Adult Atypical Teratoid/Rhabdoid Tumors

Winona W. Wu[1], Wenya Linda Bi[1], Yun Jee Kang[2], Shakti H. Ramkissoon[2], Sashank Prasad[3], Helen A. Shih[4], David A. Reardon[5], Ian F. Dunn[1]

■ BACKGROUND: **Atypical teratoid/rhabdoid tumors (AT/RTs) are highly malignant neoplasms that rarely occur in adults. Due to the complex histology of AT/RTs, the differential diagnosis of these tumors is quite challenging and increasingly relies on demonstration of characteristic *SMARCB1/INI1* inactivation in tumor cells.**

■ CASE DESCRIPTION: **A 51-year-old man presented with diplopia, lethargy, and memory deficit owing to Parinaud syndrome and hydrocephalus. Magnetic resonance imaging revealed a T2-hyperintense and homogeneously enhancing tectal mass that extended to the pineal region. Initial biopsy suggested a World Health Organization grade II myxopapillary astrocytoma. However, subsequent definitive resection revealed an AT/RT, with loss of *SMARCB1/INI1* observed through immunohistochemical staining as well as array cytogenetic analysis. Molecular profiling revealed additional mutations in *RHPN2*^{L385I}, *MDM4*^{D396G}, *FLT3*^{V194M}, and *NPRL3*^{D53N}.**

■ CONCLUSIONS: **Pathologic diagnoses in the modern era increasingly integrate molecular data for confirmation as well as prognostication. We present a rare case of a tectal AT/RT in an adult patient and report several novel mutations previously unrecognized in this tumor subtype, in addition to canonical *SMARCB1/INI1* loss. Further investigation of these novel variants may improve understanding of the pathogenesis underlying AT/RTs.**

INTRODUCTION

Atypical teratoid/rhabdoid tumors (AT/RTs) are rare and extremely aggressive malignancies of the central nervous system (CNS).[1,2] Although approximately 95% of these neoplasms occur in the posterior fossa of children under the age of 5 years,[3,4] AT/RTs also occur — albeit rarely — in adults, where they largely manifest supratentorially.[5] Since the first adult patient with a malignant CNS RT was reported in 1987, 54 adult cases (≥18 years of age) of malignant RT or AT/RT have been documented in the literature thus far (**Table 1**).[4,6-45]

Pathologically, AT/RTs are composed of sheets or nests of rhabdoid cells — characterized by eccentrically located nuclei and eosinophilic cytoplasm — that are juxtaposed to primitive neuroepithelial, mesenchymal, and epithelial components.[2,5,46] Approximately 70% of primary AT/RTs exhibit inactivation of the SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily B member 1 (SMARCB1/INI1) due to either focal deletion in or monosomy of chromosome 22.[20] While this distinctive molecular marker has greatly abetted the diagnosis of AT/RT, putative oncogenic drivers outside of SMARCB1/INI1 remain unknown in this malignancy. We report a case of a tectal region AT/RT in an adult patient with SMARCB1/INI inactivation as well as additional genetic mutations previously unreported in AT/RT, which may lend new insights into future diagnosis and management of this challenging disease.

CASE DESCRIPTION

A 51-year-old right-handed man presented with episodic and worsening diplopia, memory difficulties, and daytime lethargy over 10 months. A computed tomography scan demonstrated

Key words
- Atypical teratoid/rhabdoid tumor
- Brain tumor
- Clinical management
- Genomics
- Pineal tumor
- Rhabdoid tumor

Abbreviations and Acronyms
AT/RTs: Atypical teratoid/rhabdoid tumors
CNS: Central nervous system
FLT3: Fms-related tyrosine kinase 3
GKRS: Gamma knife radiosurgery
MDM4: Mouse double minute 4
NPRL3: Nitrogen permease regulator-like 3
RHPN2: Rhophilin-2
SMARCB1/INI1: SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily B member 1

From the [1]Department of Neurosurgery; [2]Department of Pathology, Division of Neuropathology; [3]Department of Neurology, Brigham and Women's Hospital; [4]Department of Radiation Oncology, Massachusetts General Hospital; and [5]Center for Neuro-Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, Massachusetts, USA

To whom correspondence should be addressed: Ian F. Dunn, M.D.
[E-mail: idunn@partners.org]

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Table 1. Summary of Adult Atypical Teratoid/Rhabdoid Tumor Cases Reported in the Literature: Demographics, Histopathologic Analyses, SMARCB1/INI1 Status by Immunohistochemistry or Cytogenetics, and Treatment Regimens Are Enumerated for Each Case, Where Available

			Pathology		Primary Treatment			Secondary Treatment			
Reference	Age/ Sex	Tumor Location	Positive Immunostain	INI1 Analysis	Surgery	Chemotherapy	Radiation	Surgery	Chemotherapy	Radiation	Survival (months)
Balaton et al.,1987[6]	59 M	Paravertebral	CK Vim	—	—	—	—	—	—	—	0.5
Horn et al., 1992[7]	21 M	Temporal, L	EMA Vim	—	Y (STR)	Y (multi-regimen)	N	Y (STR)	N	N	72
Cossu et al., 1993[8]	18 M	Frontal, L	CK EMA Vim	—	Y (GTR)	Y	N	Y (GTR)	Y	N	18
Fisher et al., 1996[9]	32 M	Frontal, L	CK EMA GFAP S100 Vim	—	—	—	—	—	—	—	1
Ashraf et al., 1997[10]	34 M	Parietal, L	Vim	—	Y (STR)	N	Y	Y (STR)	N	N	6
Byram et al., 1999[11]	35 M	Temporal, L	CK EMA Vim	—	Y (GTR)	N	Y	Y (GTR)	N	N	60
Sugita et al., 1999[12]	27 M	Pineal	EMA NSE S100 SMA Vim	—	Y (STR)	Y	Y	Y (STR)	N	N	24
Kuge et al., 2000[13]	32 F	Suprasellar	CK EMA SMA Vim	—	Y (STR)	N	N	N	Y (CDDP, ETO, IFNγ, IT MTX)	Y (craniospinal)	24
Arrazola et al., 2000[14]	20 M	Parietal, L	CK EMA S100 Vim	—	Y (GTR)	N	N	Y (GTR)	N	Y (craniospinal)	24+
Lutterbach et al., 2001[15]	30 F	Cerebellar	CK EMA S100 Vim	—	Y (GTR)	Y (ETO)	Y	Y (GTR)	Y (ETO)	Y	11
Bruch et al., 2001[16]	21 F	Spinal	CK EMA Vim	Monosomy 22 (FISH)	—	—	—	—	—	—	6
	34 F	Parietal	CK EMA GFAP Vim	Monosomy 22 (FISH)	—	—	—	—	—	—	6
Pimentel et al., 2003[17]	31 F	Parietal, R	GFAP NFP S100 Vim	—	Y (STR)	N	N	N	Y (ICE)	Y	6
Kachhara et al., 2003[18]	35 M	Thalamus	Vim	—	Y (STR)	N	Y	—	—	—	—
Kawaguchi et al., 2004[19]	22 M	Cerebellar	CK EMA NFP NSE SMA Vim	—	Y (STR)	Y (ICE, IT MTX)	Y (craniospinal)	—	—	—	24+
Raisanen et al., 2005[20]	20 F	Sellar	CK EMA SMA Vim	Neg	Y	Y	Y	N	Y	N	28+
	31 F	Sellar	CK EMA Vim	Neg	Y	N	Y	—	—	—	9
	45 M	Cerebellar, R	CK EMA SMA S100 Vim	Neg	Y	Y	Y	—	—	—	15+
Erickson et al., 2005[21]	20 F	Occipital, R	EMA GFAP SMA Vim CK	Pos (FISH)	Y (GTR)	N	N	N	N	Y	—

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