



## Research

# Endoscopic Transsphenoidal Approach to Somatotroph Adenomas in Pediatric Patients

## Pediatric Populasyonda Somatotrof Adenomlara Endoskopik Transsfenoidal Yaklaşım

 Melih Çaklılı<sup>1</sup>,  Savaş Ceylan<sup>2</sup>

<sup>1</sup>Kocaeli University Faculty of Medicine, Department of Neurosurgery, Kocaeli, Türkiye

<sup>2</sup>Bahçeşehir University Faculty of Medicine, Department of Neurosurgery, İstanbul, Türkiye

### ABSTRACT

**Objective:** Somatotroph adenomas account for approximately 5%-15% of pediatric pituitary adenomas and are more common in males. The aim of this study was to discuss the early and late outcomes of endoscopic pediatric growth hormone (GH)-secreting pituitary adenoma surgery performed at a high-volume tertiary hospital.

**Methods:** A total of 4875 consecutive patients underwent endoscopic transsphenoidal surgery between August 1997 and December 2022 in Kocaeli University Medical Faculty Neurosurgery Department and Pituitary Research Center. We reviewed the medical data, radiological images, and surgical videos of these patients and included 19 (0.39%) pediatric patients aged 18 years with pathologically identified GH-secreting pituitary adenoma.

**Results:** The data of 19 pediatric patients with GH-secreting pituitary adenoma were pathologically identified at our institution and retrospectively analyzed. 8 (42.1%) participants were male and 11 (57.9%) were female. Gross total resection (GTR) was performed in 10 (52.6%) patients, and subtotal resection was performed in 9 (47.4%) patients. 9 (47.4%) patients met the criteria for remission. Statistically significant results for adenoma size on GTR were obtained (p-value: 0.021). Sphenoid sinus pneumatization was not associated with resection rate (p-value 0.264). The absence of cavernous sinus invasion was significant as a positive predictive value for GTR, but it was not significant for remission (p-value:0.027-0.102, respectively).

**Conclusion:** Somatotroph adenomas in pediatric patients are rare and challenging lesions. Adenoma size and cavernous sinus invasion are effective for resection. Sphenoid sinus pneumatization does not affect the resection rate in experienced centers.

**Keywords:** Endoscopic surgery, somatotroph adenoma, pediatric

### ÖZ

**Amaç:** Somatotrof adenomlar pediatrik hipofiz adenomlarının yaklaşık %5-15'ini oluşturur ve erkeklerde daha yüksek insidans gösterir. Bu çalışmadaki amacımız yüksek volümlü üçüncü basamak merkezde gerçekleştirilen endoskopik pediatrik büyüme hormonu (GH) salgılayan hipofiz adenomu ameliyatlarının erken ve geç dönem sonuçlarını tartışmaktır.

**Gereç ve Yöntem:** Ağustos 1997-Aralık 2022 tarihleri arasında toplam 4875 hastaya endoskopik transsfenoidal cerrahi uygulandı. Bu hastaların tıbbi verilerini, radyolojik görüntülerini ve cerrahi videolarını inceledik ve patolojik olarak GH salgılayan hipofiz adenomu tespit edilen 18 yaşın altındaki 19 (%0,39) pediatrik hastayı çalışmaya dahil ettik.

**Bulgular:** Kurumumuzda patolojik olarak tanısı konan on dokuz pediatrik GH salgılayan hipofiz adenomu hastasının verileri retrospektif olarak analiz edildi. Hastaların 8'i (%42,1) erkek, 11'i (%57,9) kadındı. Hastaların 10'unda (%52,6) gross total rezeksiyon, 9'unda (%47,4) subtotal rezeksiyon gerçekleştirildi. 9 (%47,4) hasta remisyon kriterlerini karşılamıştır. Adenom boyutunun Gros total rezeksiyon (GTR) üzerindeki etkisinde istatistiksel olarak anlamlı sonuçlara ulaşılabildi (p-değeri: 0.021). Sfenoid sinüs pnömatizasyonu rezeksiyon oranları için anlamlı değildi (p-değeri 0.264). Kavernöz sinüs invazyonunun olmaması GTR için pozitif prediktif değer olarak anlamlıydı ancak remisyon için anlamlı değildi (sırasıyla p değeri: 0.027-0.102).

**Sonuç:** Pediatrik hastalarda somatotrof adenomlar nadir ve zor lezyonlardır. Adenom boyutu ve kavernöz sinüs invazyonu rezeksiyon oranları üzerinde etkilidir. Sfenoid sinüs pnömatizasyonu deneyimli merkezlerde rezeksiyon oranlarını etkilememektedir.

**Anahtar Kelimeler:** Endoskopik cerrahi, somatotrof adenom, pediatrik

**Address for Correspondence:** Melih Çaklılı, Kocaeli University Faculty of Medicine, Department of Neurosurgery, Kocaeli, Türkiye

E-mail: dr.melihcaklil@yahoo.com.tr ORCID ID: orcid.org/0000-0002-4405-0566

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## INTRODUCTION

Pituitary adenomas rarely occur in childhood, accounting for approximately 3% of all supratentorial tumors (1). They represent 2-8.5% of all pituitary tumors in children (2). Although pituitary adenomas are benign lesions, they can cause endocrinopathy due to hormone hypersecretion and/or visual disturbances due to mass effects. The majority of these adenomas are sporadic and occur at a low rate in the context of genetic syndromes or familial isolated pituitary adenomas (3).

The latest developments in endoscopic transsphenoidal approaches and advances in tools have increased the effectiveness of endoscopic transsphenoidal surgery (4). There are few studies on the endoscopic transsphenoidal approach because of the low incidence of sellar tumors in pediatric patients (5-8).

Somatotroph adenomas account for approximately 5%-15% of pediatric pituitary adenomas and are more common in males (9). The aim of this study was to discuss the early and late outcomes of endoscopic pediatric GH-secreting pituitary adenoma surgery performed at a high-volume tertiary hospital.

## METHODS

### Patient Population

A total of 4875 consecutive patients underwent endoscopic transsphenoidal surgery between August 1997 and December 2022 in Kocaeli University Medical Faculty Neurosurgery Department and Pituitary Research Center. We reviewed the medical data, radiological images, and surgical videos of these patients and included 19 (0.39%) pediatric patients aged 18 years with pathologically identified growth hormone (GH)-secreting pituitary adenoma. Patients with pathologically identified other sellar region tumors like craniopharyngioma, chordoma, Rathke cleft cyst, and other pituitary adenoma, were excluded from the study. The records of these patients were reviewed for age, sex, presenting symptoms, endocrinological findings, imaging studies, surgical outcomes, and follow-up data. Approval was obtained from Kocaeli University Non-Interventional Clinical Research Ethics Committee (decision no: KÜ GOKAEK-2024/12.20, date: 26.07.2024). Written informed consent was obtained from the families of all patients. written informed consent was obtained from the families and all patients.

### Magnetic Resonance Imaging (MRI) and Paranasal Sinus Tomography

Paranasal sinus tomography (evaluation of sphenoid sinus pneumatization and sellar type) and MRI were performed preoperatively in all patients.

Sphenoid sinus pneumatization was divided into 4 types (conchal, presellar, sellar, and postsellar) based on preoperative paranasal sinus tomography (Figure 1).

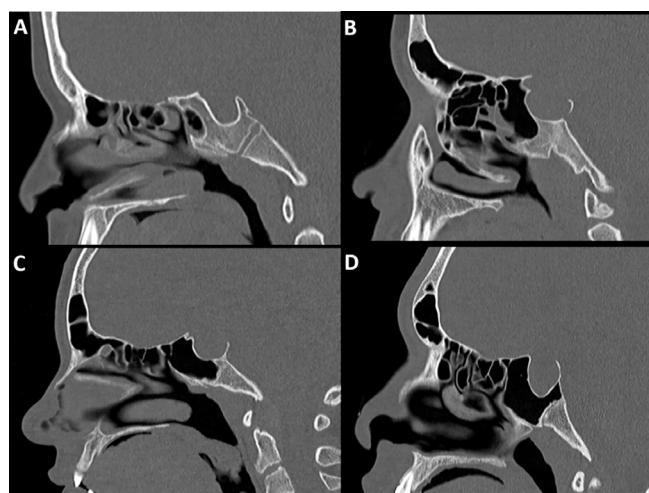
MRI was performed using 1.5-T or 3-T magnetic resonance equipment. Preoperative and postoperative (1<sup>st</sup> day, 3<sup>rd</sup> month, 1<sup>st</sup> year) MRI sequences included precontrast and postcontrast T1- weighted images in the sagittal and coronal planes, T2- weighted images and dynamic contrast-enhanced T1-weighted images in the coronal plane, and 3D volumetric neuronavigation studies.

Volumetric analyses were performed to determine preoperative and postoperative tumor volumes. One radiologist reviewed the MRI scans.

The MRI findings showed the following: gross total resection and subtotal resection were defined as no residual tumor and presence of residual tumor on postoperative MRI, respectively.

### Surgical Technique

All procedures were performed using standard endoscopic transsphenoidal approaches and, if necessary, extended endoscopic transsphenoidal approaches with an image-guided neuronavigation system. The details of the surgical procedure have been previously described (10,11). Standard techniques were used for intrasellar lesions. In the surgical approach, both nostrils were used. A 4- mm endoscope was used in all patients. In the standard approach, small sphenoidotomy is performed. The sellar base was drilled, and then the dura was opened. The aim of surgery is always to maximize the extent of resection; however, this is not possible in all cases.



**Figure 1:** Sphenoid sinus pneumatization types: A) conchal type, B) prestellar type, C) sellar type, D) postsellar type

An extended endoscopic transsphenoidal approach is required for skull base lesions extending to the suprasellar area using the infrachiasmatic corridor (12). The difference between this approach and the previous one is that the sellar base opening is extended superiorly (Figure 2).

If intraoperative cerebrospinal fluid (CSF) leakage was observed, the multilayer closure technique was used. In cases where there was no CSF leak, reconstruction was not performed.

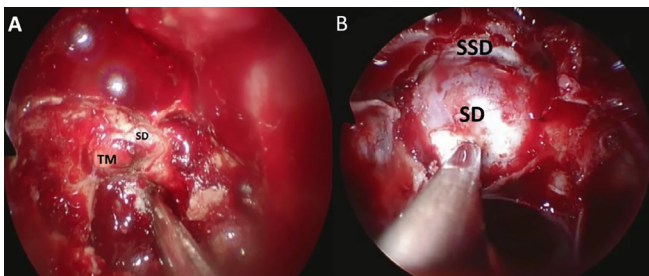
**Endocrine and Clinical Investigations**

Endocrinological functions were evaluated before and after surgery on days 1, 3, and year 1 using conventional stimulation tests. Endocrinological outcomes were assessed according to the 2010 consensus criteria. Patients were determined to have a postoperative random GH level < 1 ng/ml or a baseline GH level < 0.4 ng/ml after OGTT suppression in combination with a normal insulin-like growth factor (IGF)-1 level.

Ophthalmological examination included assessments of visual acuity, visual field function (Goldmann perimetry, and ocular motility (Hess chart).

**Statistical Analysis**

All statistical analyses were performed using IBM SPSS for Windows version 18.0 (SPSS, Chicago, IL, USA). A Shapiro-Wilk's or Kolmogorov-Smirnov tests were used to assess the assumption of normality. Continuous variables were presented depending on normal distribution with either mean±standard deviation or (in the case of non-normal distribution) median (interquartile range). Comparisons of continuous variables between groups were performed using an independent sample t-test. Associations between categorical variables were determined using the chi-square test. A p-value<0.05 was considered statistically significant.



**Figure 2:** Sellar opening differences in different approaches. A) Intraoperative view of the standard endoscopic transsphenoidal approach. TM, tumor; SD, sellar dura. B) The sellar base opening is extended superiorly in the extended endoscopic transsphenoidal approach. SD; sellar dura; SSD, suprasellar dura.

**RESULTS**

**Patients' characteristics**

The data of 19 pediatric patients with GH-secreting pituitary adenoma who were pathologically identified at our institution were retrospectively analyzed. 8 (42.1%) participants were male and 11 (57.9%) were female. The mean age was 15.8±2.1 years (Table 1). 6 (31.6%) patients had GH+prolactin (PRL) cosecretion according to their endocrinological profiles. 1 (5.3%) of 19 patients had a history of surgery in another center.

**Clinical Presentation**

Of all patients, 14 (73.7%) had hand-foot enlargement, 5 (26.3%) had headache, and 5 (26.3%) had visual field deficit (Table 2). 1 of all patients had a history of surgery in another center and were asymptomatic. During follow-up, surgical treatment was performed for the recurrent tumor.

All 6 patients with GH+PRL-secreting mixed adenoma had hand-foot growth, 3 (15.8%) had visual field deficit, 1 (5.3%) had menstrual irregularity.

**Radiology**

1 (5.3%) patient had conchal type, 2 (10.5%) patients had presellar type, 11 (57.9%) patients had sellar type, and 5 (26.3%) had postsellar type sphenoid sinus pneumatization.

1 (5.3%) patient had microadenoma, and 18 (94.7%) had macroadenoma. There were 6 (31.6%) patients presented with unilateral cavernous sinus invasion, and 3 (15.8%) with bilateral cavernous sinus invasion (Figure 3).

**Surgery and Biochemical Evaluation**

The standard endoscopic transsphenoidal approach was performed in 15 patients. The extended endoscopic transsphenoidal approach was performed in 4 patients in whom the tumor extended to the suprasellar area.

Total gross resection was performed in 10 (52.6%) patients, and subtotal resection was performed in 9 (47.4%) patients. 9 (47.4%) patients met the criteria for remission. 2 of the 9 patients were in the GH+PRL cosecretion group. 5 of 10 patients that among we could not achieve remission, GH and IGF-1 levels were reduced to normal limits with postoperative medical treatment.

**Table 1.** Demographic Findings of Patients

	n	%
<b>Patients</b>	19	100
<b>Age at surgery, and years</b>	15.8 ± 2.1 (11-18)	
<b>Sex</b>		
<b>Female</b>	11	57.9
<b>Male</b>	8	42.1

Statistically significant results for adenoma size on GTR were obtained (p value: 0.021). Sphenoid sinus pneumatization was not associated with resection rate (p-value 0.264). The absence of cavernous sinus invasion was significant as a positive predictive value for GTR, but it was not significant for remission (p-value: 0.027-0.102, respectively) (Table 3). Any complications, such as epistaxis and rhinorrhea, were not encountered in this series.

## DISCUSSION

In this study, we focused on the clinical outcomes of surgeries and the factors affecting the extent of tumor removal using the endoscopic transsphenoidal approach.

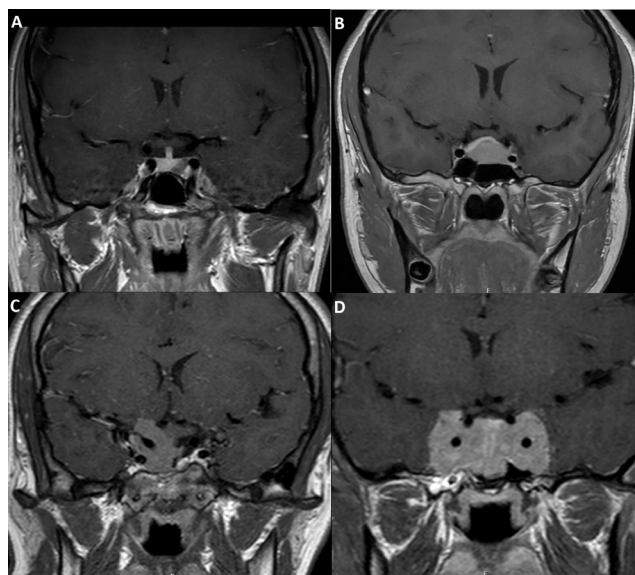
Pediatric pituitary adenomas are rare but challenging lesions, especially somatotrophic adenomas. It is found in approximately 90% of patients at the time of diagnosis (9,13). It is also seen to be invasive in 30%-60% of cases (2,14). Likewise, in our study, the percentage of macroadenomas was 94.7%. The cavernous sinus invasion rate was 47.4%, similar to the literature. It is established that childhood pituitary adenomas are more aggressive than adult pituitary adenomas (9,13-15).

The most important goal in surgery for somatotroph adenomas is to achieve GTR and remission so that the patient does not need medication during the postoperative period. However, the fact that the majority of somatotroph

**Table 2.** Characteristic Features of Patients

		<b>GH n:13</b>	<b>GH+PRL n:6</b>	<b>Total n:19</b>
<b>Preoperative symptoms</b>	Hand-foot enlargement	8 (61.5%)	6 (100%)	14 (73,7%)
	Headache	5 (38.4%)		5 (26,3%)
	Visual field deficit	2 (15.4%)	3 (50%)	5 (26.3%)
	Menstrual irregularity		1 (16.7%)	1 (5.3%)
<b>Tumor size</b>	Microadenoma	1 (7.7%)	None	1 (5.3%)
	Macroadenoma	12 (92.3%)	6	18 (94.7%)
	Giant	None	None	
<b>Sella type</b>	Conchal	1 (7.7%)	None	1 (5.3%)
	Presellar	2 (15.4%)	None	2 (10.5%)
	Sellar	6 (46.1%)	5 (83.3%)	11 (57.9%)
	Postsellar	4 (30.7%)	1 (16.7%)	5 (26.3%)
<b>CS invasion</b>		5 (38.4%)	4 (66.7%)	9 (47.4%)

GH: Growth hormone, PRL: Prolactin, CS: Cavernous sinus



**Figure 3:** Radiology of adenomas. A) Microadenoma. B) Macroadenoma. C) Unilateral cavernous sinus invasion (Right) D) Bilateral cavernous sinus invasion.

**Table 3.** Gross total resection rates

	<b>n</b>	<b>%</b>	<b>p-value</b>
<b>Number of patients</b>	19	100	
<b>CS invasion</b>			<b>0.027*</b>
<b>Yes</b>	9	47.4	
<b>No</b>	10	52.6	
<b>Sphenoid pneumatization rate of</b>			0.264
<b>Conchal</b>	1	5.3	
<b>Presellar</b>	2	10.5	
<b>Sellar</b>	11	57.9	
<b>Postsellar</b>	5	26.3	
<b>Adenoma size</b>			<b>0.021*</b>
<b>Microadenoma</b>	1	5.3	
<b>Macroadenoma</b>	18	94.7	

\*Statistically significant, CS: Cavernous sinus



adenomas in childhood are macroadenomas at the time of diagnosis and the frequent invasion of the cs decreases the GTR rate in surgical outcomes. Although we are an experienced and tertiary center in endoscopic surgery, we have shown that both are effective in this regard in the results of our study. We were able to obtain GTR results in approximately 50% of the patients.

Sphenoid sinus pneumatization did not affect GTR. There are two possible reasons for the results of our study. First, the youngest patient in our study was aged 11 years, indicating that the sphenoid sinus had already developed. Thus, a narrower and smaller sphenoid sinus was less common in our study. If younger patients could be included in the studies, more accurate results could be obtained. The second reason is that the total number of participants in this study is also small, and larger series are needed to overcome this.

In addition to GH hypersecretion, high PRL level was observed in these patients. This may be histopathologically relevant. Or loss of dopaminergic tone due to pressure on the pituitary stalk.

The only thought-provoking point in the study was that cavernous sinus invasion was not statistically significant on remission. However, the point that should be noted here is that pituitary adenomas are subtypes in the 2022 World Health Organization classification (16). Differences in subtypes affect remission. Since this subtyping was not considered in our study, the results were considered to be obtained like this.

Considering that surgical outcomes are even lower for recurrence of pituitary adenomas, surgery for pituitary adenomas, especially childhood somatotroph adenomas, should be performed by experienced surgeons at centers of excellence. Thus, better results can be achieved.

The limitation of our study is the small number of patients. Studies with higher patient numbers are needed. At the same time, studies that examine histopathological subtypes in detail are needed.

## CONCLUSION

Somatotroph adenomas in pediatric patients are rare and challenging lesions. The majority of these tumors are macroadenomas and invasive at the time of diagnosis. Adenoma size and cavernous sinus invasion are effective for resection. Sphenoid sinus pneumatization does not affect the resection rate in experienced centers. Further studies with a large number of patients are required.

## ETHICS

**Ethics Committee Approval:** Approval was obtained from Kocaeli University Non-Interventional Clinical Research Ethics Committee (decision no: KÜ GOKAEK-2024/12.20, date: 26.07.2024).

**Informed Consent:** Written informed consent was obtained from the families and all patients.

## FOOTNOTES

### Authorship Contributions

Surgical and Medical Practices: M.Ç., S.C., Concept: M.Ç., S.C., Design: M.Ç., S.C., Data Collection or Processing: M.Ç., Analysis or Interpretation: M.Ç., Literature Search: M.Ç., Writing: M.Ç.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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