Transnasal endoscopic approach for pediatric skull base lesions: a case series

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OBJECTIVE Transnasal endoscopic transsphenoidal approaches constitute an essential technique for the resection of skull base tumors in adults. However, in the pediatric population, sellar and suprasellar lesions have historically been treated by craniotomy. Transnasal endoscopic approaches are less invasive and thus may be preferable to craniotomy, especially in children. In this case series, the authors present their institutional experience with transnasal endoscopic transsphenoidal approaches for pediatric skull base tumors.

METHODS The authors retrospectively reviewed pediatric patients (age ≤ 18 years) who had undergone transnasal endoscopic transsphenoidal approaches for either biopsy or resection of sellar or suprasellar lesions between 2007 and 2016. All operations were performed jointly by a team of pediatric neurosurgeons and skull base otolaryngologists, except for 8 cases performed by one neurosurgeon.

RESULTS The series included 42 patients between 4 and 18 years old (average 12.5 years) who underwent 51 operations. Headache (45%), visual symptoms (69%), and symptoms related to hormonal abnormalities (71%) were the predominant presenting symptoms. Improvement in preoperative symptoms was seen in 92% of cases. Most patients had craniopharyngiomas ($n = 16$), followed by pituitary adenomas ($n = 12$), Rathke cleft cysts ($n = 4$), germinomas ($n = 4$), chordomas ($n = 2$), and other lesion subtypes ($n = 4$). Lesions ranged from 0.3 to 6.2 cm (median 2.5 cm) in their greatest dimension. Gross-total resection was primarily performed (63% of cases), with 5 subsequent recurrences. Nasoseptal flaps were used in 47% of cases, fat grafts in 37%, and lumbar drains in 47%. CSF space was entered intraoperatively in 15 cases, and postoperative CSF was observed only in lesions with suprasellar extension. There were 8 cases of new hormonal deficits and 3 cases of new cranial nerve deficits. Length of hospital stay ranged from 1 to 61 days (median 5 days). Patients were clinically followed up for a median of 46 months (range 1–120 months), accompanied by a median radiological follow-up period of 45 months (range 3.8–120 months). Most patients (76%) were offered adjuvant therapy.

CONCLUSIONS In this single-institution report of the transnasal endoscopic transsphenoidal approach, the authors demonstrated that this technique is generally safe and effective for different types of pediatric skull base lesions. Favorable effects of surgery were sustained during a follow-up period of 4 years. Further refinement in technology will allow for more widespread use in the pediatric population.

<https://thejns.org/doi/abs/10.3171/2019.4.PEDS18693>

KEYWORDS transnasal endoscopic approach; sellar neoplasm; suprasellar neoplasm; skull base lesion; pediatric neurosurgery; surgical technique

TRANSNASAL endoscopic approaches are well established in the adult literature as a means of resecting sellar, suprasellar, and parasellar tumors.^{5,12} Over the past century, transsphenoidal approaches have evolved significantly.¹³ The sublabial transsphenoidal approach used by Harvey Cushing and the early transnasal techniques developed by Hirsh were initially devised to reach

pituitary tumors primarily within the sellar region.¹³ Since then, the extended transnasal transsphenoidal route has been used for a variety of other skull base pathologies.¹² The development of this surgical approach has been concurrent with advancements in microscopic and endoscopic technology, allowing improved visualization through a narrow opening.^{3,13} Compared with the microscope, dif-

ABBREVIATIONS GTR = gross-total resection; STR = subtotal resection.

SUBMITTED November 15, 2018. **ACCEPTED** April 15, 2019.

INCLUDE WHEN CITING Published online June 14, 2019; DOI: 10.3171/2019.4.PEDS18693.

ferently angled lens endoscopes offer a wider field of view for the resection of parasellar and suprasellar lesions.^{5,14}

Unlike in adults, for pediatric skull base lesions a craniotomy has been the favored approach until recently. The transnasal endoscopic approach may be limited by pediatric anatomy such as an absent or incompletely pneumatized sella, narrow intercarotid distance, and small nares and nasal passages. However, this approach has the benefit of avoiding possible damage to surrounding structures from retraction during subfrontal or pterional craniotomy¹⁷ and disruption of dentition or facial development.⁴ We report our institutional experience of pediatric skull base lesions approached using a transnasal endoscopic route. We believe that this is a safe yet efficacious alternative to the traditional transcranial approach.

Methods

We performed a retrospective review of all pediatric patients who underwent transnasal endoscopic approaches for skull base lesions at our institution between 2007 and 2016. All patients were younger than 18 years at the time of their first operation. Patients were identified from a database of patients operated on by the pediatric neurosurgeons at our institution (M.S.B.E., G.A.G., and S.H.C.) and with billing codes for excision of pituitary tumor by transnasal approach (61548); neuroendoscopy, intracranial, with excision of pituitary tumor, transnasal or transsphenoidal approach (62165); craniofacial approach to intradural lesion of anterior cranial fossa (61583); malignant neoplasm of pituitary gland and craniopharyngeal duct (194.3); benign neoplasm of pituitary gland and craniopharyngeal duct (227.3); or neoplasm of uncertain behavior of pituitary gland and craniopharyngeal duct (237.0). Billing code 61548 is generally reserved for microscopic cases, but at our institution, all endoscopic cases were initially scheduled with the use of microscopes during the transitory phase. Therefore, we included 5 cases in which both a microscope and an endoscope were used but not the cases in which a microscope was used alone or as the primary means of visualization. We included patients who had undergone previous operations at our institution or elsewhere. We additionally excluded cases with 1) sublabial approaches or extension beyond a transnasal approach, 2) transnasal endoscopic approaches employed for nonneurosurgical lesions (e.g., located primarily within the nasal cavity), and 3) transnasal endoscopic procedures planned as a combined approach with a concurrent or anticipated craniotomy.

Clinical information for each patient was obtained from a de-identified chart review tool. We analyzed the pre- and postoperative neurological status. All patients underwent a complete workup by a pediatric endocrinologist and ophthalmologist when visual symptoms or signs were present. Some patients also received neuro-oncology and radiation oncology evaluations. All patients underwent preoperative and postoperative MRI with and without contrast within 24 hours of the procedure. The majority of patients underwent serial MRI at regular intervals. The preoperative T2-weighted (or, if unavailable, T1-weighted) coronal MR image was used to measure the intercarotid distance (Fig. 1).

FIG. 1. Preoperative coronal T2-weighted MR image showing the measurement of the cavernous intercarotid distance (line). Figure is available in color online only.

A method previously described in the literature was used to locate and measure the distance between the cavernous segments of the internal carotid arteries.²⁶ Operative time was gathered from anesthesia records except in cases in which the operations occurred before the full transfer to the electronic medical record system. CSF leak was defined as postoperative leakage of CSF requiring further surgical management. Recurrences were assessed only for gross-total resection (GTR) cases, as subtotal resections (STRs) and biopsy, by definition, result in residual lesions.

Institutional review board approval was obtained to review the medical records and neuroimaging studies of these patients. Patient assent and consent was obtained at the time of surgery for the use of imaging.

Results

Overall Study Population

Our series included 42 patients (28 boys and 14 girls) who had undergone a total of 51 operations. Patients were between 4 and 18 years old (median 12.3 years) at the time of their initial surgery. The most common pathological subtypes were craniopharyngioma ($n = 16$), followed by pituitary adenoma ($n = 12$), Rathke cleft cyst ($n = 4$), germinoma ($n = 4$), and chordoma ($n = 2$), with other smaller lesion subtypes ($n = 4$) (Fig. 2). The most common presenting symptoms were hormonal deficiencies (70.6%), followed by visual change (68.6%) and headache (45%). On preoperative imaging, 62.7% of the lesions had suprasellar extension, and 63% of these lesions were approached with an attempt at GTR. The preoperative cavernous intercarotid distance ranged from 8.5 to 28.3 mm (median 18.1

FIG. 2. Bar graph showing the pathological subtypes of lesions among patients included in the study. Figure is available in color online only.

mm) (Table 1). The correlation between preoperative cavernous intercarotid distance and age can be appreciated in Fig. 3.

Surgical Approach

In most of the cases, neurosurgeons and otolaryngologists jointly performed the operations. Eight operations were performed by one neurosurgeon (M.S.B.E.) without otolaryngologists. The operative technique was similar across our different neurosurgeons for similar types of pathology. Most cases were GTRs (62.7%), with fewer STRs (17.6%), including cyst aspirations, and biopsies (15.6%) (Fig. 4). The majority of GTRs were for lesions with suprasellar extension (63%). Figure 5 shows intraoperative images of a GTR. Neuronavigation was used in all cases. Many of the operations were augmented by procedures to prevent CSF leakage such as placement of an intraoperative lumbar drain (47.1%), nasoseptal flap (47.1%), or fat graft (37.3%). Reported blood loss ranged from 0 to 300 ml (median 50 ml). The median operative time was 235 minutes. Five patients had undergone prior transcranial surgery for either Ommaya reservoir placement or frontal cystic decompression; one patient had an Ommaya reservoir placed after resection (Table 1).

Postoperative Course

The majority of cases (91.7%) resulted in clinical improvement over a median follow-up of 46 months (range 1–120 months). Assessment of meaningful clinical improvement was based on patient and family reports and the clinician's evaluation during postoperative follow-up visits. Some examples of reversal or alleviation of preop-

erative symptoms consisted of resolution of headaches, improved peripheral vision in a patient with bitemporal hemianopia, and regained energy level in a fatigued patient with low cortisol level. Clinical follow-up was unavailable for 3 patients who moved out of state. In 27.5% of the cases, patients experienced postoperative complications (Table 1).

Most of the patients (76.2%) required adjuvant therapy in the form of hormonal therapy (69.0%), radiation therapy (28.6%), or chemotherapy (16.7%). Hormonal therapy was aimed at replacement ($n = 21$), suppression with cabergoline or bromocriptine ($n = 4$), or both ($n = 3$). Radiation therapy included external-beam LINAC-based therapy, with ($n = 1$) or without ($n = 10$) stereotactic radiosurgery using the CyberKnife, or brachytherapy ($n = 1$). Five patients did not have a repeat postoperative image to compare with the scan obtained immediately postoperatively. Five recurrences were reported after radiographically documented GTR (Table 2). Figure 6 demonstrates pre- and postoperative images obtained in a patient who underwent a successful GTR.

Detailed preoperative, intraoperative, and postoperative characteristics by each tumor type are as follows.

Pituitary Adenomas

There were 12 patients ranging in age from 7 to 18 years (median 11.8 years) who underwent 14 operations for pituitary adenoma. All adenomas were found to be secreting tumors, the majority of which were prolactinomas ($n = 7$) with fewer adrenocorticotrophic hormone-secreting ($n = 2$), growth hormone-secreting ($n = 1$), and mixed-secreting ($n = 2$) subtypes. Preoperatively, these patients all presented with symptoms related to pituitary hormone dysfunction. Patients with prolactinomas were offered surgical intervention after failed medical management with bromocriptine or cabergoline, marked by continued increase in prolactin levels or progressive visual loss.

Over 40% of the lesions had evidence of suprasellar extension. Gross-total resection was performed in 78.6% of the cases. Complications (14.3%) included one case of a cavernous sinus tear that was promptly repaired and another of new hormonal deficit. The majority of patients (75%) received adjuvant therapy with hormonal therapy and/or radiation therapy. Two patients underwent repeat surgery for recurrences, 4 and 5 years from the initial surgery (Table 2).

Craniopharyngiomas

A total of 22 operations were performed in 16 patients with craniopharyngiomas. Of note, during the same timeframe (2007–2016), 8 craniotomies were performed for resection of craniopharyngioma and 5 craniotomies for cyst aspiration/Ommaya reservoir placement in this population. Patients most commonly presented with visual changes (82% of cases), headache (62.5% of cases), or hormonal deficiencies (55% of cases). Visual changes included decreased visual acuity or visual field defects in 11 patients and proptosis in 1 patient. All patients with hormonal deficiencies exhibited panhypopituitarism, including growth failure and diabetes insipidus. Most of the

TABLE 1. Cohort overview by tumor type

	Overall (n = 42)	Pituitary Adenoma (n = 12)	Craniopharyngioma (n = 16)	Others (n = 14)
Total no. of ops	51	14	22	15
Median age, yrs	12.3 (4–18)	16 (7–18)	11.8 (5.9–16)	11 (4–18)
Male sex	28/42 (66.7%)	7/12 (58.3%)	11/16 (68.8%)	10/14 (71.4%)
Preop symptoms				
Headache	23/51 (45%)	7/14 (50%)	9/22 (40.9%)	7/15 (46.7%)
Visual change	35/51 (68.6%)	7/14 (50%)	18/22 (81.8%)	10/15 (66.7%)
Other CN deficits	3/51 (5.98%)	0/14 (0%)	1/22 (4.5%)	2/15 (13.3%)
Hormonal deficiency	36/51 (70.6%)	14/14 (100%)	12/22 (54.5%)	10/15 (66.7%)
Hydrocephalus/papilledema	6/51 (11.8%)	0/14 (0%)	6/22 (27.3%)	0 (0%)
Suprasellar extension	32/51 (62.7%)	6/14 (42.9%)	20/22 (90.9%)	6/15 (40%)
Median greatest tumor dimension, cm	2.5 (0.3–6.2)	1.6 (0.3–4)	3.7 (1.6–4.7)	1.9 (0.3–6.2)
Median intercarotid distance, mm	18.1 (8.5–28.3)	18.8 (14.2–24.8)	16.9 (11.4–28.3)	18.1 (8.5–26.4)
Type of op				
GTR	32/48 (62.7%)	11/14 (78.6%)	16/22 (72.7%)	5/13 (38.4%)
STR/cyst aspiration	9/48 (17.6%)	3/14 (21.4%)	5/22 (22.7%)	1/13 (7.7%)
Biopsy	8/48 (15.6%)	0/14 (0%)	1/22 (4.5%)	7/13 (53.8%)
Additional procedures				
Lumbar drain	24/51 (47.1%)	4/14 (28.6%)	14/22 (63.6%)	6/15 (40%)
Septal flap	24/51 (47.1%)	5/14 (35.7%)	9/22 (40.9%)	5/15 (33.3%)
Fat graft	19/51 (37.3%)	7/14 (50%)	14/22 (63.6%)	3/15 (20%)
Median intraop blood loss, ml	50 (0–300)	75 (50–150)	87.5 (0–300)	50 (10–125)
No. of transfusions	2/51 (3.9%)	0/14 (0%)	2/22 (9.1%)	0/15 (0%)
Median op time, mins	235 (65–439)	436 (240–436)	215 (65–439)	276 (171–405)
Median length of stay, days	5 (1–61)	4.5 (2–8)	7.5 (1–37)	4 (2–61)
Complications, any	14/51 (27.5%)	2/14 (14.3%)	9/22 (40.9%)	3/15 (20%)
CSF leak	3/51 (5.9%)	0/14 (0%)	3/22 (13.6%)	0/15 (0%)
New CN deficits	3/51 (5.9%)	0/14 (0%)	2/22 (9.1%)	1/15 (6.7%)
New hormonal deficits	8/51 (15.7%)	1/14 (7.1%)	7/22 (31.8%)	0/15 (0%)
Hemorrhage	3/51 (5.9%)	0/14 (0%)	2/22 (9.1%)	1/15 (6.7%)
Infection	2/51 (3.9%)	0/14 (0%)	1/22 (4.5%)	1/15 (6.7%)
Graft migration	2/51 (3.9%)	0/14 (0%)	2/22 (9.1%)	0/15 (0%)
Death	1/51 (2.0%)	0/14 (0%)	1/22 (4.5%)	0/15 (0%)
Median follow-up time, mos	46 (1–120)	18.5 (1–64)	57 (21–114)	46 (22–120)
No. of recurrences	5/32 (15.6%)	2/11 (18.2%)	3/16 (18.8%)	0/5 (0%)
No. of reops	9/51 (17.6%)	2/14 (14.3%)	6/22 (27.3%)	1/15 (6.7%)
Adjuvant therapy, any	32/42 (76.2%)	9/12 (75%)	14/16 (87.5%)	9/14 (64.3%)
Hormonal therapy	29/42 (69.0%)	9/12 (75%)	12/16 (75%)	8/14 (57.1%)
Radiation therapy	12/42 (28.6%)	2/12 (16.7%)	4/16 (25%)	6/14 (42.9%)
Chemotherapy	7/42 (16.7%)	0/12 (0%)	1/16 (6.3%)	6/14 (42.9%)

CN = cranial nerve.

Median values are presented as the median (range).

cases were attempted as GTRs (72.7%). The average blood loss was 109.4 ml, and 2 patients required blood transfusion. Six reoperations were performed for a recurrence of craniopharyngioma (n = 1) and a residual lesion after STR (n = 1), and 4 additional operations were performed in 1 patient with cyst reaccumulation despite multiple transnasal aspirations and prior STR (Tables 1–3).

Postoperative complications were observed in 40.9% of cases. All 3 postoperative CSF leaks (13.6%) involved lesions with suprasellar extension. There was 1 case of bacterial meningitis successfully treated with antibiotics. New hormonal deficits were observed (31.8%), most often in the form of diabetes insipidus, syndrome of inappropriate salt wasting, and panhypopituitarism. Three patients

FIG. 3. Scatterplot of age and cavernous intercarotid distance at the time of the first procedure. The red line represents a linear regression model showing the relationship between the two variables. Figure is available in color online only.

with new-onset weight gain attributable to hypothalamic obesity were included in this count, but not the patients with positive weight gain from underweight to normal weight range (n = 2), preexisting obesity (n = 5), and transient weight gain secondary to steroid use (n = 1).

One case was aborted due to excessive bone bleeding, later requiring a subfrontal craniotomy for resection. Two patients had intracranial migration of fat grafts, both of whom demonstrated acute postoperative worsening of their vision. In both instances, intracranial hypotension due to the use of a lumbar drain was felt to be causative. During the reoperation to remove both the packing material and fat graft, the fat graft was found to be compressing the optic nerve in one case and the optic chiasm in the other. Both patients saw significant improvement in their visual symptoms after the revision surgeries.

One patient died in the immediate postoperative period due to disseminated intravascular coagulation. Intraoperatively, the patient had approximately 300 ml of blood loss (estimated total blood volume from weight: 18.1 kg × 70 ml/kg = 1260 ml) from the surgical site, but hemostasis was achieved with Gelfoam. The patient was hemodynamically stabilized with a blood transfusion. CT scans obtained before transferring the patient to the ICU showed no significant intracranial hemorrhage. On arrival to the ICU, the patient started to bleed from both nares and subsequently developed coagulopathy. Bedside CT scanning revealed intraventricular and subarachnoid hemorrhages. Despite aggressive management, the patient’s condition further deteriorated to brain death.

Other Skull Base Lesions

Other less common skull base lesions included Rathke cleft cysts (n = 4), germinomas (n = 4), chordomas (n = 2), Ewing’s sarcoma (n = 1), and nongerminomatous germ cell

FIG. 4. Pie chart showing the types of surgical procedures performed for patients included in the study. Figure is available in color online only.

tumor (n = 1). One patient had a nondiagnostic pituitary stalk biopsy that demonstrated only lymphocytic infiltration (who required a repeat biopsy to rule out neoplasm after the initial sample was deemed insufficient for definitive diagnosis), and another patient with fibrous dysplasia underwent transnasal endoscopic surgery for optic nerve decompression. Detailed clinical information of this heterogeneous group of patients is available in Tables 1 and 3.

FIG. 5. Intraoperative endoscopic view demonstrating opening of the dura (A), tumor visualization (B), the optic nerve after tumor removal (C), and the third ventricle after tumor removal (D). Figure is available in color online only.

TABLE 2. Clinical characteristics of patients who had recurrence after GTR

Case No.	Type of Tumor	Context of Initial Op	1st Postop Imaging Report	Time to Recurr (mos)	Location of Recurr	Adjuvant Tx (if any)	Intervention (if any)	Disease Status on Latest FU
3	Prolactinoma	Failed medical therapy (was on bromocriptine for 1 yr w/o notable decrease in prolactin level or tumor size)	NA (lost to FU)	55	Lt side of pituitary gland	Hormonal therapy	Repeat endoscopic resection	Lost to FU
4	Pituitary adenoma (ACTH secreting)	GTR w/o trial of medical therapy	NA (outside imaging)	45	Rt side of pituitary gland	Hormonal therapy	Repeat endoscopic resection	Cushing's syndrome resolved; doing well w/ no focal neurological findings
14	Craniopharyngioma	GTR; was on hormonal therapy prior to op	Postop changes related to resection of sellar & suprasellar mass w/o specific evidence of significant residual or recurrent tumor	43	Lt cavernous sinus	Hormonal therapy	Continued hormonal therapy; no surgical intervention	Symptomatically stable
16*	Craniopharyngioma	GTR; no prior medical therapy	Interval transsphenoidal resection of the large solid & cystic sellar & suprasellar mass w/o evidence of residual enhancement	8 (since 1st op)	Adjacent to optic chiasm (suprasellar)	Irradiation, hormonal therapy	Repeat endoscopic resection	Recurred
16*	Craniopharyngioma	GTR; past irradiation	Postop changes related to transsphenoidal resection of craniopharyngioma; small enhancing tissue along rt aspect of sella likely represents postop changes	56 (since 2nd op)	Sellar & suprasellar	Hormonal therapy	CyberKnife radiosurgery	Symptom resolution; no evidence of recurrence

ACTH = adrenocorticotrophic hormone; FU = follow-up; NA = not available; Recurr = recurrence; Tx = therapy.

* Same patient who underwent 2 GTRs that both resulted in recurrences.

FIG. 6. Preoperative (A) and postoperative (B) postcontrast MR images obtained in an 11-year-old patient with a craniopharyngioma.

Discussion

Transnasal endoscopic approaches in children have mostly been reported as part of larger adult-inclusive series^{5,10,12,23} or as case reports,^{16,18,32,33,36} but they have increasingly been described in the resection of pediatric skull base lesions.^{2,4,6,9,17,30,34,40,41} Our pediatric series presents a tertiary care center's experience of implementing this surgical approach for a diverse group of sellar and suprasellar pathologies (a total of 9 different indications). Previous reports of a similar nature have been published but were either smaller in sample size^{2,4,11,17,34} or conducted in a different country.^{12,24,30,38,40,41} Larger case series from the US have been published but were all from the same institution.^{6,9,35} Among the sizable pediatric case series from American institutions, we present the longest median follow-up time of 4 years.^{2,4,6,34}

Pituitary Adenomas

In their series of 56 pediatric patients with pituitary adenomas, Zhan et al. reported a high rate of GTR (87.5%).⁴¹ These authors additionally described a smaller subset of 11 adolescent patients with similar outcomes.⁴⁰ Their patients were between 10 and 18 years old, with the majority (91%) older than 15 years.⁴¹ Therefore, many of their patients had skull base anatomy closer to adult size.⁴⁰ These patients primarily presented with visual deficits and symptoms related to hormonal deficits, with clinical improvement immediately after surgery.^{40,41} In our study, we saw similarly high rates of overall clinical improvement (92%). Given what they deem to be comparable rates of safety and efficacy with the adult population, these authors advocate for the use of the endonasal endoscopic approach for pediatric pituitary adenomas.

Craniopharyngiomas

A number of series have also described transsphenoidal, but not purely transnasal endoscopic, resection of craniopharyngiomas in children with good outcomes.^{1,22,38}

These series primarily utilized the operating microscope for visualization. In their series of 22 patients, Jane et al. included 2 children who underwent a purely endoscopic endonasal resection of their craniopharyngiomas, which they acknowledged has since become the predominant surgical technique.¹⁵ Their rate of GTR (68%) was similar to ours (62.7%) but had a higher rate of new hormonal deficits (67% cases of panhypopituitarism, 56% cases of new diabetes insipidus).

Other Skull Base Lesions

The endoscopic transnasal approach has also been described in the setting of other skull base lesions.^{4,6,34} Kasam et al. reported their institutional experience of expanded endoscopic endonasal approaches for optic nerve decompression and CSF leak repair in addition to tumor resection.¹⁷ In this series, 2 of 25 patients (8%) had postoperative CSF leakage, although increasing use of a nasoseptal flap was thought to reduce this risk.¹⁷ They later reported using a nasoseptal flap in 41.4% of cases, with 48% of patients having intraoperative and 10.5% postoperative CSF leakage in their full series of 133 pediatric patients undergoing the same procedure.⁶

Based on 33 children who underwent endoscopic endonasal approaches for neoplasms, congenital malformations, and skull base defects, Banu et al. reported a GTR rate (75%) comparable to ours (62.5%).⁴ Interestingly, they found that the patient's age did not significantly impact the extent of resection or overall clinical outcome.⁴ In their series of 97 adult and 3 adolescent patients, de Divitiis et al. suggested that the endoscopic endonasal approach allows for safe resection of a diverse array of pathologies.⁸ While most of our patients had pituitary adenomas and craniopharyngiomas, we also included a few patients with other skull base pathologies (e.g., Ewing's sarcoma, optic nerve compression from fibrous dysplasia). Some authors might argue that a transnasal approach should be limited to tumors contained within the sella or below the diaphragma sellae.^{1,31} It is our experience in children that the

TABLE 3. List of individual patients, by tumor type

Case No.	Age (yrs), Sex	Subtype	Preop Signs/Symptoms	Suprasellar Extension	Tumor Dimension (cm)	Op Type
Pituitary adenoma (n = 12)*						
1	11, M	Pituitary adenoma (mixed prolactin, GH secreting)	HAs, bitemp hemianopia, DI, elevated growth hormone & prolactin, hypothyroidism	Yes	3.6	GTR
2	17, F	Pituitary adenoma (mixed prolactin, GH secreting)	Acromegaly	No	1.1	GTR
3	17, F	Prolactinoma	HAs, blurry vision, fatigue, weight gain, elevated prolactin/galactorrhea, amenorrhea, temp dysregulation, frequent urination	Yes	1.7	GTR
	22			No	1.4	GTR
4	17.5, M	Pituitary adenoma (ACTH secreting)	Weight gain, acne, fatigue, increased cortisol	No	NA	GTR
	21			No	NA	GTR
5	17, F	Prolactinoma	HAs, fatigue, amenorrhea, galactorrhea	No	0.8	GTR
6	7, M	Pituitary adenoma (GH secreting)	Eye deviation, ptosis, acromegaly	No	0.9	GTR
7	16, M	Pituitary adenoma (ACTH secreting)	Cushing's disease	No	0.3	GTR
8	18, F	Prolactinoma	Visual field deficit, elevated prolactin	No	1.5	GTR
9	7.9, F	Prolactinoma	HAs, visual loss, bitemp hemianopia, weight gain, amenorrhea, elevated prolactin, DI	Yes	2.6	STR
10	13.5, M	Prolactinoma	HAs, bitemp hemianopia, optic atrophy, elevated prolactin, DI	Yes	4	STR
11	16, M	Prolactinoma	HAs, visual loss, bitemp hemianopia, elevated prolactin	Yes	2.1	GTR
12	13, M	Prolactinoma	Visual loss, elevated prolactin	Yes	2.7	STR
Craniopharyngioma (n = 16)						
13	14, F		HAs, vision loss	Yes	2.4	GTR
14	12.5, F		HAs, bilat hemianopia	Yes	3.5	GTR
15	13, F		HAs, blurry vision, papilledema, obstructive hydrocephalus	Yes	3.9	GTR
16	15, M		Rt eye vision loss, visual field cuts, poor appetite, constipation, dry skin	Yes	4	GTR
	17			Yes	1.7	GTR
17	9, M		HAs, visual field deficit, proptosis, congestion, rhinorrhea, airway obstruction	No	1.6	STR
	10			No	2.3	GTR
18	8, M		Bitemp hemianopia, panhypopituitarism	Yes	4	GTR
19	11, F		HAs, papilledema	Yes	2.1	GTR
20	14, M		Visual loss, bitemp hemianopia	Yes	3.7	GTR
21	12, F		Visual problems, growth failure, fatigue	Yes	3.6	STR × 4, GTR
22	6.5, M		Visual field deficit, panhypopituitarism, hydrocephalus, vomiting	Yes	4.4	GTR
23	9.8, M		HAs, weight loss, N/V, papilledema	Yes	3.7	GTR
24	10, M		HAs	Yes	4.7	Biopsy
25	13.5, M		HAs, growth retardation, hydrocephalus, vomiting	Yes	4.5	GTR
26	11.5, M		HAs, blurry vision	Yes	4.3	GTR
27	14, M		Visual loss, panhypopituitarism	Yes	1.8	GTR
28	5.9, M		HAs, optic nerve compression, panhypopituitarism, hydrocephalus, N/V	Yes	4.4	GTR

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TABLE 3. List of individual patients, by tumor type

Case No.	Age (yrs), Sex	Subtype	Preop Signs/Symptoms	Suprasellar Extension	Tumor Dimension (cm)	Op Type
RCC (n = 4)						
29	14, F		HAs, impaired vision	No	1.1	GTR
30	5, M		HAs, vision loss, visual field deficit, panhypopituitarism	Yes	2.7	STR
31	18, F		HAs, blurry vision, bitemp hemianopia, pituitary apoplexy, dizziness	No	1	Biopsy
32	11, M		Visual loss, bitemp hemianopia, hormone deficiencies	Yes	2.4	GTR
Germinoma (n = 4)						
33	11, F		Fatigue, DI	No	NA ("bright spot")	Biopsy
34	16, M		Vision loss, panhypopituitarism	Yes	2.5	GTR
35	7, F		DI	Yes	0.55	Biopsy
36	11.5, M		Panhypopituitarism	Yes	NA	Biopsy
Chordoma (n = 2)						
37	11, M		HAs, diplopia, CN VI palsy	No	0.3	GTR
38	11, M		HAs, double vision, CN VI palsy	No	3.2	GTR
Other (n = 4)						
39	10, M	Lymphocytic cells	DI, elevated growth hormone	No	NA (enhancing stalk)	Biopsy
40	4, M	Ewing's sarcoma	HAs, proptosis, poor appetite, drowsiness, nasal discharge	No	6.2	Biopsy
41	16, M	Nongerminomatous germ cell tumor	HAs, visual loss, photophobia, N/V panhypopituitarism, elevated beta-HCG & AFP	Yes	1.4	Aborted due to bony bleeding
42	13, M	Optic canal decompression	Progressive blindness	NA	NA	Other

AFP = alpha-fetoprotein; bitemp = bitemporal; DI = diabetes insipidus; GH = growth hormone; HA = headache; HCG = human chorionic gonadotropin; N/V = nausea/vomiting; RCC = Rathke cleft cyst.

endoscopic transnasal approach can be used for GTR of intrasellar as well as suprasellar lesions while minimizing postoperative complications. Compared with open resection, endoscopic approaches have shorter hospital stays, fewer blood transfusions, and lower postoperative pain scores.³⁰ Our median blood loss was 50 ml, and the length of stay was 5 days.

Special Considerations in the Pediatric Population

Anatomical Limitations

In children, the anatomical limitations of endoscopic endonasal approaches are dependent on age-related parameters of the face and skull base.⁴ While intracranial measurements usually reach 95% of adult size at 10 years of age, facial measurements only appear to be at 85% of adult size. Skull base pathology itself can disrupt normal anatomical dimensions that subsequently hinder endonasal access.⁴ The intercarotid distance at the level of the cavernous sinus is significantly smaller in children, but inferiorly at the superior clivus, it does not appear to vary

significantly with age.^{4,29,37} The ability to perform a GTR is related to the intercarotid distance and the lateral extent of the tumor into the cavernous sinus or middle cranial fossa.²⁹ Wider intercarotid distance and shorter nare-dens working distance are associated with better resection outcomes.^{4,39} In our study, the cavernous intercarotid distance of the overall study cohort, whose mean age was in the early teens, was comparable to the length reported in adults.²⁶ The lack of significant difference in cavernous intercarotid distance between adults and children older than 9 years has been previously reported.³⁷ However, in our experience with children younger than 10 years, the approach was often limited by the narrow approach afforded into the sella. In addition, 11 children demonstrated growth failure, which may have resulted in smaller skull base anatomical structures for age, further complicating surgical access. As expected, intercarotid distance was positively correlated with age (Fig. 3) and inversely related to operative times. As the exact operative times were often unavailable for many patients, a formal regression analysis was deferred.

Sellar pneumatization, or lack thereof, is another consideration unique to the pediatric population. Children often do not have a pneumatized sella, a process which begins around the age of 3 years and continues into the teenage years.^{20,37} In children with growth hormone deficiency, the sella is delayed in pneumatization. Children with a nonpneumatized sphenoid required drilling out of the sphenoid bone to gain access to the tumor. Furthermore, the lack of landmarks in the absence of sellar pneumatization such as the optico-carotid recess makes localization challenging.²⁰ In these cases, beginning with a pediatric endoscope (2.7 mm) and transitioning after the initial exposure to an adult-sized endoscope (4 mm) can facilitate visualization.²⁰ Smaller children may therefore require a sublabial approach in order to have enough working space for instrument placement and for greater intra- and suprasellar exposure.^{7,15,19,28}

Surgical Instruments

At our institution, a 45° angled endoscope was used for lateral and superior views of the tumor. Once in the intracranial space, we used a variety of endoscopes with angles ranging from 0° to 45° for adequate visualization depending on the suprasellar extent of the lesion. Transnasal microscopic instruments were used for dissection and resection. The NICO Myriad device (NICO Corp.), an aspiration device designed for the neuroendoscope,²⁷ was not utilized based on surgeon preference and experience with adult cases at our institution.

The manipulation of operative instruments poses unique challenges in children. Instrumental limitations of this approach have been noted in the adult literature as well. For instance, intranasal drills generate bone dust but may lack built-in irrigation and suction functionality, hindering the achievement of ideal visualization.²⁵ Even when performed correctly, irrigation results in transient yet complete obliteration of the surgical field in the narrow sinonasal corridor. Such challenges are only magnified in the pediatric population, especially in the absence of microscopic instruments designed solely for children to accommodate for their diminutive anatomical structures.²⁴ Passage of multiple instruments within the confines of the tight operative field requires dynamic movement and careful positioning. In our experience, the ability to simultaneously place 3 instruments (endoscope, drill, and suction or bipolar electrocautery) was especially limited in children younger than 8 years or in those with a nonpneumatized sella. This difficulty persisted despite the use of pistol-grip bipolar forceps, suggesting that the development of specialized instrumentation for young children would enhance our ability to resect complex suprasellar lesions. Different pathologies may present additional challenges for instrument manipulation, such as a small bony opening that is further decreased by hyperostosis of the sphenoid bone due to pituitary tumor or tissue with increased vascularity in the context of Cushing disease that requires meticulous hemostasis.

Structural Preservation

Compared with craniotomy, an endoscopic endonasal approach can help limit brain retraction and prevent po-

tential neurocognitive effects in children.¹⁷ An endoscope may circumvent facial retraction injury from the speculum used during a traditional craniofacial approach.¹⁷ Additionally, the endoscopic approach allows dentition and facial growth plates to be preserved, which are important advantages in the pediatric population.^{17,28} Studies from the otolaryngology literature indicate that children who have undergone endoscopic sinus surgery do not differ later in life regarding development of facial anatomical dimensions.²⁰

Surgical Approach and Adjunctive Procedures

Literature on pediatric skull base lesions suggests that tumor consistency plays an important role in deciding whether a GTR is feasible and should be attempted.^{1,29} Fibrous tumors may be more difficult to resect using a transnasal approach.²⁹ Some authors have argued that suprasellar calcifications in craniopharyngiomas warrant a transcranial approach.¹ Firm or adherent suprasellar tumors or reoperations pose a higher risk of damaging the optic chiasm, carotid arteries, or other surrounding brain structures as well as a greater risk of bleeding.²⁹

In addition to the main procedure, placement of nasoseptal flaps, fat grafts, and lumbar drains may be considered. In children younger than 10 years, a nasoseptal flap may not be of sufficient size to cover a large skull base defect.²⁰ At our institution, packing of the sella with fat was used initially but was later discontinued, as this was no longer deemed necessary to achieve an adequate barrier to CSF leak. The use of a nasoseptal mucosal flap and packing of the sella with Gelfoam was adequate to prevent a CSF leak. A lumbar drain was placed in the operating room for CSF diversion to lower intracranial pressure when a higher chance of CSF leakage was expected, such as with tumors with significant supra- and parasellar extension. In fact, we observed postoperative CSF leakage only in craniopharyngiomas with suprasellar and/or parasellar extension, which necessitated intraoperatively entering the subarachnoid space, and not in intrasellar lesions. Our practice has evolved from open lumbar CSF drainage at the height of the foramen magnum to a controlled drainage of only 10 ml per hour to minimize the risk of postoperative CSF leakage when intraoperative CSF was observed.

Operative Environment and Training

Endoscopic neurosurgery represents an important collaboration between otolaryngology and neurosurgery. Hardy famously adopted many of the tools used by otolaryngologists to resect not only pituitary tumors but also other skull base lesions.¹³ Increased comfort level with extended endoscopic endonasal approaches in the adult population has led to their wider application in children.²⁰ Tools such as neuronavigation, intraoperative Doppler, and neuromonitoring can facilitate this approach.^{4,28} Intraoperative neuromonitoring is effective for detecting cranial nerve dysfunction during tumor dissection and can help mitigate damage to surrounding structures, and this technique is especially valuable during staged procedures and reoperations.⁹ There is a distinct learning curve associated with transnasal endoscopic surgeries that must also be

overcome for complex surgeries in the pediatric population.²¹

Study Limitations

We report only our own institutional experience, and, as with any surgical approach, there exists a distinct learning curve. However, the collaborative relationship between pediatric neurosurgeons and otolaryngologists has allowed our team to become experienced with this approach, and the evolution in our practice over time (e.g., discontinuation of fat grafts due to complications) reflects the process of gathering institutional knowledge. Long-term clinical follow-up was possible for the majority of patients, but as patients move into adulthood, availability of clinical records was limited by whether they were followed by an adult neurosurgeon at our institution. Despite the lack of uniformly obtainable data for all patients, the median follow-up time of our study cohort was 46 months, which is longer than that in previously published pediatric case series on transnasal endoscopic approaches in the US. Multiple pathologies were discussed in this case series, as might be expected in the pediatric population, but the variety of conditions treated by this surgical approach suggests its applicability to many different pediatric diseases. Given the rare incidence of many pediatric skull base lesions, only a few case series on this topic have focused on a single pathological condition.

Conclusions

This single-institution case series suggests that transnasal endoscopic approaches have utility for diagnosing and treating pediatric skull base lesions with a high likelihood of symptomatic relief. In particular, for prolactinomas, resection can be considered when medical therapy has failed or is not well tolerated. For craniopharyngiomas, resection can remove or debulk selected complex tumors, obviating either postoperative irradiation or chemotherapy. Favorable surgical outcomes require careful patient selection and an experienced team of surgeons. Further development in imaging, simulation techniques, and instrumentation will allow for careful preoperative planning and improved resection via minimally invasive exposure, thereby expanding the current use of this microsurgical approach.

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Disclosures

Dr. Hwang: consultant for Medtronic and Canon. Dr. Patel: consultant for Medtronic, Stryker, IntersectENT, and Optinose.

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Conception and design: Edwards, Quon. Acquisition of data: all authors. Analysis and interpretation of data: Edwards, Quon, Kim. Drafting the article: Edwards, Quon, Kim. Critically revising the article: Edwards, Quon, Kim. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Edwards. Statistical analysis: Kim. Administrative/technical/material support: Edwards, Quon, Kim. Study supervision: Edwards.

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