



## Endoskopik Endonazal Yaklaşım Uygulanan En Genç Klival ve Suprasellar Atipik Teratoid/Rabdoid Tümör ve Literatürün Taranması

### The Youngest Case of Clival and Suprasellar Atypical Teratoid/ Rhabdoid Tumor Treated with an Endoscopic Endonasal Approach and a Review of the Literature

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#### ÖZ

Atipik teratoid/rabdoid tümör (ATRT), merkezi sinir sisteminin (MSS) nadir görülen, son derece agresif malign embriyonal bir neoplazmıdır ve genellikle 3 yaş altındaki çocukları etkiler. Bu tümörler, SMARCB1 (INI1) gen inaktivasyonu ile karakterize edilir ve heterojen patolojileri nedeniyle tanı koymada zorluklar yaşanabilir. ATRT genellikle posterior fossada görülürken, sellar ve suprasellar yerleşimler özellikle pediatrik hastalarda oldukça nadirdir.

Bu çalışmada, pitoz ve kraniyal sinir tutulumuyla başvuran 17 aylık bir erkek çocuk sunulmaktadır. Manyetik rezonans görüntüleme (MRG), klivusu destrükte eden, suprasellar ve preoptin sistemlere uzanan ve kavernöz sinüsü invaze eden sellar yerleşimli bir tümör ortaya koymuştur. İki aşamalı endoskopik transsfenoidal cerrahi uygulanarak subtotal rezeksiyon sağlanmıştır. Histopatolojik analiz, SMARCB1 ekspresyon kaybı ve %40–50 Ki-67 proliferasyon indeksi ile ATRT tanısını doğrulamıştır. Hasta, adjuvan kemoterapi ve radyoterapi almış; ancak başvurudan 9 ay sonra solunum yetmezliği nedeniyle kaybedilmiştir.

Literatür taramasında, ATRT'nin agresif klinik seyri, karmaşık cerrahi zorlukları ve kötü sonuçları vurgulayan toplam 39 sellar ATRT vakası incelenmiştir. Sellar ATRT'lerin yönetiminde endoskopik transsfenoidal cerrahi, multimodal tedaviyle birlikte en uygun yaklaşım olarak önerilmektedir. Bu vaka, klival ATRT'li en genç hasta ve literatürde belgelenen ilk pediatrik suprasellar ATRT vakasını temsil etmektedir. Erken tanı, yenilikçi tedavi stratejileri ve bu zorlu hastalık için daha fazla araştırma gerekliliğini vurgulamaktadır.

**Anahtar Kelimeler:** atipik teratoid/rabdoid tümör, endoskopik transsfenoidal cerrahi, pediatrik suprasellar AT/RT, klival AT/RT

#### ABSTRACT

Atypical teratoid/rhabdoid tumor (ATRT) is a rare, highly aggressive malignant embryonal neoplasm of the central nervous system (CNS), primarily affecting children under the age of 3. These tumors are characterized by the inactivation of the SMARCB1 (INI1) gene and exhibit heterogeneous pathology, frequently leading to diagnostic challenges. ATRT commonly arises in the posterior fossa, while sellar and suprasellar locations are rare, particularly in pediatric patients.

We report the case of a 17-month-old male presenting with ptosis and cranial nerve deficits. Magnetic resonance imaging (MRI) revealed a sellar tumor extending into the suprasellar and preoptine cisterns, with clival destruction and cavernous sinus invasion. Endoscopic transsphenoidal surgery was performed in two stages, achieving subtotal resection. Histopathological analysis confirmed ATRT with loss of SMARCB1 expression and a Ki-67 proliferation index of 40–50%. The patient received adjuvant chemotherapy and radiotherapy but succumbed to respiratory failure nine months after presentation.

A comprehensive literature review identified 39 sellar ATRT cases, highlighting their aggressive clinical course, complex surgical challenges, and poor outcomes. Endoscopic transsphenoidal surgery, combined with multimodal therapy, remains the optimal approach for managing sellar ATRTs. This case represents the youngest patient with clival ATRT and the first pediatric suprasellar ATRT reported in the literature, emphasizing the need for early diagnosis, innovative treatment strategies, and further research to improve outcomes.

**Keywords:** atypical teratoid/rhabdoid tumor, endoscopic transsphenoidal surgery, pediatric suprasellar AT/RT, clival AT/RT

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## INTRODUCTION

Atypical teratoid/rhabdoid tumor (AT/RT) is a rare malignant embryonal neoplasm of the central nervous system (CNS).[1–5] It is typically characterized by scattered rhabdoid cells and large epithelioid cells.[6] Additionally, these tumors may exhibit primitive neuroepithelial, epithelial, and mesenchymal components. Due to their heterogeneous pathology and histological features, AT/RT is frequently misdiagnosed as other types of embryonal tumors.[7–11]

AT/RT is defined by its aggressive and invasive behavior. The prognosis is generally poor, with a median survival of less than one year. AT/RT predominantly affects children under the age of 3, with the highest incidence occurring between birth and 2 years of age.[3,11,12] In the pediatric population, it accounts for approximately 6% of malignant CNS tumors.[2,11] The posterior fossa is the most common location for AT/RT, especially in children under 2 years of age. However, it has also been reported in other locations, such as the extramedullary region.[1,3,4,7,13,14] Although rare in the sellar region, AT/RT has not been previously reported in the pediatric suprasellar region.

Depending on its anatomical location and size, AT/RT can compress adjacent critical structures, leading to neurological symptoms. The current treatment approach is multidisciplinary and includes surgery, chemotherapy, and radiotherapy.[8,10,15] For sellar and parasellar lesions, surgical approaches may involve either microscopic or endoscopic techniques. Endoscopic transsphenoidal surgery is considered the optimal method due to its low complication rates, ease of surgical manipulation, and high rates of tumor resection.

This study aims to share our experience with endoscopic transnasal surgery in a patient with sellar AT/RT while reviewing the existing literature on AT/RT. This case represents the youngest patient with clival AT/RT and the first pediatric suprasellar AT/RT reported in the literature.

## REVIEW

### Material and Methods

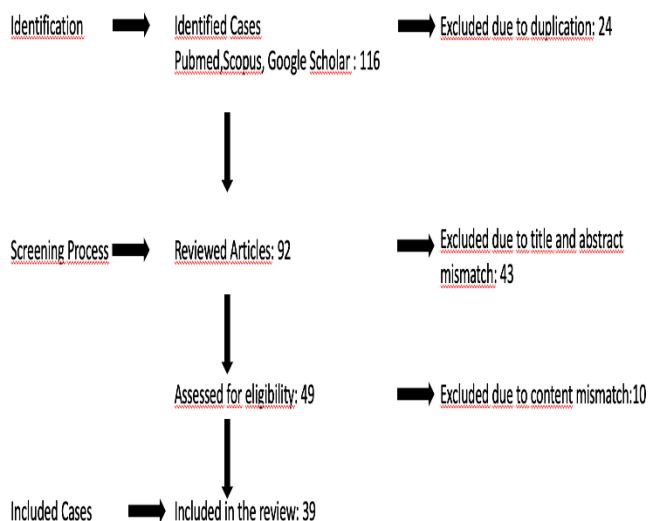
After obtaining written informed consent from the patient's family, medical records, imaging studies, laboratory test results, histopathology reports, and follow-up notes were reviewed.

To compile cases of sellar AT/RT, a comprehensive search was conducted using the PubMed, Scopus, and Google Scholar databases. Keywords such as "sellar," "parasellar," and "atypical teratoid/rhabdoid tumor" were utilized, and only cases with SMARCB1/INI1 mutation confirmed via immunohistochemistry were considered. Case reports and case series with complete follow-up data were included in the quantitative analysis. Full-text articles were independently reviewed by two authors.

### Systematic review

After removing duplicate studies, a total of 92 studies were screened, of which 43 were excluded. Excluded studies included those not directly related to sellar AT/RT and articles for which full text was unavailable. Following the review of full-text articles, 10 additional studies were excluded due to the lack of specific information on AT/RT cases. Consequently, a total of 39 cases, including the case reported in this study,

were included in the final analysis, as detailed in Figure 1.



**Figure 1.** Flow diagram of our literature search

## RESULTS

### Clinical Features

Immunohistochemical analyses revealed a loss of INI1 expression in all but two cases. Symptoms were reported as headache and visual disturbances in 67% of patients, while 33% presented with only visual changes. The duration of headaches ranged from one week to three months, whereas the duration of visual disturbances varied from six days to five months.

### Radiologic Findings

On MRI examinations, tumor sizes ranged from 1.6 to 3.63 cm, with 66.7% of cases demonstrating heterogeneous contrast enhancement. Cavernous sinus invasion was reported in 44.4% of cases, and cystic components were observed in 22.2%. Two patients presented with pituitary apoplexy.

### Survival Outcomes

Median survival was found to be 28 months in patients who underwent total resection, compared to 7.5 months in those who underwent subtotal resection; however, this difference was not statistically significant ( $p = 0.15$ ). Among 23 patients who received chemoradiotherapy, the median survival was 27 months, whereas in 15 patients who did not receive this treatment, the median survival was only 2 months. This difference was statistically significant ( $p = 0.0052$ ).

### Alternative Therapies

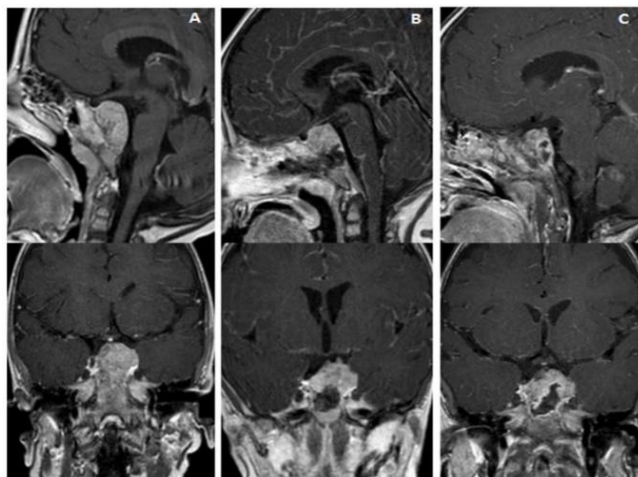
Chemotherapy regimens varied, with the most common combination being ifosfamide, cisplatin, and etoposide (37.5%). Two patients received high-dose chemotherapy with autologous stem cell transplantation, while 14 patients did not receive any chemotherapy. Intrathecal chemotherapy was administered to three patients, one of whom was treated with a combination of methotrexate, topotecan, etoposide, and thiotepa based on pediatric protocols.

In patients receiving radiotherapy, total doses ranged from 20 to 66 Gy. Focused radiotherapy was administered in 10 patients, craniospinal radiotherapy in seven, and seven patients did not receive radiotherapy.

#### Case Example

A 17-month-old male presented with a sudden onset of ptosis in the left eyelid. Initially, his family consulted an ophthalmologist, and magnetic resonance imaging (MRI) led to his referral to our clinic. At presentation, the left third and sixth cranial nerves were affected, while other cranial nerves remained intact. No motor or sensory deficits were identified. A comprehensive hormonal profile revealed adrenocorticotrophic hormone (ACTH) deficiency with a low serum cortisol level (6 µg/dL), prompting the initiation of hydrocortisone replacement therapy. No other pituitary hormone deficiencies were detected; levels of prolactin, TSH, FT4, IGF-1, FSH, LH, and estradiol were within normal ranges. Additionally, there were no signs of diabetes insipidus.

Contrast-enhanced MRI revealed a tumor measuring 26 × 26 × 18 mm in the sellar region, extending into the suprasellar and prepontine cisterns, invading the left cavernous sinus, and destructing the clivus. (Figure 2)



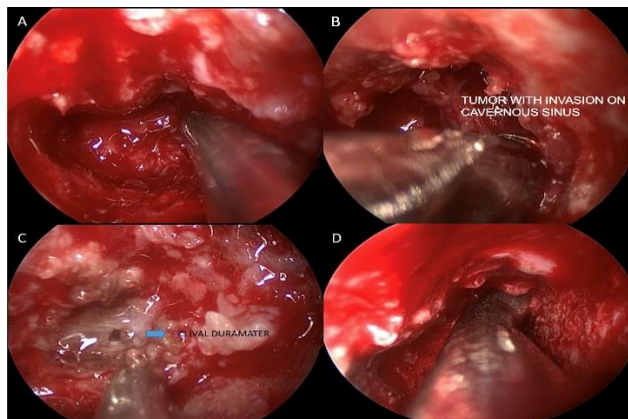
**Figure 2.** (A) T1 weighted images (TIWIs) contrast-enhanced pre-operatively on coronal and sagittal images illustrates a mass which seen hyperintense in the sellar region which reached suprasellar and prepontine cistern, invaded left cavernous sinus and destructed clivus.

(B) Post-operative contrast-enhanced TIWIs on coronal and sagittal images shows residual tumor (after first operation).

(C) TIWIs contrast-enhanced post-operatively on coronal and sagittal images (after second operation).

The patient underwent endoscopic transsphenoidal surgery with neuronavigation guidance. The tumor, originating from the clivus and invading the suprasellar and prepontine cisterns as well as filling the sphenoid sinus, was solid, viscous, and mildly calcified. As a result, ultrasonic aspiration was unsuccessful, necessitating sharp dissection. During the initial surgery, the patient's young age and narrow anatomical structures limited endoscopic manipulation. Furthermore, subtotal resection was performed due to tumor invasion into the left upper

cavernous sinus and its proximity to critical neurovascular structures. The clival portion of the tumor was excised, but the suprasellar portion was left in situ. (Figure 3)



**Figure 3.** (A) Tumor in sphenoid sinus is removed by endoscopic endonasal approach.

(B) Tumor in left cavernous sinus is removed by suction.

(C) After puncture, cerebrospinal fluid comes to suction, this shows it is reached clival dura.

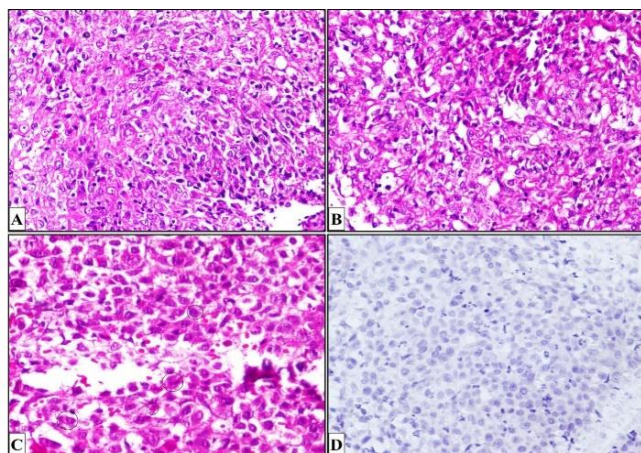
(D) Tumor is removed from intrasellar and suprasellar regions subtotally.

The initial postoperative period was uneventful. Two days later, a second surgery was performed to remove the residual tumor. During this procedure, a portion of the residual tumor was excised without compromising the patient's neurological function or causing complications. Postoperative imaging confirmed subtotal tumor resection, with residual tissue invading the left upper cavernous sinus left intact (Figure 2).

Histopathological analysis identified a poorly differentiated (grade IV) neoplasm composed of medium to large cells with vesicular nuclei, prominent nucleoli, and pale, eosinophilic cytoplasm. Immunohistochemical evaluation demonstrated that the tumor was negative for mesenchymal, neuronal, neuroendocrine, glial, melanoma, hematopoietic, keratin, and other tumor markers. The loss of nuclear SMARCB1/INI1 (BAF47 clone) expression and the presence of the germ cell marker SALL-4 confirmed the diagnosis of atypical teratoid/rhabdoid tumor (AT/RT). The Ki-67 proliferation index was measured at 40–50%, indicating high tumor aggressiveness. (Figure 4)

Postoperatively, the patient was referred to the pediatric oncology clinic for adjuvant therapy, including radiotherapy and chemotherapy. Whole-body staging scans (neuroaxis, thoracic, and abdominal CT) revealed no secondary lesions. The patient was treated with a combination of high-dose cyclophosphamide, cisplatin, vincristine, and etoposide. However, the patient succumbed to respiratory failure nine months after presentation.





**Figure 4.** Microscopic images of atypical teratoid / rhabdoid tumor (ATRT).

A, Histological sections show a highly cellular tumor composed of poorly cohesive primitive cells with large nuclei, prominent nucleoli, and scant eosinophilic cytoplasm.

B, Neoplastic cells with eccentrically placed vesicular nuclei with prominent nucleoli, eosinophilic cytoplasm, as characteristics of rhabdoid cells.

C, Local neoplastic cells with mitotic figures (black circles), (hematoxylin and eosin; 200 $\times$ ).

D, Immunohistochemically negative neoplastic rhabdoid cells for integrase interactor 1 (INI1) protein (200 $\times$ ).

## DISCUSSION

Malignant CNS embryonal tumors composed of poorly differentiated cells including rhabdoid cells which occur in young children. AT/RT is a rare and highly malignant tumor of the CNS, it occurs in infancy and childhood. Diagnosis is typically confirmed by the inactivation of the SMARCB1 (INI1) gene or, less frequently, the SMARCA4 (BRG1) gene. ATRT accounts for 1–2% of pediatric brain tumors and approximately 6% of all malignant CNS tumors in the pediatric population.[9,16,17] The average age at diagnosis is 2.9 years, with three-quarters of cases occurring in children aged 3 years or younger, predominantly in males.[7,12,15] ATRT most commonly arises in the posterior fossa and cerebellum, but other potential locations include the supratentorial region, pineal gland, and spinal cord.[6,9]

The most common region of AT/RT is posterior fossa and cerebellum. The other possible regions are supratentorial space, pineal and spinal regions, particularly the sellar area. This finding aligns with previous literature.[7,10] Approximately half of sellar ATRT cases occur in female patients, with most aged around 45–46 years.[3,10] (5, 6) While male predominance is observed in pediatric ATRT cases, female predominance is notable in sellar ATRT. This disparity has been hypothesized to relate to increased mitotic activity in the female pituitary gland throughout life.[18,19] However, male predominance persists in ATRTs arising in other locations.

## Patient Demographics and Clinical Characteristics

The clinical presentation of ATRT varies depending on tumor location and patient age. Both pediatric and adult cases commonly present with signs of increased intracranial pressure or localized neurological deficits.[2] Frequent symptoms include cranial nerve palsies (most commonly involving the 6th and 7th cranial nerves), headaches, vomiting, lethargy, developmental delay, and hemiplegia secondary to mass effect.[12] In supratentorial ATRTs, especially those in the sellar region, persistent headaches and visual disturbances are frequently reported. These symptoms can mimic those of benign sellar lesions, such as pituitary macroadenomas. However, ATRT is distinguishable by its aggressive nature and propensity for invading surrounding tissues.[10]

## Histological and Molecular Characteristics

Histopathologically, ATRT is characterized by the presence of rhabdoid cells, which feature eccentric round nuclei, open chromatin, prominent nucleoli, and large cell bodies with characteristic cytoplasmic inclusions. The morphological features of the cells are highly variable, ranging from small, spindle-shaped cells to large cells with irregular borders.[20] Loss of INI1 expression plays a central role in the immunohistochemical diagnosis of ATRT. In our case, the cells were large neoplastic cells with large nuclei, prominent nucleoli and eosinophilic cytoplasm without hyaline inclusions. Historically, these tumors were often classified as primitive neuroectodermal tumors (PNETs), but the 2016 WHO classification of CNS tumors now distinguishes ATRTs by their association with SMARCB1 mutations.[9]

## Radiological Characteristics

Radiologically, ATRT exhibits characteristic findings on computed tomography (CT), including heterogeneous contrast enhancement, calcifications, cyst formation, and hemorrhage. (10) On magnetic resonance imaging (MRI), ATRTs typically show low signal intensity on T2-weighted images and heterogeneous enhancement following gadolinium administration. However, histopathological and radiological similarities may lead to misdiagnosis with other tumors, such as medulloblastomas, ependymomas, choroid plexus carcinomas, and immature teratomas.[7,15] In our case, the patient's age, neuroimaging features, and clival destruction initially led to a misdiagnosis of chordoma or craniopharyngioma.

## Additional Therapies and Prognosis

Multimodal treatment approaches are recommended for ATRT. Maximal surgical resection is followed by aggressive chemotherapy and radiotherapy. The most commonly used chemotherapeutic agents are platinum-based or alkylating agents. However, treatment outcomes remain poor due to the tumor's aggressive nature. Median progression-free survival is reported as 4.5 months, with overall survival averaging 6 months.[12,15] Total resection is often challenging due to tumor size, infiltration of surrounding tissues, and the young age of patients at diagnosis. The primary goal of surgery is to achieve diagnosis and reduce tumor burden.[2]

In our case, endoscopic transsphenoidal surgery (ETS) was chosen. ETS is the most suitable surgical approach for intrasellar and suprasellar

lesions. This technique provides the surgeon with a wide panoramic view and improved maneuverability for gross total tumor resection. Additionally, its minimally invasive nature offers better postoperative comfort compared to other surgical approaches. In pediatric patients, where nasal sinuses are often underdeveloped, neuronavigation guidance is recommended to optimize surgical outcomes.[21–24]

We present the case of a 17-month-old boy with left eye ptosis, managed successfully with endoscopic transsphenoidal surgery (ETS) based on our extensive experience with endoscopic skull base procedures. While preoperative imaging initially suggested a diagnosis of chordoma or craniopharyngioma, histopathological analysis confirmed the tumor to be an atypical teratoid/rhabdoid tumor (AT/RT). To our knowledge, this is the youngest reported case and the third documented instance of clival AT/RT. Furthermore, this case represents the first reported pediatric sellar AT/RT, underscoring the importance of considering AT/RT in the differential diagnosis of pediatric sellar and parasellar tumors.

## CONCLUSION

Atypical teratoid/rhabdoid tumors (ATRTs) are highly aggressive malignancies with distinct characteristics based on patient age and tumor location. While commonly observed in the posterior fossa of infants, adult cases frequently arise in the supratentorial region, particularly in the sellar area, and display unique clinical and demographic features. Accurate diagnosis, facilitated by immunohistochemical analysis confirming SMARCB1 (INI1) gene inactivation, remains crucial due to the tumor's ability to mimic other CNS lesions. Multimodal treatment, including maximal safe surgical resection, aggressive chemotherapy, and radiotherapy, offers the best chance for disease control, though outcomes remain poor due to the tumor's aggressive nature. Our case highlights the importance of endoscopic transsphenoidal surgery as a minimally invasive and effective approach for sellar and suprasellar ATRTs, especially in pediatric patients. Continued research is essential to improve therapeutic strategies and outcomes for this challenging disease.

**Conflict of Interest:** All authors contributing to the article have no conflict of interest regarding the materials and methods used or the findings stated in this study.

**Informed Consent:** Informed consent was obtained from the patient's parents for this study.

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