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TECHNICAL NOTE

Combined endoscopic and microscopic management of pediatric pituitary region tumors through one nostril: technical note with case illustrations

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Abstract
Objective Sellar and parasellar lesions in the pediatric population have traditionally been approached through either a transsphenoidal hypophysectomy or craniotomy or a combination of the two, with the surgical approach being dictated by the anatomical location and extent of the pathology. The introduction and evolution of the endonasal endoscopic technique has provided a minimally invasive method alone or in combination with the operative microscope for removal of these lesions in the pediatric population. The authors have implemented in their practice the use of endonasal endoscopic-assisted microsurgery in the pediatric population harboring sellar and/or lesions extending to the suprasellar space and report our experience in nine patients.
Materials and methods Five craniopharyngiomas, one Rathke's cleft cyst, and two pituitary tumors were treated via endonasal endoscopic-assisted microsurgery. Histopathologic examination revealed lymphocytic hypophysitis in one patient with an enhancing lesion in the pituitary stalk. The approach utilized by the authors is performed through one nostril without any resection of the nasal turbinates or nasal septum. The middle turbinate is displaced laterally, while the nasal septum is moved medially.
Conclusion Gross total, near-total, and subtotal resections and a diagnostic biopsy were obtained in six, one, one, and one patients, respectively. The authors were able to safely perform this procedure in nine pediatric patients, and the lack of turbinate or septum resection minimized postoperative discomfort.

Keywords Endoscope · Hypophysectomy · Endonasal · Transsphenoidal · Sellar · Parasellar

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Introduction

Sellar and parasellar lesions in the pediatric population include a vast array of tumors. Approximately 90% of neoplasms arising in the sellar and parasellar region are craniopharyngiomas with less than 10% including pituitary adenomas, Rathke's cleft cysts, germinomas, hamartomas, lipomas, teratomas, dermoid cysts, and epidermoid cysts [9, 50, 51, 75, 77, 80, 84]. Craniopharyngiomas typically present in the first and second decades of life and also in the fifth decade resulting in a bimodal age distribution [91]. Pituitary adenomas account for under 3% of tumors in the pediatric population with prolactinomas predominating as the major histologic subtype, followed by adrenocorticotropic hormone (ACTH)-secreting adenomas [7, 50]. Traditionally, these lesions have been treated by a transsphenoidal hypophysectomy and/or craniotomy depending on findings with neuroimaging.

The transsphenoidal approach is a versatile option for access to various lesions of the pituitary gland and sellar region [32, 38, 43, 53, 63, 65–68, 97, 98]. It offers a less traumatic route to the sella turcica, avoids brain retraction, and provides good visualization of the sellar and parasellar region [22]. In 1907, a pituitary tumor was successfully

removed through a transsphenoidal approach by Schloffer [33, 70, 87, 96]. Harvey Cushing [21] operated on 231 pituitary tumors through the sublabial transsphenoidal approach with a mortality rate of 5.6% [46]. Cushing started utilizing this approach in 1912 when he combined the submucosal resection of Hirsch with the sublabial incision of Halstead [19, 40, 46, 47]. Hardy [43] subsequently modified the procedure with microsurgical techniques, including the addition of the operating microscope and fluoroscopy. Advances in neurosurgical techniques have led to less invasive methods for the treatment of these lesions, including transnasal endoscopic transsphenoidal surgery [10, 12, 13, 15, 20, 23–25, 36, 39, 42, 44, 45, 54, 56, 58, 59, 61, 64, 71, 85, 90, 99, 100, 102]. Initial endoscopic procedures to the sella used the sublabial and/or transseptal approaches, although the sublabial approach has been associated with upper lip and incisor paresthesias [55, 57, 79, 88]. The operative microscope provides a good field depth and excellent stereoscopic three-dimensional view of the surgical area of interest, in addition to a more comfortable working surgical corridor after an intranasal speculum has been situated. An endoscope can be used as a complement to microsurgery during and/or after the removal of the lesion and to provide a more detailed exploration of the sellar and suprasellar regions, especially when examining difficult angles and large lesions. Endoscopy provides excellent visualization of sellar anatomical landmarks and the lesion of interest, and recent reports have documented the utilization of the endoscope in pediatric patients for sellar region tumors [24, 34, 35, 50, 52, 60, 72]. In contrast to adults, a child's nostril may be too small for the introduction of an intranasal speculum. Introduction of the endoscope into a nostril may be the only way to gain access followed by placement of a pediatric self-retaining speculum. In contrast to our practice, some surgeons advocate making an incision in the posterior nasal septum to enable greater access [30].

In this report, we report our experience with the utilization of a combination of both the microscope and endoscope in transnasal transsphenoidal approaches for sellar and suprasellar lesions through a single nostril in nine pediatric cases.

Clinical material and methods

During the last 15 months, nine endoscopic-assisted endonasal transsphenoidal microsurgical procedures were performed for sellar and/or suprasellar lesions. This series consists of five craniopharyngiomas, one Rathke's cleft cyst, one prolactinoma, one ACTH-producing adenoma, and one lymphocytic hypophysitis. There were five girls and four boys in this series (Table 1).

Preoperative and postoperative ophthalmological and endocrinological evaluations were performed. Preoperative brain magnetic resonance imaging (MRI) was obtained, and an immediate postoperative MRI was obtained with subsequent follow-up scans every 4 to 6 months. The operative microscope (Carl Zeiss Surgical, Inc., OPMI® Pentero™) in combination with 0° and 30° endoscopes (Karl Storz Endoscopy-America, Inc.) was utilized in all cases. The endoscope was utilized for approach and resection and/or to assess the presence of any residual tumor and the degree of decompression. All of the operations were performed by the same two surgeons (GIJ, AQH).

Surgical preparation

General anesthesia induction is followed by endotracheal intubation. In patients with clear suprasellar extension that may be a higher risk for intraoperative and postoperative cerebrospinal fluid leaks, initially, the patient is placed in the lateral decubitus position, and the lumbosacral spinal region is prepped and draped for placement of a lumbar drain. Next, the patient is placed in the supine position with

Table 1 Demographics, presenting symptoms, radiographic findings, and pathology of the nine pediatric patients that underwent surgery

Characteristics	No. of patients
Age (mean±standard deviation)	11.1±5.2 (range, 3–17)
Gender	
Male	4
Female	5
Presenting symptoms	
Duration of symptoms (months) [median (IQR)]	7 (0.5–10.5)
Headache	6
Visual deficit	2
Visual field deficit	2
Nausea or vomiting	1
Endocrinopathy	6
Prolactinoma	1
Cushing's disease	1
Panhypopituitary	1
Diabetes insipidus	2
Growth hormone deficiency	1
Radiographic findings	
Size (cm) [median (IQR)]	2.5±1.6
Optic chiasm compression	4
Suprasellar extension	4
Cavernous sinus invasion	1
Pathology	
Craniopharyngioma	5
Pituitary adenoma	2
Rathke's cleft cyst	1
Lymphocytic hypophysitis	1

the head located on a horseshoe that is attached to the table by a Mayfield adaptor. The nasal cavities are prepped with Betadine paint and the abdomen is prepped in the usual sterile fashion. Once the area of the nose and abdomen are draped, Afrin®-soaked cotton pledgets are placed in both nasal cavities. A fluoroscopy C-arm is draped in a sterile fashion and placed at the head of the patient with the fluoroscopy monitor situated lateral to the C-arm. The approach is made from the right-hand side for the right-handed surgeons and for lesions that are in the midline and/or lesions that are eccentric to the left of the sella towards the cavernous sinus. The operative microscope and the endoscope are also draped in the usual sterile fashion. Ipsilateral to the surgeon, a table-mounted pneumatic arm is attached to hold the endoscope. This pneumatic arm facilitates maneuverability of the endoscope and is placed caudal to the head to avoid interference with fluoroscopy.

Surgical technique

A small transverse incision is made in the left lower abdominal quadrant or semicircular around the belly button, and Bovie cautery is utilized to circumferentially harvest a large piece of adipose tissue for patients with large lesions and/or patients that have a cerebrospinal fluid leak at the end of the procedure. The right lower abdominal quadrant is not used so that other physicians will not mistake an incision in this region in the pediatric population for a previous appendectomy. After closure of the wound, attention is turned to performing the endonasal transsphenoidal hypophysectomy.

Oxymetazoline (Afrin)®-soaked cotton pledgets are placed in each nasal cavity and removed after 5–10 min to aid in hemostasis. A handheld pediatric intranasal speculum is inserted into the nasal cavity, and a #2 penfield is utilized to move the middle turbinate laterally without any resection. In the case of our youngest patient (3 years), a small narrow-caliber handheld nasal speculum had to be used because of the small size of the nostrils. The nasal septum is moved medially without any resection, and fluoroscopic images are serially taken to localize the sphenoid sinus with the aid of the penfield and/or the suction tip. Once the sphenoid ostia are identified, the #2 penfield is used to open a window into the sphenoid sinus and to move the septum laterally with the preservation of the contralateral mucosa. The rostrum is identified to localize the midline and partially resected along with the anterior wall of the sphenoid sinus using kerrison punches and pituitary rongeurs. An Anspach drill with a 3-mm diamond drill bit is utilized to remove the anterior wall of the sella (catalog #MA15–8NSDC; 3-mm coarse diamond matchstick (15 mm), used in minimal access attachment #MA-D20 with 15-cm bearing sleeves). Sometimes, we use the same drill in the resection of the anterior rostrum. The dura is incised in a cruciate fashion with a #11 scalpel blade. Ringed curettes (Endoscopic Endonasal Pituitary Set, Integra Catalog #RN-5000) are used to remove the pathology, and specimens are submitted to the pathologist for histologic examination. The pituitary gland is identified and protected during the operation. A Valsalva maneuver is induced to bring suprasellar pathology into the sella to facilitate resection.

The endoscope is mobilized into the operative field for the surgical approach and/or to obtain better visualization within the sella turcica (Fig. 1). Any remaining pathology is removed, and the endoscope is taken out of the surgical field once the surgeon has achieved satisfactory resection. The harvested fat graft is cut, wrapped in Surgicel® (Johnson & Johnson), and placed into the sell turcica. DuraGen® (Integra LifeSciences Corp) is placed over the fat graft and Tisseel® is (Baxter International) inserted. A Synthes bioabsorbable miniplate is used to reconstruct the anterior wall of the sella (catalog #851.009.01S). The nasal septum and concha are moved back into their respective anatomical locations, and oxymetazoline (Afrin)®-soaked cotton pledgets are placed in each nasal cavity to aid in hemostasis. This nasal packing is removed just prior to extubation. If a cerebrospinal fluid (CSF) leak is not observed, the lumbar drain is removed prior to extubation. Otherwise, the drain is left in place postoperatively if a CSF leak is observed during the case.

Results

Nine transnasal endoscopic-assisted microsurgical procedures were performed for sellar and intrasellar lesions in this cohort of pediatric patients ranging in age from 3 to 17 years (Table 2). The mean follow-up period was 9.5± 4.5 months (range, 1–17 months). Preoperative MRI demonstrated a mean size of 2.5±1.6 cm for the lesions. Six patients had a gross total resection of their tumors, while one patient had a near-total resection as revealed by postoperative MRI. One patient had a diagnostic biopsy for a pituitary stalk lesion that caused diabetes insipidus (DI), and the final pathology revealed lymphocytic infiltration without neoplastic cells or granuloma formation. One subtotal resection was observed for a craniopharyngioma with local recurrence necessitating postoperative radiation treatment. Adjuvant postoperative radiation therapy was also administered to the patient with a near-total resection of a craniopharyngioma. Four patients underwent lumbar drain placement, in which three had their drains removed immediately upon completion of the operation, and one patient developed a CSF leak during surgery that resolved

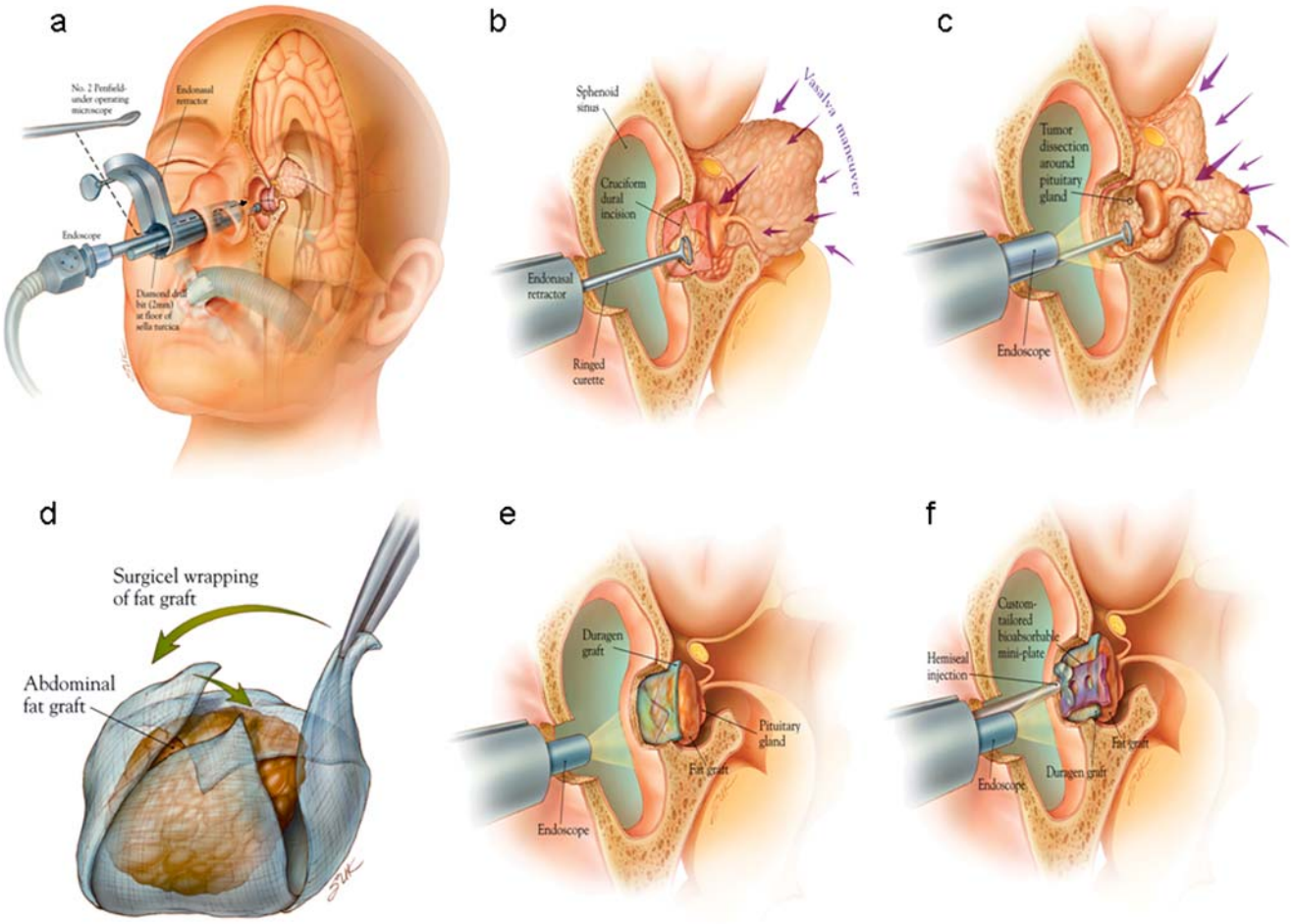

Fig. 1 **a** The intranasal speculum is in place as a working corridor for the endoscope. A 2-mm diamond burr is used to drill the anterior wall of the sella turcica. **b** Cruciform dural incision. **c** A ringed curette being used for tumor removal after the dural incision with identification of the pituitary gland. Valsalva maneuver for assistance in bringing the tumor down from the suprasellar region. **d** Wrapping of the harvested fat graft in Surgicel® (Johnson & Johnson). **e** Placement of the fat graft into the sella and sphenoid sinus followed by the placement of duragen. **f** Placement of the synthes bioarbsorbable miniplate (catalog #851.009.01S). Fibrin glue (Tisseel® [Baxter International]) is utilized for reinforcement

with lumbar drainage, in which the lumbar drain was removed on postoperative day 4. The mean hospital stay was 5±2 days.

Four patients had preoperative visual deficits, including two with bitemporal hemianopsia, and no patient experienced any worsening of vision postoperatively. The two patients with bitemporal hemianopsia had a craniopharyngioma. In one patient with a preoperative bitemporal hemianopsia, there was no improvement in vision after surgery at 17 months follow-up. The remaining patients had improvement of their vision at the 12-month follow-up. Furthermore, six patients had DI, in which two had the diagnosis prior to surgery. Four of the six patients continue to require desmopressin acetate (DDAVP), including two craniopharyngioma patients, one with the diagnosis of a Rathke's cleft cyst and another with a diagnosis of chronic inflammation of the pituitary gland at 3-, 12-, 13-, and 1-month follow-up, respectively. Two craniopharyngioma patients had panhypopituitarism after surgery, in which one had the diagnosis preoperatively. One patient continues to be treated with hormonal replacement therapy at 17 months follow-up and is followed closely by endocrinology with regularly scheduled clinic visits at the discretion of the endocrinologist. The other patient is being treated for hypothyroidism at 12-month follow-up. There were no intraoperative or postoperative deaths or any significant neurological deficits.

Illustrative cases

Case 1

History and presentation A 10-year-old boy presented with a 1-year history of headaches and nocturnal enuresis. His

Table 2 Perioperative characteristics and postoperative outcomes of the nine pediatric patients that underwent surgery

Outcome	No. of patients
Operative	
Lumbar drain	4
Fat graft	4
CSF leak	1
Estimated blood loss (cc) [median (IQR)]	50 (15–50)
Extent of resection	
Gross total resection	6
Near-total resection	1
Subtotal resection	1
Diagnostic biopsy	1
Hospital stay	
Duration, days (mean±standard deviation)	5±2
Complications	
Diabetes insipidus	6
Panyhypopituitary	2
CSF leak	0
Perioperative death	0
Neurological outcomes	
Vision improved	2
Vision maintained	7
Vision worsened	0
New motor, sensory, language deficit	0
Local recurrence	1
Postoperative radiation	2
At last follow-up	
Vision outcome	
Vision stabilization	9
Vision worsened	0
Preoperative symptoms	
Symptoms improved	7
Symptoms maintained	2

physical examination was remarkable for decreased visual acuity in the right eye, 20/25, and a bitemporal hemianopsia. A brain MRI revealed a 1.7×1.9×2.8-cm cystic mass in the sellar and suprasellar region with optic chiasm compression (Fig. 2a,b). Preoperative endocrinologic evaluation revealed central diabetes insipidus and hypothyroidism.

Operation and postoperative course The patient underwent endonasal endoscopic-assisted microsurgical resection, via thyroid-stimulating hormone (TSH), of the lesion. Histopathologic examination of the specimen revealed the lesion to be a craniopharyngioma. A postoperative CSF leak was not observed, and postoperative MRI demonstrated gross total resection and decompression of the optic chiasm (Fig. 2c,d). An endocrinologist was consulted, and the patient was maintained on Synthroid and DDAVP for his hypothyroidism and diabetes insipidus, respectively. Based on his last endocrinology clinic visit, which was 1 year after surgery, he continues to be maintained on these medications. Ophthalmologic examination revealed 20/20 visual acuity in both eyes and full visual fields to confrontation testing bilaterally. He was discharged on postoperative day 3.

Case 2

History and presentation A 14-year-old girl presented to the emergency department with severe headaches and emesis. A head computed tomography demonstrated a 3-cm intracranial lesion in the sellar region without mass effect. A brain MRI was performed and revealed a mass with intrasellar and suprasellar components. The intrasellar component measured 1.7×1.0×1.3 cm, and the suprasellar component measured 2.6×2.0×2.5 cm with optic chiasm compression (Fig. 3a–c). An endocrinologic evaluation revealed normal pituitary function, and ophthalmologic workup did not reveal any visual deficits.

Operation and postoperative course An endoscopic-assisted microsurgical resection of the lesion was performed using the endonasal route for TSH. Pathologic analysis determined the lesion to be Rathke's cleft cyst. A postoperative cerebrospinal fluid leak was noted, which resolved with a lumbar drain in place, which was removed on postoperative day 4. The patient developed diabetes insipidus requiring DDAVP, which she is still taking based on her last endocrinology clinic visit 8 months after surgery. A postoperative MRI demonstrated gross total resection and decompression of the optic chiasm (Fig. 3d–f). No postoperative visual deficits were observed. She was discharged after achieving satisfactory control of her diabetes insipidus.

Discussion

Sellar and parasellar lesions in the pediatric population are approached through either a craniotomy or transsphenoidal hypophysectomy. The surgical approach is usually determined by the anatomic relationship of the suprasellar pathology to surrounding structures and if an intrasellar component is present. A craniotomy is typically performed for lesions with only a suprasellar location, although extended transsphenoidal approaches are being utilized [14, 26, 35, 62, 101]. Transsphenoidal hypophysectomies are conducted for pathology located in the intrasellar and/or suprasellar compartments [5, 41, 64, 65].

Pituitary adenomas occur infrequently in the pediatric population, and our series included two patients, in which there was a nonsecreting tumor in one patient and

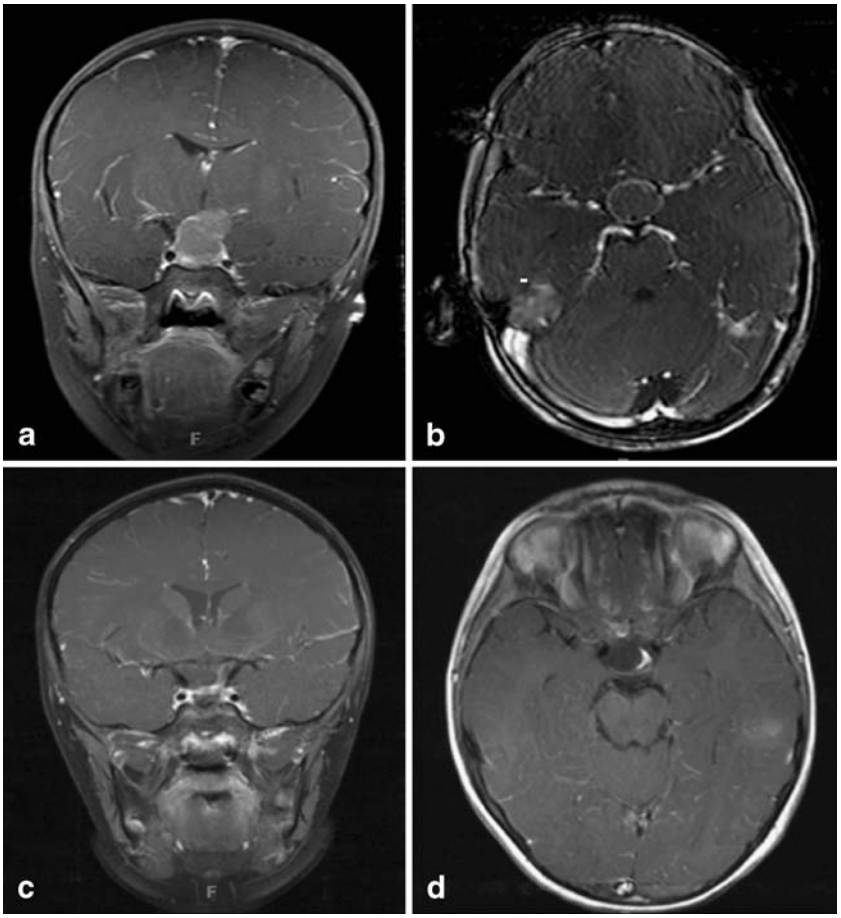

Fig. 2 Preoperative and postoperative MRI scans showing the craniopharyngioma and subsequent resection in a 10-year-old boy with a 1-year history of headaches and nocturnal enuresis. A bitemporal hemianopsia was detected on exam. **a**, **b** Preoperative coronal and axial postcontrast MRI scans. **c**, **d** Postoperative coronal and axial postcontrast MRI scans

Cushing's disease in another. Cushing's disease is rare in children and can result in significant morbidity and mortality if left untreated [58]. Rapid diagnosis and treatment are important for the maintenance of cognitive and physical development [31, 58]. These lesions are typically treated via a transsphenoidal approach [8, 43, 58, 73, 81, 93].

Traditionally, lesions with a predominant suprasellar location, such as craniopharyngiomas, have been approached through a craniotomy with increased risk of morbidity and mortality contingent upon the experience of the surgeon [29, 32, 80]. Recent reports have advocated stratification of craniopharyngiomas by location and the extent of hypothalamic involvement in an attempt to determine which lesions are more amenable to gross total resection or subtotal resection followed by potential radiotherapy to reduce devastating morbidity and deterioration in the quality of life [29, 78, 82, 83, 94]. Hypothalamic dysfunction, including endocrinopathy and hyperphagia, motor and/or sensory deficits, decline in cognitive function, and worsening of vision after surgery are major concerns with craniotomies for these lesions [3, 17, 27, 28, 32, 37, 78, 82, 89, 103]. Transnasal endoscopic-assisted microsurgery provides a less invasive approach for these lesions that can be performed safely, but endocrinopathy, worsening of vision, and postoperative obesity, particularly with the extended transsphenoidal approach, can occur although at a lower rate when compared to craniotomy [1, 4, 15, 18, 24, 26, 32, 35, 59, 86, 95].

The endonasal transsphenoidal route offers a less traumatic route for the resection of sellar and parasellar lesions, especially in the pediatric population. Both the microscope and endoscope are effective methods for the transsphenoidal approach to these lesions. The microscope offers stereoscopic three-dimensional visualization, in addition to illumination and magnification of the operative field and sometimes the distinction of the plane between the tumor and the normal pituitary. Endoscopy allows for a

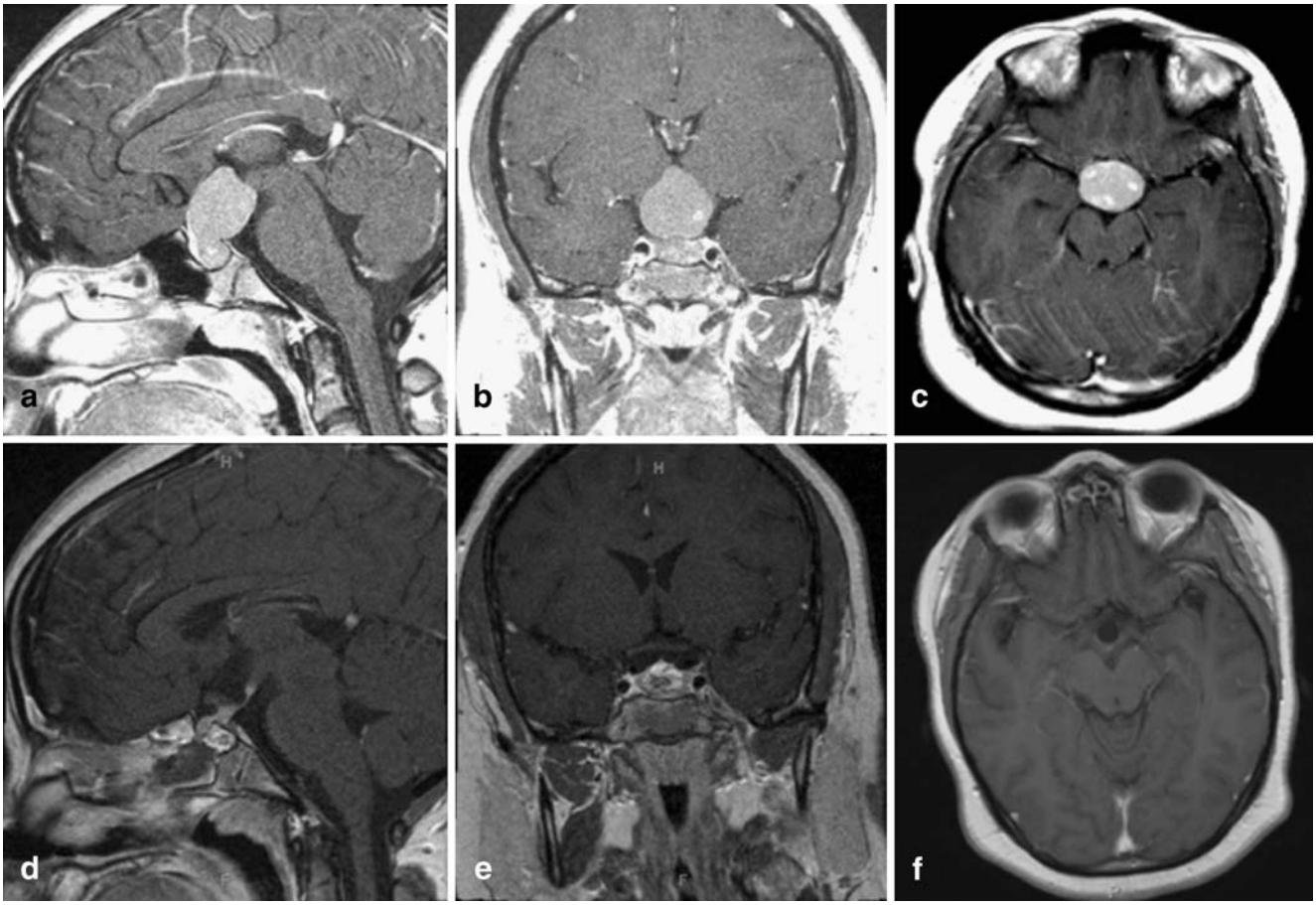

Fig. 3 Preoperative and postoperative MRI scans demonstrating the Rathke's cleft cyst and resection in a 14-year-old girl who presented with severe headaches and emesis. **a**–**c** Preoperative sagittal, coronal, and axial postcontrast MRI scans, respectively. **d**–**f** Postoperative sagittal, coronal, and axial postcontrast MRI scans, respectively

larger and closer view of the surgical field, particularly providing better anatomical detail and visualization of any residual pathology, and a lower complication rate [11]. Endoscopy has been shown, through anatomic studies, to provide a volume of exposure superior to that of the operating microscope [92]. In addition, diagnostic biopsies can be performed for pituitary lesions utilizing this method. In our case series, one patient presented with diabetes insipidus, in which a brain MRI demonstrated a pituitary stalk lesion. A biopsy was performed, and the final histopathologic examination revealed lymphocytic hypophysitis. Although rare, cases of lymphocytic hypophysitis have been reported in the pediatric population [2, 6, 16, 48, 49, 69, 74, 76]. Therefore, the microscope and endoscope can be utilized to complement each other in endonasal transsphenoidal hypophysectomies with excellent results as represented by our case series and two case illustrations.

The technique employed by the authors offers a less invasive method for approaching the sella turcica and suprasellar region. There is no resection of the turbinates or nasal septum; however, the degree of difficulty of the operation is increased, especially in younger patients with a small pituitary fossa and/or the absence of sphenoid sinus aeration in some cases. Although more technically challenging since the surgeon is working through a narrower corridor without the aid of turbinate and/or septum resection, our series of patients demonstrates that this method can be safely performed with good operative outcomes. A majority of our patients had a gross total resection of their lesions. An observed advantage of not resecting any turbinate or nasal septum was the minimal postoperative discomfort in our patients.

Conclusions

Endonasal transsphenoidal hypophysectomy through endoscope-assisted microsurgery can be safely used to extirpate sellar and parasellar lesions in the pediatric population. Our method may be more technically challenging but can be

safely performed for lesion extirpation while minimizing postoperative discomfort. As endoscopic techniques continue to evolve, this combined approach will only be enhanced while minimizing any associated morbidity and mortality.

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