Human Pathology (2014) **45**, 185–188

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Human PATHOLOGY

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Case study

Atypical teratoid/rhabdoid tumor with ganglioglioma-like differentiation: case report and review of the literature☆,☆☆

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Received 31 May 2013; revised 29 July 2013; accepted 31 July 2013

Keywords:
Atypical teratoid rhabdoid tumor;
INI1;
Ganglioglioma;
Pediatric brain tumor

Summary Atypical teratoid/rhabdoid tumor (AT/RT) is a highly aggressive embryonal tumor of the central nervous system, which typically affects young children. A characteristic feature of AT/RT is a polyphenotypic immunoprofile and ultrastructural diversity. The morphologic and antigenic heterogeneity of AT/RT give it the potential to mimic other embryonal central nervous system tumors, epithelial neoplasms or mesenchymal tumors. Alternatively, "collision-type" tumors have been published, in which AT/RT coexists with a separate low-grade central nervous system tumor. Here, we report a case of AT/RT with morphologic and immunohistochemical evidence of extensive ganglioglioma-like differentiation with only a small focal primitive component and minimal rhabdoid cytology. Fluorescence in situ hybridization and immunohistochemistry demonstrated INI1/BAF47 gene/protein losses in both histologic components. To the best of our knowledge, this is the first reported case of AT/RT with extensive ganglioglioma-like differentiation. This unique case supports the notion that routine application of INI1 stains/in situ hybridization can capture AT/RT with unexpected patterns of differentiation.

1. Introduction

Atypical teratoid/rhabdoid tumors (AT/RT) are highly aggressive central nervous system (CNS) malignancies with a propensity for morphologic and antigenic heterogeneity. AT/RT represents the CNS manifestation of the malignant rhabdoid tumor (MRT) family harboring inactivation of the *SMARCB1* gene. Prior to the early 1990s, a subset of embryonal CNS tumors, mostly in young children, was recognized for their unusually aggressive clinical behavior. These cases were typified by variable numbers of tumor cells with rhabdoid morphology and coexpression of neuroglial, epithelial, and mesenchymal antigens [1-3]. Subsequently, reports of monosomy 22 by karyotype began the slow but steady evolution defining the diagnosis using genetic criteria [4-6].

Several investigators confirmed via immunohistochemical methods the lack of expression of the INI1 protein in the

☆ The authors acknowledge no conflicts of interest during the preparation of this manuscript.
☆☆ Funding disclosures: none.
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0046-8177/$ – see front matter © 2014 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.humpath.2013.07.039

vast majority of malignant rhabdoid tumors (including AT/RT). Thus, this genetic signature (and its immunohistochemical corollary) is accepted as a near definitional feature of malignant rhabdoid tumors [7-9]. Furthermore, the routine application of INI1 immunohistochemistry, often in combination with fluorescence in situ hybridization (FISH) studies to detect deletions of the *INI*1 gene, has helped to broaden the histologic spectrum encountered in AT/RT, including rare examples where the rhabdoid cells are inconspicuous.

Here, we report an unusual case of AT/RT with extensive gangliogliomatous differentiation. To the best of our knowledge, this pattern has not been reported elsewhere in the literature.

2. Materials and methods

2.1. Case report

The patient is a 4-year-old girl with a 3-month history of headache and worsening clumsiness. Two weeks prior to presentation, she experienced intermittent nausea with vomiting. Upon admission for acute ataxia, a computed tomographic scan showed a large posterior fossa tumor. Preoperative magnetic resonance imaging scans demonstrated a large, inhomogeneously enhancing, 4 × 4 × 7 cm mass filling the fourth ventricle with anterior displacement and compression of the dorsal brainstem.

A gross total resection was completed.

2.2. Histology and immunohistochemistry

Formalin-fixed, paraffin-embedded tissue was cut in 4-μm thick sections (Leica Semiautomated Microtome RM2245, Leica Microsystems, Wetzlar, Germany) and stained with hematoxylin and eosin.

Immunohistochemistry was performed on 4-μm thick paraffin-embedded sections using commercially available antibodies under different antigen retrieval techniques, using an automated stainer. Absence of INI1 staining (CellMarque, clone MRQ-27, Rocklin, CA, USA) was interpreted as loss of protein expression in the context of a lack of nuclear reactivity in tumor cells with positive staining in background endothelial cells and lymphocytes. The MIB-1 (Ventana, clone 30-9, Tucson, AZ, USA) proliferation index was estimated as the highest number of positive tumor cells in a representative low-power field (100×), as a fraction of total tumor nuclei.

2.3. Cytogenetics and FISH

Karyotype analysis was performed by Mayo Medical Laboratories (Mayo Clinic, Rochester, MN, USA) using standard techniques. Fluorescence in situ hybridization (FISH) was performed on formalin-fixed, paraffin-embedded tissues using the custom-labeled BAC clone RP11-80O7 (Bluegnome, Cambridge, UK), the target of which lies 3.4-kb distal to the *SMARCB1* locus at 22q11.23, and a probe for the *SMARCB1* locus itself.

3. Results

Histologically, the tumor demonstrated 2 distinct morphologies. The first was a highly cellular component exhibiting primitive features, as evidenced by tumor cells bearing scant cytoplasm, angulated hyperchromatic nuclei, frequent mitoses, and sheet-like growth (Fig 1A). The second, and predominant pattern, resembled ganglioglioma, including numerous, variably sized, dysmorphic ganglion cells with frequent binucleation, along with rare elongate,

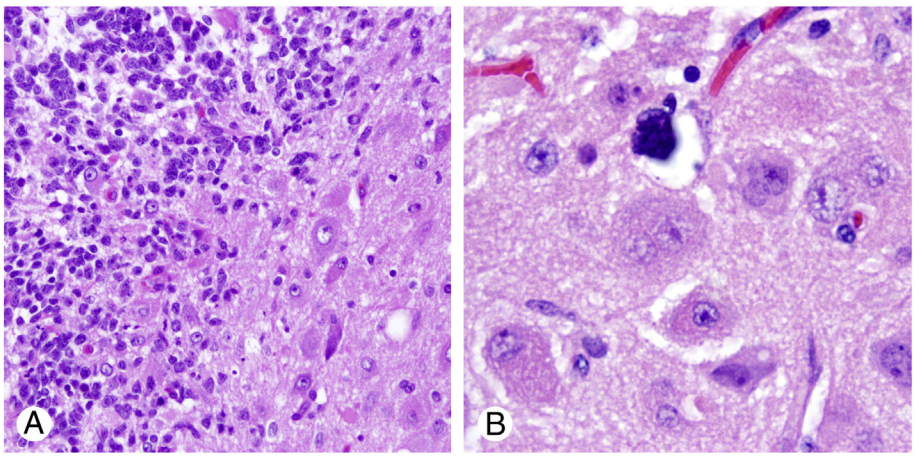

Fig. 1 A and B, Sections of the tumor show two distinct tumor morphologies. A, Low-power view showing an embryonal component typical of AT/RT and a gangliogliomatous component, which represented the majority of the tumor (H&E section, 100×). B, High-power view of the gangliogliomatous component (H&E section, 400×). Abbreviation: H&E, hematoxylin and eosin.