

Atypical Teratoid/Rhabdoid Tumor of the Sellar Region: A Case Report and Review of the Literature

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Abstract

Atypical teratoid/rhabdoid tumors (AT/RTs) are rare and aggressive pediatric malignant rhabdoid tumors (MRTs) that occur within the brain. The majority of these tumors occur in the cerebellum. Only 45 cases of adults with AT/RTs have been reported in the literature to date. We present a case of sellar and suprasellar AT/RT in a 40-year-old female patient with this rare entity. To our knowledge, this is the 14th case of an adult-onset AT/RT in the sellar and suprasellar region.

Keywords: Atypical teratoid/rhabdoid tumor; Sellar/suprasellar lesion; Surgery

Introduction

Atypical teratoid/rhabdoid tumors (AT/RTs) are rare and aggressive pediatric malignant rhabdoid tumors (MRTs) that occur within the brain [1]. It is initially reported in 1987 and subsequently, defined as a distinct central nervous system (CNS) neoplasm in 1996. It is added to the World Health Organization (WHO) Brain Tumor Classification in 2007 (grade IV) [2, 3]. Histologically, AT/RTs are known that they are composed of diffuse proliferation of atypical large cells showing eccentrically located nuclei and abundant eosinophilic cytoplasm (rhabdoid features) with prominent nucleoli [4]. AT/RTs are characterized by biallelic loss of SMARCB1 (SWI/SNF-related, matrix-associated, actin-dependent regulator of chromatin, subfamily b, member 1). Here, we report a case of AT/RT that originated in sellar and suprasellar region in a 40-year-old

female patient with brief review of this aggressive tumor in adult population.

Case Report

A medically free 40-year-old female, presented to the emergency department with a history of severe headache and right eye decrease vision. It was associated with nausea, vomiting and photosensitivity for the last few days. Clinical examination revealed decreased vision of the right eye and third nerve palsy of the same side. She denied any history of prolactinoma, constitutional symptoms or family history of pituitary tumors. Magnetic resonance imaging (MRI) and computed tomography (CT) scan showed sellar and suprasellar lesion that was invading the cavernous sinus bilaterally, but more into the right side and protruding through the sella turcica.

Preoperative MRI identified a large sellar enhancing lesion with cystic degeneration measuring $2.9 \times 1.7 \times 2.3$ mm (Fig. 1).

Hormone profiles including cortisol, plasma adrenocorticotropic hormone (ACTH), thyroid hormones such as thyroid-stimulating hormone (TSH) and T4, follicle stimulating hormone (FSH), luteinizing hormone (LH) and growth hormone, prolactin were normal.

Classical transnasal endoscopic approach was performed with subtotal resection of the sellar and suprasellar lesion. The tumor was rubbery and fibrotic which was unusual to pituitary adenoma.

The histopathological study revealed a high-grade densely cellular neoplasm (Fig. 2). Tumor cells were large-sized, polygonal in shape and arranged in sheets. The cytoplasm was eosinophilic with focal eccentric eosinophilic globular inclusions. The nuclei were oval-shaped and pleomorphic with prominent nucleoli (Fig. 3). First differential diagnosis was pituitary adenoma, as it is the most common tumor in the sellar region. Other differential diagnoses include glioma and AT/RTs. Negative staining for pituitary panel, chromogranin and synaptophysin ruled out pituitary adenoma and other neuroendocrine tumors as well. Glial fibrillary acidic protein (GFAP) was negative excluding glial tumor. Immunohistochemical stain for INI-1 (BAF-47) was negative in the tumor nuclei (Fig. 4). The morphologic characteristics and immunoprofile were diagnostic of AT/RT.

Postoperatively, the patient developed diabetes insipidus (DI), which was treated by desmopressin. After that, she was referred to oncology team and started on chemoradiation ther-

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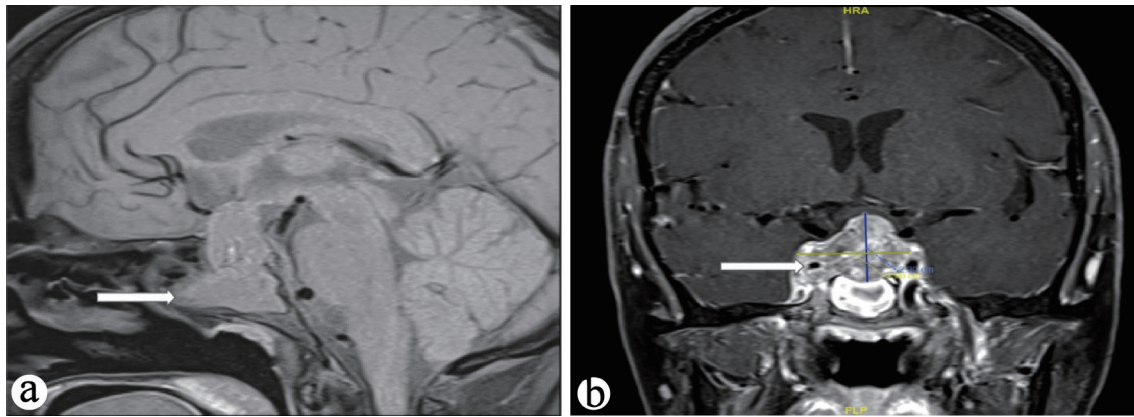


Figure 1. (a) T1-weighted MRI sagittal images showing large intrasellar mass (arrow), (b) T1-weighted MRI coronal images showing large intrasellar mass encasing right internal carotid artery (arrow). MRI: magnetic resonance imaging.

apy. One month later the patient died due to respiratory failure secondary to acute respiratory distress syndrome in shock state and acute kidney injury.

Discussion

AT/RTs are aggressive pediatric malignant brain tumors that accounts for approximately 1-2% of pediatric cancers of the CNS [5]. The majority of these tumors (approximately 60%) occur in the posterior cranial fossa (particularly the cerebellum) [6]. Only 45 cases of adults with AT/RTs have been reported in the literature to date [5]. Ostrom et al reported that the most common location in adults is the cerebral hemisphere, followed by the sellar region [7]. In contrast, Chan et al found that the most common location was the sellar region (46%), followed by cerebral hemisphere (32%) [8]. Sellar AT/RTs were reported to be almost exclusively in females and not in the pediatric population [9, 10]. Recently, it has been reported in the sellar region, with only 14 cases reported in the literature to date including our case (Table 1) [4, 6, 11-19]. All 14 cases are female of age range between 20 and 61 years old, and most of the cases presented with visual disturbance and ocular palsies.

Radiological findings of sellar AT/RTs are non-specific but are remarkably similar to pituitary adenoma; the lesions

are isointense on T1-weighted imaging and enhance following gadolinium administration [12]. Histologically, AT/RTs are composed of diffuse proliferation of atypical large cells showing eccentrically located nuclei and abundant eosinophilic cytoplasm (rhabdoid features) with prominent nucleoli [4].

SMARCB1/INI1 is one of the core subunit proteins of the ATP-dependent SWI/SNF chromatin remodeling complex, and is identified as a potent and *bona fide* tumor suppressor [20]. Interactions have been demonstrated between SMARCB1/INI1 and key proteins in various pathways related to tumor proliferation and progression: the p16/RB pathway, WNT signaling pathway, sonic hedgehog signaling pathway and Polycomb pathway [20]. The molecular changes in AT/RTs include a mutation in one allele with a second allele loss due to monosomy 22, deletion of 22q11.2, or an acquired copy number neutral loss heterozygosity [21, 22]. Sellar AT/RTs also have a higher prevalence of biallelic INI1 alterations compared to AT/RTs in other locations [9]. Loss of expression of INI1 as detected by immunohistochemical staining correlates with deletion and mutations of the *INI1* gene [23]. The differential diagnosis of sellar mass includes pituitary adenomas (85%), followed by craniopharyngioma (3%), Rathke cleft cyst (2%), and meningioma (1%) [24]. Pituitary adenoma shows uniform nuclear morphology with moderately abundant cytoplasm, and the neoplastic cells are highlighted by synaptophysin and chromogranin. Craniopharyngioma has a distinct morphology

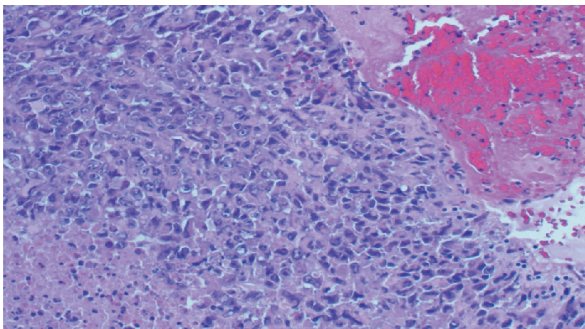


Figure 2. The tumor is composed of sheets of undifferentiated cells with large area of necrosis and hemorrhage (H&E stain, $\times 200$ magnifications). H&E: hematoxylin and eosin stain.

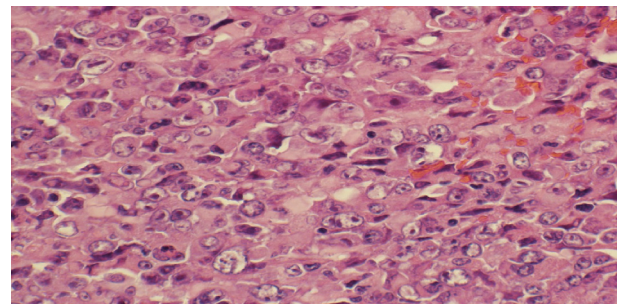


Figure 3. The tumor is composed of medium sized to large cells with prominent nucleoli and some with peripherally placed nuclei (H&E stain, $\times 400$ magnifications). H&E: hematoxylin and eosin stain.

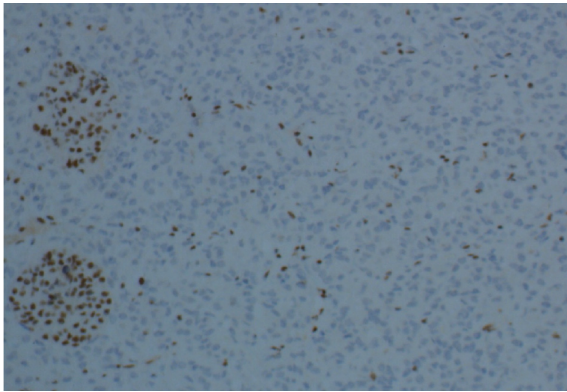


Figure 4. INI-1 (BAF-47) immunostaining shows loss of nuclear staining in the tumor nuclei and positive in the endothelial cells and residual entrapped pituitary tissue (× 200 magnification).

that the neoplastic cells are forming nodules or trabeculae of squamous epithelium, with peripheral nuclear palisading that surrounds looser plumper cells called “stellate reticulum”. In addition, nodules of anucleated squamous (“ghost” cells) and “wet” keratin are usually present. Rathke cleft cyst is a cyst lined by columnar ciliated epithelium with goblet cells. Meningioma usually has syncytial cells that have round uniform nuclei with intranuclear pseudo inclusions.

The prognosis of AT/RT is poor both in adults and in the pediatric population. Chan et al reported the average survival rate of adult AT/RT was 20 months [8]. This is comparable to the reported median survival of 13.5 to 16.8 months in the pediatric population [10, 25]. Long-term survival is possible in adult AT/RT cases after a combined approach including surgery, adjuvant radiotherapy, and chemotherapy [17, 26].

Conclusions

AT/RT is not limited to pediatric age group or to cerebellum, it should be considered in the differential diagnosis of malignant sellar lesion in adult patients. There is no specific radiological features that are available to differentiate AT/RT from pituitary adenoma, both of which represent as a sellar mass. Histologically, high grade features in form of necrosis, hemorrhage and frequent mitosis in adult sellar tumor should raise the possibility of ATRT. Use of BAF- 47(INI-1) immunohistochemical antibodies is the simple and quick tool to confirm the diagnosis. This high grade tumor with dismal outcome is surgically treated followed by radiochemotherapy.

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Table 1. Summary of Previously Described Reports of Sellar AT/RTs and the Present Case

Year	Age/sex	Presentation	Treatment	Outcome	Reference	
1	2000	32/F	Visual disturbance	Resection, radiation, and chemotherapy	28 months (dead)	[12]
2	2005	20/F	Visual disturbance	Resection, radiation, and chemotherapy	28 months (survived)	[13]
3	2005	31/F	Not mentioned	Resection and radiation	9 months (dead)	[13]
4	2008	56/F	Diplopia	Resection and radiation	23 months (dead)	[14]
5	2010	46/F	Headache	Not mentioned	Not mentioned	[15]
6	2011	61/F	Diplopia	Resection	3 months (dead)	[16]
7	2011	57/F	Diplopia	Resection, radiation, and chemotherapy	6 months (survived)	[16]
8	2013	60/F	Headache and diplopia	Resection, radiation, and chemotherapy	30 months (dead)	[17]
9	2013	43/F	Headache and diplopia	Resection and radiation	2 weeks (survived)	[18]
10	2014	44/F	Visual disturbance	Resection, radiation, and chemotherapy	17 months (dead)	[19]
11	2014	42/F	Visual disturbance	Resection, radiation, and chemotherapy	27 months (survived)	[5]
12	2015	36/F	Headache and blurred vision	Resection, radiation, and chemotherapy	29 months (dead)	[20]
13	2017	35/F	Headache, diplopia, and amenorrhea	Resection, radiation, and chemotherapy	37 months (survived)	[7]
14	Present case	40/F	Headache, right oculomotor palsy with decreased vision	Resection, radiation, chemotherapy	2 months	

Conflict of Interest

The authors declare that they have no conflicts of interest.

Informed Consent

The patient died shortly after the surgery.

Author Contributions

Raghad Bokhari wrote the whole manuscript. Mohammed Ba-
faqeeh was the surgeon who did the surgery and provided the
notes. Saad Al-Obaysi provided the radiology images with ex-
planation for each image. Areej Al-Aman provided the clinical
information. Wafa Alshakweer reviewed the manuscript.

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