion type (endocrine-inactive adenoma, endocrine-active adenoma, Rathke's cleft cyst, apoplexy, hypophysitis, craniopharyngioma, or other), number of prior pituitary surgeries, endonasal surgical approach (49 endoscopic versus 966 microscopic operations), location of the lesion (suprasellar, sellar, or sellar with suprasellar extension), and the presence of preoperative hypopituitarism. Records were also reviewed for duration and location of headache, as well as to classify apoplexy as subacute versus acute as we have described previously [19].

2.3. Variables recorded post-operatively

Post-operative notes as well as follow-up records form clinic visits were carefully reviewed to assess for symptomatic improvement of headaches as well as any other presenting complaints. Operative notes as well as post-operative MRI scans were carefully reviewed to evaluate extent of resection and patients were categorized as either having undergone gross total or subtotal resection.

2.4. Statistical methods

In conducting parametric comparisons of greater than two variables with a continuous dependent variable, we utilize the analysis of variance (ANOVA) test, and when comparing greater than two proportions we used a chi-squared test. The Student's t test was used for parametric comparison between two variables, while Fisher's exact test was utilized when comparing two proportions. P values <0.05 are deemed statistically significant and all P values are 2 tailed. Multivariate logistic regression was used to correlate preoperative variables with postoperative improvement of headache.

3. Results

3.1. Participants

Our study cohort comprised 916 patients who underwent 1015 operations. At the time of the initial operation, the mean age was 47 years (4–93) with 492 female patients (54%). The mean size among all lesions was 2.0 cm (3 mm–6.7 cm). Diagnoses included endocrine active (36%) or inactive (30%) adenomas, Rathke's cleft cysts (10%), craniopharyngioma (4%), apoplexy (5%), hypophysitis (2%), and miscellaneous pathology (13%).

3.2. Characterization of preoperative headache

Before the 1015 operations, 329 patients (32%) presented with a headache. Of these 329 patients, 241 patients (73%) presented with headache as their chief complaint, while 88 patients (27%) had headache as a secondary symptom associated with a different chief complaint. Of the 241 patients with headache as their chief complaint, 84 patients (35%) presented with headache as their only complaint, while 157 (65%) had headache as the chief complaint associated with other secondary symptoms. Of the patients who reliably localized their headache, locations included: 25 bifrontal (28%), 23 frontal (26%), 23 retro-orbital (26%), 9 temporal (10%), and 8 occipital (9%). Of 471 patients with adenomas not invading the cavernous sinus, 127 (27%) had headache, comparable to the 51 of 155 (33%) patients with unilateral cavernous sinus invasion and the 13 of 44 (30%) patients with adenomas invading both cavernous sinuses ($P > 0.05$). Of all patients who reliably gave a duration of their headache, median duration was 2 months (range = 1 day to over 30 years). Apoplexy patients reported a much shorter duration of headache (mean = 4 days; median = 7 days; range = 1–10 days) than non-apoplexy patients (median = 2 months; range = 4 days to over 30 years) ($P < 0.05$). For patients with headache as a chief complaint, the mean duration was 17 months (range = less than 24 h to over 30 years), compared to a mean of 11 months for patients with headache as a secondary complaint.

3.3. Variables associated with headache

Multivariate analyses revealed diagnosis ($P = 0.001$), younger age ($P = 0.001$), and female gender ($P = 0.006$) to be associated with headache, while lesion size, suprasellar extension, number of the operation, vision loss, and hypopituitarism were not associated with headache as a presenting complaint (Table 1).

Patients with apoplexy had the highest percentage of headache at 84%, followed by Rathke's cleft cysts (RCC) (60%), hypophysitis (50%), and craniopharyngioma (46%) while endocrine inactive and active adenomas had lower rates of headache (28–29%) ($P < 0.05$) (Fig. 1). Apoplexy patients had high rates of headaches regardless of whether their presentation was acute (symptoms for 1 day, 89%