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FOCUS SESSION

The endoscopic endonasal approach for pediatric craniopharyngiomas: the key lessons learned

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Abstract

Purpose The aim of this study is to highlight the role of the endoscopic endonasal approach (EEA) in pediatric craniopharyngiomas by reviewing our experience and the key lessons learned from the application of this approach in children.

Methods Between 1998 and 2017, 12 pediatric craniopharyngiomas were treated via EEA at our institution. Demographic data, preoperative assessment, tumor features, surgical results, complications, and recurrences were analyzed.

Results Visual defects were the most frequent presenting sign. Seven craniopharyngiomas were infradiaphragmatic, and five were supradiaphragmatic. The EEA was successfully performed in all cases with no complication related to children's sinonasal anatomy. Gross total resection (GTR) rate was of 75%. Endocrinological disturbances improved in one case (20%) and worsened in three (60%). New onset of diabetes insipidus was observed in four (36%) children. Visual defect improved in 91% of cases, with no new postoperative deficit. Postoperative cerebrospinal fluid (CSF) leak occurred in one patient (8%). Three patients (27%) experienced tumor regrowth, and one craniopharyngioma recurred (mean follow-up, 78 months).

Conclusions The EEA offers a straight route to the sellar-suprasellar, making it the ideal approach for pediatric infradiaphragmatic craniopharyngiomas. In supradiaphragmatic craniopharyngiomas, the extended EEA provides a clearer and close-up visualization of the tumor-hypothalamus interface, which can grant better results in terms of quality of life. The pediatric skull base anatomy should not represent a contraindication for the endoscopic technique. Larger series encompassing a wider spectrum of pediatric craniopharyngiomas are needed to further support the benefits of this surgical approach.

Keywords Craniopharyngiomas · Endoscopic endonasal approach · Pediatric

Introduction

Craniopharyngiomas are histological benign tumors that can be burdened by a severe clinical course, mostly related to their tendency to involve a great number of vital neurovascular structures and the high rates of recurrence. They present with a bimodal distribution, being frequent at childhood (mean age 5–14 years) and late adulthood (mean age 50–74 years). Pediatric craniopharyngiomas, representing 30–50% of the cases, are the most commonly diagnosed tumors of the sellar and suprasellar region in children [1–3]. Childhood-onset craniopharyngiomas are almost diagnosed as adamantinomatous histological subtype, and are frequently associated with cystic components, irregular interface, and adhesion to surrounding structures. Aside of the sellar region, craniopharyngiomas develop into surrounding areas of the skull base, tightly adhering to optic nerves and chiasm, internal carotid arteries, third ventricle—above all its floor, hypothalamus and pituitary gland, thus causing a variety of symptoms [4–6].

The optimal treatment of pediatric craniopharyngiomas is complete surgical resection with preservation of hypothalamic and visual functions; subtotal resection should be preferred in certain unfavorable cases at high risk or to permit adequate psycho-motor development [7–13]. As a result, outcome assessments in the pediatric population focus more on quality of life rather than radical removal.

According to the pattern of growth of most craniopharyngiomas, the transsphenoidal route has been

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advocated for the surgical management of these lesions since its introduction in the early 1960s by Gerard Guiot [14]. This technique initially was reserved only for lesions with a cystic component, with a minimal suprasellar extension, in patients with an enlarged sella, preferably with panhypopituitarism. The transsphenoidal microsurgical approach allows a shorter and direct route to the tumor as compared with transcranial approaches, obviating the need of brain retraction and neurovascular manipulation [15–20]. Recently, the endoscope perfectly suited this scenario, bringing further advantages in terms of visualization and safety: a wider, close-up view of the surgical field over the vital neurovascular structures along with the chance of bringing the eye inside the sellar and suprasellar areas [21–29]. The transsphenoidal endoscopic technique has been adopted according to conventional indications and, along with the increasing technological progress and surgeons' confidence, extended for the treatment of supradiaphragmatic craniopharyngiomas. The introduction of the so-called extended endoscopic transsphenoidal approaches provided a greater exposure of the subchiasmatic and retrochiasmatic areas, as well as of the stalk–infundibulum axis, permitting safe surgical maneuvers inside the crucial areas along the growth path of craniopharyngiomas [30–40].

The endoscopic endonasal approach (EEA) is nowadays widely accepted for the treatment of craniopharyngiomas in the adults, while pediatric reports are still sparse in the literature [11, 39, 41–45]. Herein we review our consecutive series of 12 pediatric craniopharyngiomas treated by endoscopic endonasal approach and the key lessons learned from the application of this approach.

Methods

Patient population

Between 1998 and 2017, 12 children (8 males and 4 females, mean age 12 years, range 7–16 years) underwent surgery for the removal of a craniopharyngiomas via an endoscopic endonasal approach at our institution. Among them, four (36%) had previously been surgically treated via a transcranial route; one had received also radiotherapy. The mean follow-up was 78 months (range 18–256 months). Demographic data, preoperative assessment (endocrinological and visual status and presenting signs), tumor features, surgical results, and complications and recurrences were retrieved from our electronic database (FileMaker Pro 11, FileMaker, Inc.).

Preoperative assessment

Upon admission, patients underwent basal and dynamic hormonal status evaluation. Partial hypopituitarism was defined when two axes had deficiencies, and panhypopituitarism was present when three or more axes were deficient. All patients were evaluated preoperatively for visual acuity, and computerized visual field examination was performed. In the postoperative course these examinations were performed at 3 months and 1 year after surgery; they were further repeated when clinically appropriate.

Surgical procedures

According to lesions features and main purpose of the surgery, patients underwent a standard endoscopic endonasal approach to the sellar region in case of infradiaphragmatic lesions, whereas an "extended" approach (i.e., transtuberculum-transplanum) was run in case of supradiaphragmatic tumors. Detailed depiction of these approaches has been extensively described in previous publications [32, 37, 38]. In one case of infradiaphragmatic craniopharyngioma, at the end of tumor removal, cistosphenoidotomy was performed [46, 47]. The endoscopic endonasal approach for the removal of an infradiaphragmatic craniopharyngioma is a two-surgeon, three- or four-handed technique along a binostril surgical corridor: a wide anterior sphenoidotomy is achieved and parasellar areas are exposed over the posterior wall of the sphenoid sinus. The sellar floor is opened and bimanual dissection is performed under endoscopic visual control between close-up and panoramic views. On the other side, in cases of craniopharyngiomas with prevalent extension in the supradiaphragmatic space, the so-called extended technique is adopted: bone is removed off the superior half of the sella and the planum sphenoidale is opened. A complete removal of the tuberculum sellae is accomplished, including medial optocarotid recess, in order to access the suprasellar area and gain adequate exposure for tumor resection.

Results

Signs and symptoms

Upon hospital admission, visual defects were the most frequent sign in both groups of craniopharyngiomas, accounting overall for a 92% rate of incidence, followed by endocrinological disturbances (75%). The predominant visual defect was bilateral temporal hemianopia (45%). Panhypopituitarism and partial hypopituitarism were observed in 5 (45%) patients each; two children were preoperatively diagnosed with diabetes insipidus. No hydrocephalus or other neurological defects were present at admission. Two of the five children harboring supradiaphragmatic craniopharyngioma showed hypothalamic symptoms, namely, bulimia/obesity (40%).

Table 1 Patients' and tumors' characteristics of 12 pediatric craniopharyngiomas treated by endoscopic endonasal approach

Demographic characteristics		Tumor features			Signs and symptoms at presentation	
Age	Previous treatment	Extension	III ventricle involvement	Consistency	Endocrinological	Visual
10		Supradiaphragmatic preinfundibular	Compressed	Cystic-solid with calcification	Partial hypopituitarism	Left eye acuity reduction
10	TCA + RT	Infradiaphragmatic intra-suprasellar	Uninvolved	Mainly cystic	Panhyopopituitarism	Bitemporal hemianopsia
16		Infradiaphragmatic intra-suprasellar	Uninvolved	Mainly cystic		Bitemporal hemianopsia
13	TCA	Supradiaphragmatic preinfundibular	Compressed	Cystic-solid with calcification	Partial hypopituitarism	Right amaurosis and left temporal hemianopsia
10		Infradiaphragmatic intra- para-suprasellar	Uninvolved	Cystic-solid	Partial hypopituitarism	
7	TCA	Infradiaphragmatic intra-suprasellar	Uninvolved	Cystic-solid with calcification	Partial hypopitutarism	Bitemporal hemianopsia
12	TCA	Infradiaphragmatic intra-para-suprasellar	Uninvolved	Cystic-solid with calcification	Panhypopituitarism and DI	Bilateral superior quadrantopsia
11		Infradiaphragmatic intra-suprasellar	Uninvolved	Mainly cystic with calcification	Panhypopituitarism	Bitemporal hemianopsia
8		Infradiaphragmatic intra-suprasellar	Compressed	Mainly cystic with calcification	Panhypopituitarism and DI	Bilateral superior quadrantopsia
11		Supradiaphragmatic preinfundibular suprasellar	Compressed	Mainly cystic with calcification	Partial hypopituitarism	Right temporal hemianopsia
10		Supradiaphragmatic preinfundibular	Compressed	Cystic-solid		Right amaurosis
10		Supradiaphragmatic retroinfundibular	Invaded	Cystic-solid with calcification	Panhypopituitarism	Bitemporal hemianopsia

Demographic characteristics	Signs and symptoms at presentation	Outcome				
Age	Hypothalamic	Extent of resection	Endocrinological	Visual	Hypothalamic	Recurrence/regrowth and further treatment
10		STR	Worsened	Improved	Unchanged	Regrowth; extended EEA + RT
10		STR	Unchanged and new onset DI	Improved	Unchanged	Regrowth; EEA + cistosphenoidotomy
16		GTR	Unchanged	Improved	Unchanged	
13		STR	Unchanged	Improved	Unchanged	Regrowth; lost at follow-up
10		GTR	Improved	Unchanged	Unchanged	Recurrence; EEA + cistosphenoidotomy + RT
7		GTR	Worsened and new onset DI	Improved	Unchanged	
12		GTR	Unchanged	Improved	Unchanged	
11		GTR	Unchanged	Improved	Unchanged	
8		GTR	Unchanged	Unchanged	Unchanged	
11	Bulimia/obesity	GTR (two-staged planned procedure)	Worsened and new onset DI	Improved	Unchanged	TCA for the known residual tumor
10		GTR	Unchanged	Improved	Unchanged	
10	Bulimia/obesity and memory deficit	GTR	Unchanged and new onset DI	Improved	Unchanged	

DI diabetes insipidus, EEA endoscopic endonasal approach, GTR gross total resection, RT radiotherapy, STR subtotal resection, TCA transcranial approach

Tumor features

The majority of craniopharyngiomas were infradiaphragmatic lesions (58%); all of them were intra-suprasellar lesions, and in two cases parasellar extension was present. The main extension of the supradiaphragmatic craniopharyngiomas (5 cases, 42%) was preinfundibular in four patients and retroinfundibular in one child, with third ventricular invasion. In regard to consistency, cystic-solid tumors were prevalent (58%), with calcifications of different degrees present in 67% of cases. Table 1 summarizes patients' and lesions' characteristics in our series.

Sinonasal corridor and skull base closure

The transsphenoidal approach was successfully performed in all cases with no complication related to children's sinonasal anatomy. We used a 2.7-mm Ø endoscope to operate on the youngest children in our series, i.e., ≤ 7 years old, according to the evidence of narrow nasal cavities. The surgical approach was performed with no restrictions and, though, we adopted the standard 4-mm endoscope. We found a fully pneumatized sphenoid sinus in 83% (10/12) of cases. In two children (7 and 8 years old) harboring a presellar sphenoid sinus, the anterior wall of the sella was reached with cautious drilling of the soft cancellous bone, under neuronavigation guidance. In all cases of extended EEA, the anterior pneumatization of the sphenoid sinus at the tuberculum sellae allowed a safe and adequate bone removal to access the suprasellar space. Intercarotid distance never represented a limitation for the approach, neither for infradiaphragmatic or supradiaphragmatic craniopharyngiomas. No differences with the adult patients were noted with regard to harvesting of the nasospetal flap (required in 25% of cases): dimension of the nasal septum resulted capable of anterior cranial fossa reconstruction in all cases with preservation of the olfactory functions. In two cases of EEA, treated prior to the adoption of the nasospetal flap, a multilayer reconstruction of the skull defect was performed.

Extent of resection

We achieved a gross total resection (GTR) rate of 75%. In one child harboring a supradiaphragmatic craniopharyngioma a two-staged procedure was planned in order to obtain a gross total resection: indeed, a primary extended endonasal approach followed by transcranial approach for the residual tumor after 3 months were needed. The GTR rate for primary tumors (87%) was higher than in recurrent craniopharyngiomas (50%). When considering the extent of resection in the group of patients with lesions involving the supradiaphragmatic space, the GTR rate was considerably lower as compared to infradiaphragmatic lesions (60% versus 86%).

Outcomes

The two patients presenting with normal anterior pituitary function remained unchanged. Partial hypopituitarism remained unchanged in one case (20%), while improved in one case (20%) and worsened in three children (60%). New onset of diabetes insipidus was observed in four (36%) children. We reported no transient hypothalamic disturbance and/or alteration. Concerning visual disturbances, we noted an overall improvement of the visual defect in 91% of cases, while 17% remained unchanged, with no new postoperative visual defect. Postoperative cerebrospinal fluid (CSF) leak occurred in one patient (8%), who harbored a supradiaphragmatic craniopharyngioma: no second surgery was required and leak resolved with fibrin glue injection into the sphenoid sinus according to the so called "awake sealant technique" [48].

Recurrence

Rate of recurrence was higher in patients with supradiaphragmatic craniopharyngiomas (40%) compared with patients harboring an infradiaphragmatic tumor (29%). In case of gross total resection, recurrence was observed in one case (12%); in case of subtotal resection, tumor regrowth was always observed. Within the time frame of the study, three patients (27%) experienced tumor regrowth and one craniopharyngioma recurred (9%). In two cases of infradiaphragmatic tumors, cistosphenoidotomy was performed because of the predominant cystic component of the recurrence [46, 47]. After second surgery, two children received radiotherapy. One patient was admitted to another institution for the treatment and though lost at follow-up.

Discussion

The optimal surgical management of pediatric craniopharyngiomas should take into account relevant tumor aspects and morphological features as well as the patients' clinical status. When tumor growth is confined to the infradiaphragmatic space, the transsphenoidal approach is the ideal route even in pediatric patients, with excellent results and lower morbidity [11, 16, 32, 33, 38, 39, 49–51]. However, pediatric craniopharyngiomas often exceed the boundaries of the sellar area and develop into the supradiaphragmatic space, involving vital neurovascular structures. Hypothalamus involvement is very common in pediatric craniopharyngiomas at the time of diagnosis, so that surgical resection has to be measured to grant the best achievable long-term quality of life [2, 7, 52–54]. Upon the observation of dramatically diminished quality of life in children affected by surgical-related hypothalamic dysfunction, Puget

et al. endorsed a hypothalamus-sparing surgery [9]. The anatomical relationships of a craniopharyngioma with the neurohypophysis and, in particular, the hypothalamus should guide the surgical management of these lesions in the pediatric population.

With the present study, we provide our experience on the endoscopic endonasal approach for the treatment of craniopharyngiomas in children. The vast majority of studies in the literature focuses on a variety of pediatric skull base pathologies or data reports of mixed series in both adults and children populations [18, 22, 31, 32, 40, 55–58]. In the present series, the majority of treated craniopharyngiomas were infradiaphragmatic; as reported in previous studies the intra-suprasellar, eventually infradiaphragmatic lesions, are better amenable to the transsphenoidal corridor [8, 11, 17, 30, 35, 37, 38, 40, 44, 59]. Infradiaphragmatic craniopharyngiomas can be removed via a "standard" approach to the sellar region. It should be emphasized that infradiaphragmatic does not mean small lesion; indeed, such lesions can be extremely large, extending into the suprasellar space and displacing the chiasm posteriorly and superiorly, but not disrupting the arachnoidal membrane of the suprasellar cistern. The endoscope allows the surgeon to easily assess the completeness of tumor removal, explore the inner aspect of the cyst wall, the hidden corners behind the collapsed suprasellar cistern, and verify the possible presence of CSF leak after skull base closure. The EEA should be considered as the ideal treatment for infradiaphragmatic pediatric craniopharyngiomas, allowing higher chances of gross total removal through a safe and direct surgical corridor. However, also infradiaphragmatic craniopharyngiomas may recur. In case of cystic relapse, the endoscopic technique gives another surgical opportunity, namely, the placement of a silicon intracystic catheter in order to evacuate the cyst's content into the sphenoid sinus, the so-called cistosphenoidotomy [46, 47]. In our experience, cistosphenoidotomy was adopted in two recurring cystic craniopharyngiomas and one incompletely resected cystic tumor (Fig. 1). Thereafter, no new recurrence was seen. However, it is mandatory to underline that breaching of the suprasellar cistern represents an absolute contraindication for this technique.

In supradiaphragmatic craniopharyngiomas, the transsphenoidal route has been gaining land with the definition of the "extended" EEA, and only few reports exist concerning the use of this technique in the pediatric population [42–45, 60]. The extended approach to the suprasellar area affords a panoramic view and greater exposure of the neurovascular structures of the retrochiasmatic, infrachiasmatic, retrosellar, and ventricular area. Selection criteria for the best surgical route remain the same as for the adult population: chiasm position and distance from the pituitary gland, stalk-infundibulum axis position, parasellar tumor extension, neurovascular tumor encasement, intercarotid distance, sellar size, and above all relationship with the third ventricle floor. Similarly, contraindications for the extended EEA in pediatric patients do not differ from the adult population: tumors with far-lateral extension beyond the internal carotid arteries or far-anterior extension, purely intraventricular tumors, and tumors with major suprasellar calcifications. The endonasal route allows to access lesions from the inferior aspect, namely, the infrachiasmatic, so that dissection and removal maneuvers can be performed without any need of vessels or optic apparatus manipulation. The most important advantages in considering an extended EEA for craniopharyngioma resection is the better visualization of the optic chiasm and of the stalk–infundibulum axis; it is possible to identify and dissect the walls of the third ventricle and the hypothalamus, distinguishing them from the tumor as well permitting a safe resection, without any brain retraction (Figs. 2 and 3), albeit the position of the infundibulum has not been preoperatively defined, especially in case of large tumors [61]. Even when preoperative prediction is inaccurate, the endoscopic approach consents to modify the surgery accordingly.

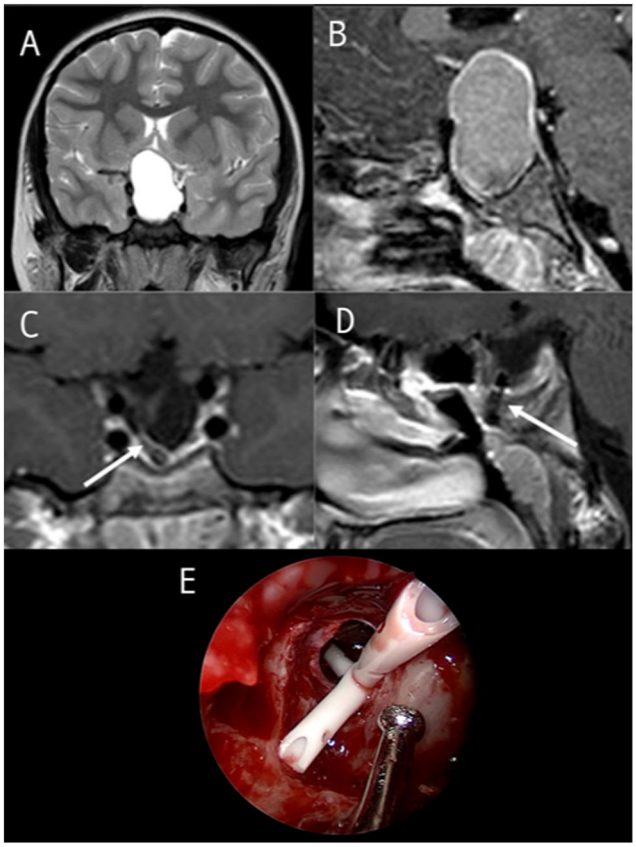

Fig. 1 Preoperative MRI images (**a** coronal T2-weighted and **b** postcontrast sagittal) of a recurrent pediatric cystic infradiaphragmatic craniopharyngioma. Postoperative MRI (**c**, **d**) show complete removal of the tumor, obtained through a standard endoscopic endonasal transsphenoidal approach, and the cistosphenoidotomy (withe arrow). Intra-operative images (**e**) of the sellar surgical cavity and of the placement of the catheter in order to evacuate the cyst's content to the sphenoid

Endoscopic endonasal approach for craniopharyngiomas seems to offer similar outcomes in both adulthood and childhood [8, 33, 40, 50, 51]. Comparing our results in the pediatric population with the wider experience in adults, no significant

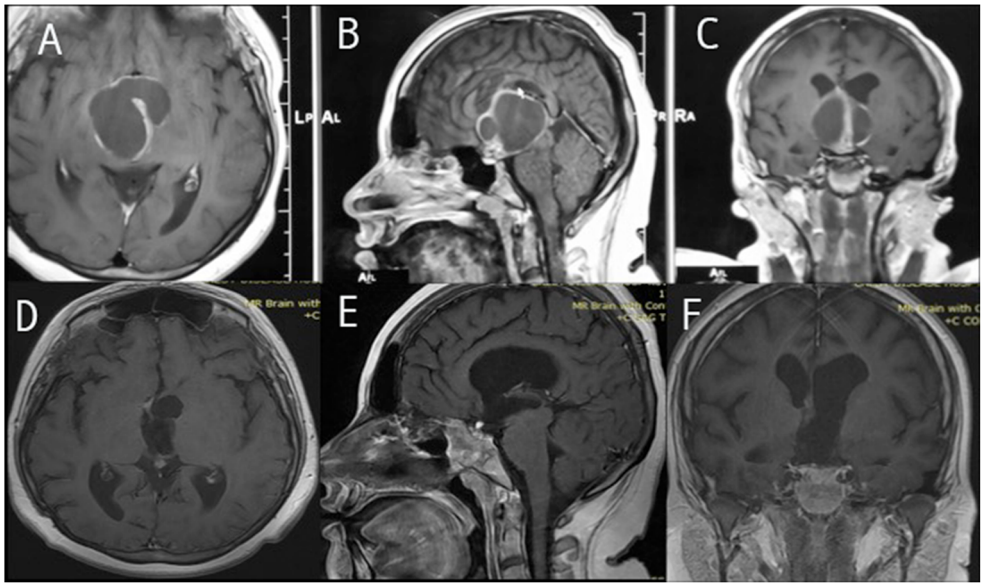

Fig. 2 Preoperative MRI (**a**–**c**) showing a suprasellar supradiaphragmatic pediatric craniopharyngioma, mainly cystic with III ventricle involvement. Postoperative MRI (**d**–**f**) demonstrates the complete removal of the tumor through an extended endonasal endoscopic approach

differences were observed in respect to extent of resection, and/or endocrine outcomes; the rate of improvement in postoperative visual functions was higher within the pediatric cohort [32]. CSF leak remains one of the most feared complication; however, as reconstruction techniques moved forward, with the boost taken from the use of pedicled nasoseptal flaps, the risk dropped to a 7%, indeed very close to the adult population [33, 44, 59, 62, 63]. The outcomes we retrieved at our center are concordant with results reported by others [42, 44, 59].

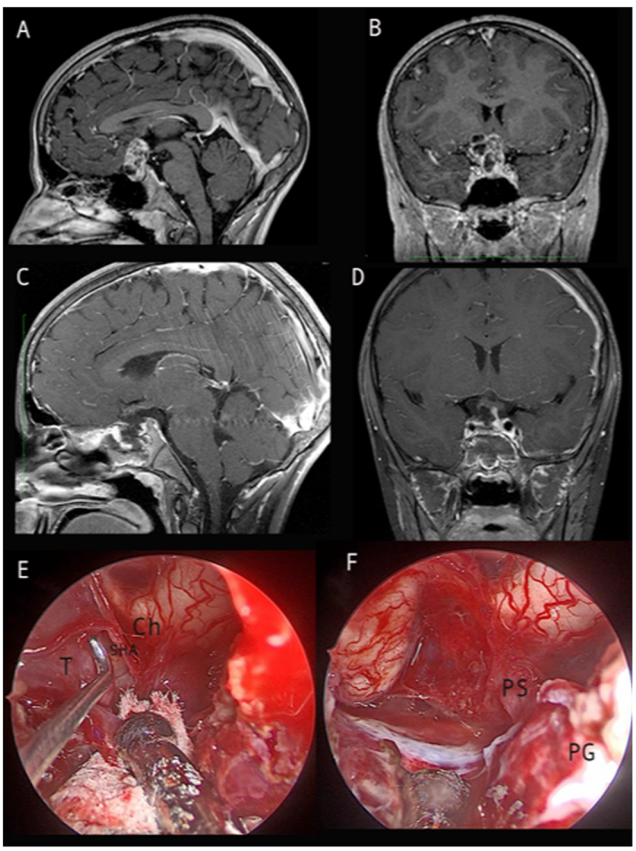

Fig. 3 Preoperative (**a**, **b**) and postoperative (**c**, **d**) MRI of a supradiaphragmatic craniopharyngiomas operated on by extended EEA, achieving a gross total resection. The close-up view offered by the endoscope discloses the tumor-optic nerves interface and surrounding vessels (**e**). At the end of the removal, the preserved pituitary stalk resulted free from the tumor (**f**). Ch optic chiasm, PG pituitary gland, PS pituitary stalk, SHA superior hypophyseal artery, T tumor

One main concern with the endonasal corridor when dealing with children is the pediatric sinonasal anatomy, i.e., small nostrils, narrow nasal cavities, and reduced/absent pneumatization of the sphenoid sinus [21, 22]. By eliminating the need for the speculum and thanks to the intrinsic features of the endoscopic technique, the transsphenoidal approach can be considered the less traumatic route, virtually suitable in children of any age; in addition, the shorter working distance from the nasal aperture to the suprasellar compartment counterbalances the difficulties of a narrower nasal corridor. In some cases of small nostrils the 2.7-mm Ø scope can be used instead of the standard 4 mm Ø [64]. From 2 years over, the gradual aeration of the sphenoid sinus increases with age in a linear fashion and reaches maturation at 7–10 years. The incompletely pneumatized sphenoid sinus should be also considered as important factor during EEA in children. With the use of neuronavigation, safe drilling of the sphenoid immature cancellous bone can be achieved regardless the pneumatization degree and though the absence of crucial landmarks such as the optic, the carotid and the sellar prominences [65–67]. The sequential pneumatization of the sphenoid sinus—i.e., from anterior to posterior—has a positive effect on the safety and feasibility of extended EEA in children; indeed, the bony recesses that open the suprasellar corridor—tuberculum sellae and the medial opto-carotid recesses—can be recognized and removed even in very young

children. Furthermore, previous studies have shown that the cavernous intercarotid distance is an independent factor from the degree of sphenoid sinus pneumatization, with no statistically significant difference between patients after the age of 2 years [66, 68]. So, in pediatric patients when the sinonasal corridor is done, there is enough space to work safely and attempt tumor removal. In our experience, encompassing patients from 7 to 16 years old, the sinonasal anatomy encountered during EEA for pediatric craniopharyngiomas was similar to the adult population.

Finally, it is worth reminding that EEA for craniopharyngiomas in pediatric population requires adequate understanding of the disease, proper anatomical knowledge, and dedicated expertise in the field of endoscopic skull base surgery, in order to fulfill the steep learning curve of this technique [69, 70].

Conclusions

The endoscopic endonasal approach with its variations deserves to be taken into account among the wide kaleidoscope of surgical strategies for the management of pediatric craniopharyngiomas. Indications respond to proper selection criteria and the sinonasal and cranial base pediatric anatomy should not be considered a contraindication for the endoscopic technique. The EEA offers a straight route to the sellar-suprasellar area with no need of manipulation of the surrounding neurovascular structures, which are ideal features for the treatment of pediatric infradiaphragmatic craniopharyngiomas. Besides, in supradiaphragmatic craniopharyngiomas the main advantage of extended EEA is a clearer and close-up visualization of the tumor-hypothalamus interface, which can grant better results in terms of quality of life. Larger series encompassing a wider spectrum of pediatric craniopharyngiomas, with different morphological features, are needed to further support the benefits of this surgical approach.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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