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FOCUS SESSION

Outcomes following endoscopic endonasal resection of sellar and supresellar lesions in pediatric patients

Christoforos Koumas[1] · Anya Laibangyang[1] · Shanna L. Barron[2] · Mark A. Mittler[1,2] · Steven J. Schneider[1,2] · Shaun D. Rodgers[1,2]

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Abstract

Purpose The endoscopic endonasal approach (EEA) is a credible surgical alternative for the resection of sellar and suprasellar lesions such as pituitary adenomas, craniopharyngiomas, and Rathke cleft cysts. However, its application to pediatric patients poses several unique challenges that have not yet been well evaluated. The authors evaluate the safety, efficacy, and outcomes associated with the use of the EEA for treatment of these pathologic entities in pediatric patients.

Methods Retrospective review of 30 patients between the ages of two and 24 who underwent endoscopic endonasal resection of sellar or suprasellar lesions between January 2010 and December 2015. Endocrinological and ophthalmological outcomes, as well as extent of resection and complications were all evaluated.

Results Gross total resection was achieved in eight of the nine pituitary adenomas, nine of the 12 craniopharyngiomas, and six of the nine Rathke cleft cysts. Of the 30 patients, 22 remained disease free at last follow-up. A total of six patients developed hypopituitarism and five developed diabetes insipidus. Eleven patients experienced improved vision, sixteen experienced no change, and one patient experienced visual worsening. Postoperative cerebrospinal fluid leak was seen in a single case and later resolved, vasospasm/stroke was experienced by 10% of patients, and new obesity was recorded in 10% of patients. There were no perioperative deaths.

Conclusions Endoscopic endonasal resection is a safe and effective surgical alternative for the management of sellar and suprasellar pathologies in pediatric populations with excellent outcomes, minimal complications, and a low risk of morbidity.

Keywords Pediatric neurosurgery · Endoscopic · Endonasal · Sellar · Suprasellar

Introduction

Pituitary adenomas, craniopharyngiomas, and Rathke cleft cysts (RCC) are common sellar and suprasellar pathologies in pediatric patients. These lesions are mostly benign but can cause significant morbidity due to endocrinopathies, visual disturbances, and severe headaches. Surgical resection of such pathologies is dangerous due to markedly complex nature and potential for damage to neighboring structures including the pituitary, optic tracts, and hypothalamus. Limited visualization and restricted maneuverability previously limited the use of the endoscopic endonasal approach (EEA) in the resection of these pathologies. However, recent advancements in endonasal endoscopic neurosurgery and refinements in techniques and instruments suggest EEA is a promising minimally invasive and effective technique in treatment of sellar and suprasellar pathologies [19].

Despite such advancements, application of the EEA in pediatric populations has been limited due to unique challenges such as smaller skull base and sellar compartment, more narrow corridor between the carotid arteries, incomplete sphenoid sinus pneumatization, and developmental craniofacial asymmetry [3, 9, 25, 26, 31]. We present a series of 30 pediatric patients who underwent endoscopic endonasal resections for sellar and suprasellar pathologies. We seek to evaluate surgical, endocrine, and ophthalmologic outcomes as well as any complications to determine safety, efficacy, and outcome of this surgical approach in the pediatric population.

✉ Shaun D. Rodgers
srodgers@northwell.edu

[1] Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY, USA

[2] Division of Pediatric Neurosurgery, Cohen Children's Medical Center, 410 Lakeville Road, Suite 204, New Hyde Park, NY 11042, USA

Methods

Study population

After obtaining institutional review board approval, we reviewed medical records and imaging studies of 30 pediatric patients with sellar and suprasellar pathologies treated with endoscopic endonasal neurological surgery between January 2010 and December 2015 at the Steven and Alexandra Cohen Childrens Medical Center of NY by the investigators involved with this study. The ages of patients ranged from 2 to 24, and mean age was 14. There was a male:female ratio of 10:20. No patient was excluded or lost to follow-up. The mean follow-up period was 39 months.

Clinical outcomes

Before and after surgery, each patient underwent formal endocrine assessment, ophthalmological assessment, and neuroimaging. Neuroimaging included magnetic resonance imaging and/or computed tomography, both with and without contrast (Fig. 1).

Pathological diagnosis was confirmed after surgical resectionbiopsy. We recorded presenting symptoms, any previous treatment, ophthalmological and endocrine preoperative and postoperative function, extent of resection, and complications. Postoperative obesity was also evaluated based on BMI. Extent of resection was determined by postoperative MR imaging within 24 h of surgery and repeated at 3 months to confirm extent of tumor removal. Size and extension of all neoplasms are recorded through neuroradiology, and we note any recurrence or residual disease on postoperative scans up until September 1, 2016.

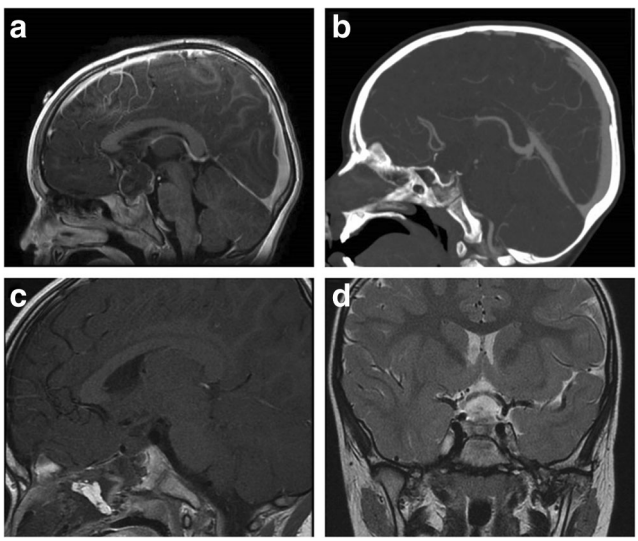

Fig. 1 **a** Preoperative sagittal contrast-enhanced MR image of 2-year-old patient with a suprasellar cystic craniopharyngioma. **b** Preoperative shows two calcifications in craniopharyngioma as well as non-aerated sinuses. **c** Postoperative sagittal view of same patient showing pedicle of endonasal flap, fat packing of nose, and GTR of lesion. **d** Postoperative coronal view of same patient showing pedicle of endonasal flap, fat packing of nose, and GTR of lesion

Results

In our series of 30 total pediatric patients with sellar and/or suprasellar pathologies, pathologic diagnosis identified 9 patients with pituitary adenomas, 12 with craniopharyngiomas, and 9 with RCC. Twenty-five patients presented with a new tumor and 5 presented with recurrent disease. All 5 of the patients with previous disease (4 recurrent craniopharyngiomas and 1 recurrent prolactinoma) received their prior treatment from our practice; one underwent prior craniotomy, three underwent craniotomy and radiation, and one underwent prior endoscopic endonasal (EE) resection for the prolactinoma.

All 12 of the craniopharyngiomas were confirmed by pathology to be of the adamantinomatous subtype. The mean volume of the craniopharyngiomas was 11.8 cm^3 and volumes ranged from 0.5 to 43.4 cm^3 (Table 1, Fig. 2). Four of the 12 craniopharyngiomas only had suprasellar involvement, and the other 8 also had extension into the third ventricle. The pituitary adenomas had a mean volume of 1.3 cm^3 with a range from 0.032 to 6.9 cm^3. Of the 9 pituitary adenomas, 7 were functioning and 1 was non-functioning, and 1 was indeterminate due to extensive necrosis secondary to pituitary apoplexy. Immunopathology identified 5 prolactin-secreting adenomas and 2 that were ACTH and prolactin positive. Three had suprasellar extension and 2 extended into the cavernous sinus. The RCCs had a mean volume of 0.7 cm^3 and ranged in volume from 0.15 to 1.3cm^3. Suprasellar extension was identified in 7 of the 9 patients with RCCs.

Surgical outcome

Overall, 23 of 30 patients (77%) had gross total resection (GTR) determined by 3-month postoperative neuroimaging. Specifically, GTR was achieved in 8 (89%) of the pituitary adenomas, 9 (75%) of the craniopharyngiomas, and 6 (67%) of the RCCs. As of September 1, 2016, there are 22 disease-free patients (73%), and there has been residual or recurrent disease in 8 patients (27%). Of the 8 patients who experienced recurrent or residual diseases post-resection, one was a planned debulking of a prolactinoma followed by pharmacotherapy with cabergoline postoperatively, and another 3 had already experienced recurrence of their craniopharyngioma previously.

Of the 25 patients presenting with a new, non-recurrent disease, 20 (80%) did not experience recurrence or residual disease and 5 (20%) did. Three of these recurrences were

Table 1 Surgical outcomes by pathology

	Number of patients (%)			
	Pituitary adenoma ($n = 9$)	Craniopharyngioma ($n = 12$)	Rathke cleft cyst ($n = 9$)	Total ($n = 30$)
Average volume	1.3 cm^3	11.8 cm^3	0.7 cm^3	–
GTR on 3 month FU	8 (88.9)	9 (75.0)	6 (66.7)	23 (76.7)
Remained disease free	8 (88.9)	8 (66.7)	6 (66.7)	22 (73.3)

RCCs, one was craniopharyngioma, and the other was the aforementioned debulked prolactinoma.

Clinical presentation

The most common clinical presentation included endocrinopathies in 21 (70%) patients and headaches in 19 (63.3%) patients. Other common presenting symptoms included visual disturbances, symptoms of diabetes insipidus, and symptoms of hydrocephalus (Table 2).

Endocrine outcome

Overall, 7 patients had normal pituitary function preoperatively and another 5 had elevated prolactin due to stalk effect. Fourteen patients had completely normal pituitary function postoperatively. Preoperative endocrine evaluation detected hyperprolactinemia consistent with prolactinoma (> 200 ng/mL) in 5 patients (17%), central hypothyroidism in 2 patients (7%), and 1 patient had hypercortisolism secondary to an ACTH and prolactin-producing pituitary adenoma. Eight patients (28%) had panhypopituitarism preoperatively. Of the patients with panhypopituitarism, 5 were due to recurrent craniopharyngiomas, 2 were secondary to new craniopharyngiomas, and 1 was from a pituitary adenoma with apoplexy.

While 7 craniopharyngioma patients experienced panhypopituitarism prior to surgery, all 12 patients experienced panhypopituitarism postoperatively. There was no new postoperative panhypopituitarism in the pituitary adenoma group. Hormonal remission was achieved in 100% of the patients with functioning tumors. One patient with RCC had endocrinopathy postoperatively in the form of adrenal insufficiency and hyperprolactinemia. All 12 patients suffering from hyperprolactinemia preoperatively, including those from stalk effect, had normal prolactin levels postoperatively. Both patients with central hypothyroidism preoperatively had normal TSH levels postoperatively. The patient with Cushing's disease preoperatively also had normal 8 am cortisol postoperatively.

The number of craniopharyngioma patients experiencing central diabetes insipidus increased from 8 preoperatively to 12 postoperatively. None of the 9 pituitary adenoma patients had permanent DI postoperatively. Three experienced a transient period of DI postoperatively. The number of RCC patients with DI increased from 1 to 2 after surgery, and 1 additional patient experienced transient DI postoperatively.

Ophthalmological outcome

In the preoperative ophthalmological evaluation, 7 patients (23%) had visual field cuts determined by Humphrey visual field testing, 7 patients (23%) had diplopia, and 1 patient had both. Of the 7 patients with visual field cuts, 3 were unilateral temporal hemianopia and 4 were bitemporal hemianopia. Postoperatively, ophthalmological examination identified 4 patients with visual field cuts and no patients with diplopia. Eleven patients (37%) experienced improvement in their vision, 16 (53%) patients experienced no change, and one (3%) patient experienced visual worsening.

Complications

CSF leakage was seen in only 1 patient (3%). This patient underwent pituitary macroadenoma resection and had heavy coughing and retching in the immediate post-operative period which likely partially dislodged the seal and contributed to the development of a leak. The transient CSF leak was resolved by re-exploration with repacking and lumbar drain. During re-exploration, the leak was identified and a small two-layer inlay was made with Durepair inside the dura, followed by onlay of Durepair then Duragen. This was secured with cartilaginous piece from anterior to posteior, a transverse piece of vomer, followed by Valsalva to check for leak. The patient had an excellent recovery and experiences normal endocrine, visual, gustatory, and olfactory function without any complaints of headaches, fatigue, polyuria, or polydypsia. No evidence of bacterial meningitis was seen in this patient.

Three patients (10%) had vasospasm/stroke, all after craniopharyngioma resection. This involved one patient with silent stroke of right thalamic region, one patient with thalamic stroke causing decreased level of consciousness requiring 3-month inpatient stay, and one patient with vasospasms leading

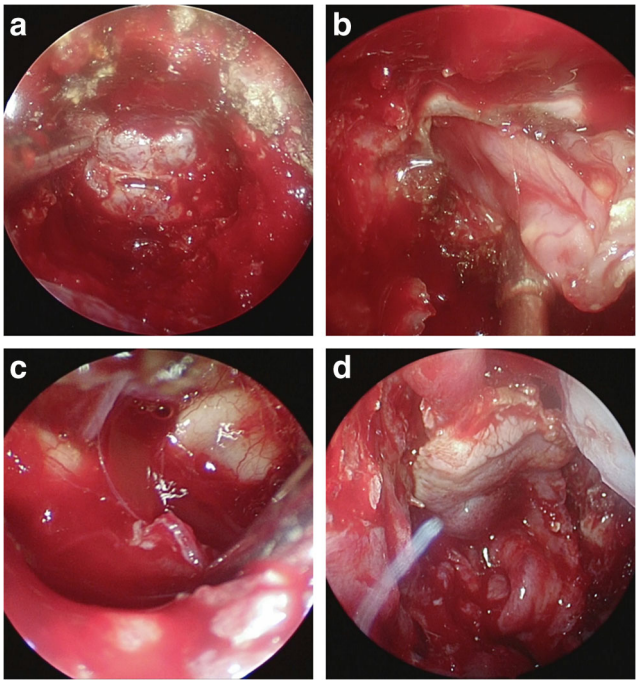

Fig. 2 **a** Intraoperative photos during total resection of suprasellar cystic craniopharyngioma in 2-year-old patient. Complete sphenoid drill out of non-aerated sinus with exposure from optic nerve to optic nerve. **b** Tumor capsule being delivered with calcifications visible in tumor. **c** Bilateral optic nerves with bilateral A1 arteries coming into ACOM complex and residual pituitary stalk at bottom of image, consistent with low stalk section. **d** Endonasal flap with pedicle following multilayer closure

to large watershed stroke proved by magnetic resonance angiography.

One craniopharyngioma patient who presented to us with hydrocephalus required external ventricular drain for persistent hydrocephalus postoperatively. The patient then had an infected ventriculostomy and CSF was positive for gram-positive cocci. He had a cisternogram to rule out CSF leak, then a ventriculoperitoneal shunt was inserted after CSF cultures were negative.

New obesity was also recorded in 3 patients (10%) which included two craniopharyngiomas and one RCC. There was a 0% perioperative mortality rate in this study.

Discussion

When dealing with sellar and suprasellar pathologies in the pediatric population, skilled and cautious management is warranted to achieve complete resection without compromising neurological, ophthalmological, and endocrinological function. Although craniotomy has been tradition surgical treatment, outcomes have varied and more recent studies highlight the benefits of an endoscopic endonasal approach [19]. EEA obviates the need for brain retraction by creating an ventromedial corridor to the sellar, suprasellar, and parasellar compartments, providing visualization up to the floor of the hypothalamus and roof of the third ventricle [6, 29, 34]. This extensive visualization facilitates high rates of gross-total resection and positive outcomes, while absence of brain retraction minimizes frequency of post-operative complications.

In this series, we record 77% gross total resection rate overall and 80% GTR rate where GTR was planned. Furthermore, a mean follow-up period of 39 months found no residual or recurrent disease in 73% of all patients and in 80% of patients initially presenting to us with non-recurrent/non-residual disease. For pituitary adenomas, craniopharyngiomas, and RCC, the GTR rates were 89%, 75%, and 69%, respectively. These rates slightly exceed those reported in a similar study by Chivukula et al. which reported GTR rates of 70%, 56.2%, and 72.7% for pituitary adenomas, craniopharyngiomas, and RCCs, respectively [9]. The resections were achieved with limited frequency of complications, including 30% new DI (17% permanent), 20% new endocrinopathy, 10% new obesity, 3% CSF leak, and 0% peri-operative mortality (Table 3). These resection rates support the efficacy of the EEA in pediatric populations, while the low complication rates support its safety and low-morbidity. These results reflect a promising positive trend in EEA GTR rates which are correlated with greater extent of resection and improved outcomes with lower recurrence rates [10, 30]. Furthermore, this study reports 37% of patients experienced improvement in their vision and 37% had improvement in anterior pituitary function. In all, the application of the EEA to pediatric populations is a safe and effective minimally invasive approach to sellar and suprasellar lesions and it is capable of excellent outcomes with limited complications.

Endocrinological outcomes reported in this study are consistent with those reported. Our frequent rates of diabetes insipidus are consistent with literature findings that DI is the most frequent post-operative complication following EEA [9, 37].

Most postoperative endocrinopathies occurred following craniopharyngioma resection. Similarly, craniopharyngioma resection reports a prevalence of post-operative anterior pituitary dysfunction rates from 57.1 to 100% [4, 5, 7, 11, 12, 18, 20, 28, 40]. Moreover, pre-existing endocrinopathies rarely recover after craniopharyngioma resection [8, 14, 22–24]. Chivukula et al. reported that all pediatric craniopharyngioma patients required hormone replacement postoperatively with 50% new anterior pituitary endocrinopathy and 68.8% permanent DI [9]. Therefore, complete resection and cure was the goal in all of the surgeries, which explains why 100% of the craniopharyngioma patients experienced hypopituitarism and DI postoperatively with 42% new endocrinopathies and 33% new DI. When dealing with aggressive lesions with extensive adhesions such as craniopharyngiomas, high likelihood of postoperative endocrinopathies were tolerated to achieve total cure and avoid the potential morbidity associated with

Table 2 Summary of major presenting symptoms by pathology

Number of patients (%)

Presenting symptom	Pituitary adenoma ($n = 9$)	Craniopharyngioma ($n = 12$)	Rathke cleft cyst ($n = 9$)	Total ($n = 30$)
Endocrinopathies*	8 (88.9)	8 (66.7)	5 (55.6)	21 (70.0)
Headaches	6 (66.7)	6 (50.0)	7 (77.8)	19 (63.3)
Visual disturbances	4 (44.4)	6 (50.0)	5 (55.6)	15 (50.0)
Diabetes insipidus	0	8 (66.7)	2 (22.2)	10 (33.3)
Hydrocephalus	0	3 (25.0)	1 (11.1)	4 (13.3)
Nausea/vomiting	0	2 (16.7)	1 (11.1)	3 (10.0)
Weight gain	1 (11.1)	0	1 (11.1)	2 (6.7)
Pituitary apoplexy	2 (22.2)	0	0	2 (6.7)
Memory issues	0	1 (8.3)	0	1 (3.3)
Weight loss	0	1 (8.3)	0	1 (3.3)

*Excludes DI

repeated surgery for any residual or recurrent disease. We believe the GTR and cure rates reported in the present study support such an approach.

The most important outcome of RCC resection is resolution of the headache and endocrinopathies that patients classically present with. [9]. Aho et al. reported that improvements in symptoms are expected after surgical decompression of the optic apparatus and hypothalamic-pituitary axis [1]. Although RCC had the lowest GTR rates in this study, the 88% rate of symptom resolution, compared to rates of 37–92% in the literature, indicates these were successful outcomes [1, 2].

The visual outcomes recorded were very promising, with only one patient experiencing worsening in vision postoperatively. This was a 5-year-old with an extremely large (5.8 × 4.4 × 3.4 cm) suprasellar mass extending into the interhemispheric fissure who experienced persistent headache in the postoperative period. Ophthalmological assessment found optic nerve pallor, small right esotropia, and bitemporal hemianopia. The outcome could be attributed to intraoperative manipulation of the optic chiasm secondary to tumor invasion or hydrocephalus causing chiasmal compression. Series of radical EE resections record visual deterioration in approximately 15% of patients, which is a higher prevalence than recorded in this study [15, 35, 41]. Visual field cuts persisted in 4 other patients in this study, but no patient experienced diplopia postoperatively.

The most common surgical complication recorded in the literature following EEA is cerebrospinal fluid leak. Previously reported rates of this complication after transsphenoidal resection range from 2 to 13%, with rates of 8–13% in pediatric patients [13, 16, 17], while the rates following EE craniopharyngioma resections are notably higher and range from 0 to 58% [4, 5, 7, 11, 12, 18, 20, 28, 40]. Most series have reported decrease in rates of leakage corresponding with the surgeon's learning curve and proficiency in the surgery. Additionally, the introduction of the novel nasoseptal flap in the reconstruction of the skull base by Hadad et al. in 2006 has resulted in a drastic drop in rates of CSF leaks after EEA [21]. In our series, a single CSF leak was surgically resolved without any further complications. The use of EEA with high rates of GTR and low rates of CSF leak indicates this is an increasingly safe approach.

Pediatric patients with brain tumors, specifically craniopharyngiomas, are at a very high risk for development of hypothalamic obesity after tumor therapy [32, 33, 36, 38, 39]. Koutourousiou et al. recorded a 33.3% new obesity rate in pediatric patients after EE craniopharyngioma resections [27]. Leng et al. recorded a 39% weight gain (> 9% increase in BMI) after EE craniopharyngioma resections in adult patients [29]. In our series, 10% of these patients developed new postoperative obesity, which may be attributable to intraoperative damage to the hypothalamus or postoperative glucocorticoid therapy which both independently increase BMI.

Perhaps the most surprising finding in this study was vasospasm/stroke in 3 craniopharyngioma patients. This result supports the need for cautious management when attempting to resect aggressive and recurrent lesions with extensive adhesions. Despite the spatial relationship of these pathologies to the cavernous sinuses and the narrow corridor seen in pediatric patients, vascular injury to the internal carotids was avoided in all patients.

We consider outcomes of three different pediatric pathologies to evaluate efficacy of EEA, which means generalizing and simultaneously considering outcomes of a heterogeneous group of pathologies. Future studies focusing on each pathologic entity individually will be crucial to further enhancing our understanding of EE outcomes in pediatric populations. Lastly, further studies with larger

Table 3 Summary of postoperative complications by pathology

Number of patients (%)				
Complication	Pituitary adenoma ($n = 9$)	Craniopharyngioma ($n = 12$)	Rathke cleft cyst ($n = 9$)	Total ($n = 30$)
New transient DI	3 (33.3)	4 (33.3)	2 (22.2)	9 (30.0)
New permanent DI	0	4 (33.3)	1 (11.1)	5 (16.7)
New endocrinopathy*	0	5 (41.7)	1 (11.1)	6 (20.0)
Headaches	2 (22.2)	1 (8.3)	1 (11.1)	4 (13.3)
New obesity	0	2 (16.7)	1 (11.1)	3 (10.0)
Vasospasm/stroke	0	3 (25.0)	0	3 (10.0)
CSF leak	1 (11.1)	0	0	1 (3.3)
New visual deficit	0	1 (8.3)	0	1 (3.3)
Bacterial meningitis†	0	1 (8.3)	0	1 (3.3)

*Excludes DI

† Source was infected ventriculostomy

sample size, younger study population, and longer follow-up period will be critical for complete and accurate evaluation of the EEA in pediatric populations.

Conclusions

This small case series of pediatric patients underscores the ability of the EEA to achieve complete resection and limit recurrences while minimizing risk of postoperative morbidity due endocrinopathies, visual disturbances, headaches, or CSF leaks. Difficulties with preventing vascular damage are highlighted in this series. These findings support the favorable use of EEA for resection of these lesions in pediatric populations. We hope that this study contributes to further understanding and advancement of this approach that will translate to improved outcomes for pediatric patients.

Compliance with ethical standards

Conflict of interest The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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