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Primary Adult Atypical Teratoid Rhabdoid Tumor of Spine : Extremely Rare Case and Review of Literature

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Abstract

Atypical teratoid rhabdoid tumors (ATRTs) constitute a rare, highly malignant aggressive central nervous system embryonal neoplasms. While spinal ATRTs are exceptionally uncommon, their clinical significance is underscored by the aggressive nature of the disease and the formidable challenges they pose to diagnosis and management. Characterized by a distinctive histopathological profile, ATRTs exhibit features of primitive/ undifferentiated cells with variable rhabdoid morphology. These tumors are linked to biallelic inactivation of the INI1 (SMARCB1) gene or rarely SMARCA4, contributing to their pathogenesis. This scientific exploration is regarding a thirty-nine-year-old female who presented with sudden onset weakness in both the lower limbs and MRI study of cervical spine revealed as extra axial enhancing lesion at D1-D2 level suggestive of meningioma followed by histological diagnoses of primary adult ATRT of the spine. The case report aims to delve into the unique aspects of ATRTs arising in the spinal cord, providing an overview of their clinical presentation, histopathological characteristics, and the challenges associated with diagnosis. Furthermore, the review will discuss current perspectives on the molecular mechanisms underlying spinal ATRTs, emphasizing the significance of the INI1 gene alterations.

Keywords: ***ATRT; Adult; Spinal location; SMARCB1(INI1)***

1. Introduction

Atypical teratoid rhabdoid tumors (ATRTs) constitute a rare, highly malignant aggressive central nervous system embryonal neoplasms [1]. Atypical Teratoid Rhabdoid Tumor (ATRT) is defined as a high-grade malignancy composed of poorly differentiated cells and a variable number of rhabdoid cells with a potential to differentiate along neuroepithelial, epithelial and mesenchymal cell line. Predominantly recognized for their occurrence in the pediatric population, ATRTs have been

documented in various anatomical locations, including the spinal cord [2]. ATRT is estimated to occur in 1%-2% of all pediatric CNS tumors, and 10%-20% of CNS tumors in children under 3 years old.

ATRT can occur throughout the neuraxis but supratentorial location is more common involving the cerebral hemispheres, ventricles, pineal region followed by infratentorial location involving the cerebellar hemispheres and brainstem. While spinal ATRTs are exceptionally uncommon, their clinical significance is underscored by the aggressive nature of the disease and the formidable challenges they pose to diagnosis and management.

Clinical presentation is variable and depends on the age, location of tumor and size. Specific symptoms include headache, vomiting, cranial nerve palsies, paresthesias and hemiplegia.

Characterized by a distinctive histopathological profile, ATRTs exhibit features of primitive/ undifferentiated cells with variable rhabdoid morphology. These tumors are linked to biallelic inactivation of the INI1 (SMARCB1) gene or rarely SMARCA4, contributing to their pathogenesis [3-5]. Despite their rarity in adult populations, spinal ATRTs necessitate a comprehensive understanding due to their potential impact on neurological function, morbidity, and overall survival.

There is no standard recommendation of treatment for these tumors due to their low prevalence and high mortality rates. There is strong evidence of multimodal treatment with studies suggesting complete resection of tumor is the cornerstone of treatment, and the use of trimodal treatment comprising surgery with adjuvant RT and CT improves OS.

Understanding the intricacies of spinal ATRTs is paramount for advancing diagnostic precision, therapeutic strategies, and prognostic assessments in the pursuit of improved outcomes for affected individuals. This scientific exploration aims to delve into the unique aspects of ATRTs arising in the spinal cord, providing an overview of their clinical presentation, histopathological characteristics, and the challenges associated with diagnosis. Furthermore, the review will discuss current perspectives on the molecular mechanisms underlying spinal ATRTs, emphasizing the significance of the INI1 gene alterations.

3. Case Report

A thirty-nine-year-old female, known diabetic on treatment presented with sudden onset weakness in both the lower limbs for two weeks followed by bowel involvement with loss of bowel control leading to bowel incontinence with paraesthesia of both lower limbs. She also had a decrease in sensation from abdomen to lower limbs on both sides. On examination, decreased power in both limbs (1/5).

MRI study of cervical spine with whole spine screening revealed as extra axial enhancing lesion at D1-D2 level approximately measuring 30 mm in posterior dural space causing cord indentation resulting in cord edema, with possibility of meningioma to be considered (FIG. 1). Patient underwent a D1-D3 Laminectomy and near total excision of the tumor was performaed. Intra operative findings revealed a pinkish grey color, soft, suckable, moderately vascular tumor with intramedullary extension. The sample was sent to histopathology lab for an examination.

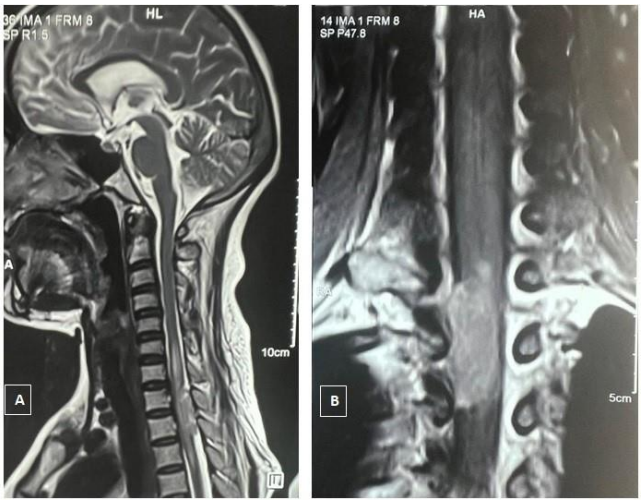

FIG. 1A &B. **MRI Saggital and coronal sections of cervico dorsal Spine showing extraaxial enhancing lesion at D 1- D2 level in the posterior dural space measuring ~3 Cms, causing cord indentation resulting in cord edema.**

Routine histopathology sections reveal cellular lesion with sheets of polygonal cells separated by thin vasculatures. The cellular lesion seen as syncytial and diffuse sheeting pattern composed predominantly of rhabdoid morphology with enlarged eccentric nuclei, open vesicular nuclei and typical abundant homogenous eosinophilic cytoplasm. Foci showed plump spindled cells (FIG. 2). There were focal moderate to severe anisonucleosis with occasional binucleate and multinucleate forms. Miotic figures were seen 8-10/hpf. A morphological diagnosis of Tumors with Rhabdoid Morphology was entertained with differential diagnosis of Rhabdoid meningioma, Chrordoma, Germ cell Tumor and Malignant Rhabdoid Tumor (AT/RT) were considered. The lesional cells showed strong patchy positivity to EMA and CK with negative stains to GFAP, HMB45, Desmin, SALL4, Brachyury. Immunohistochemcial studies showed rhabdoid cells with typical diffuse loss of INI 1 protein (SMARCB1) staining (FIG. 3,4).

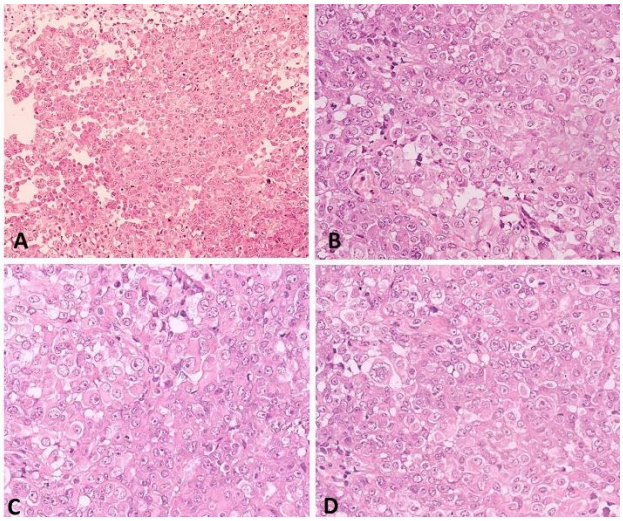

FIG. 2. **Syncytial sheets separated by capillary network composed of of large polygonal cells with rhabdoid morphology with enlarged eccentric open vesicular nuclei, prominent nucleolus and typical abundant homogenous eosinophilic cytoplasm (H&E, Ax100; B,C,D x400).**

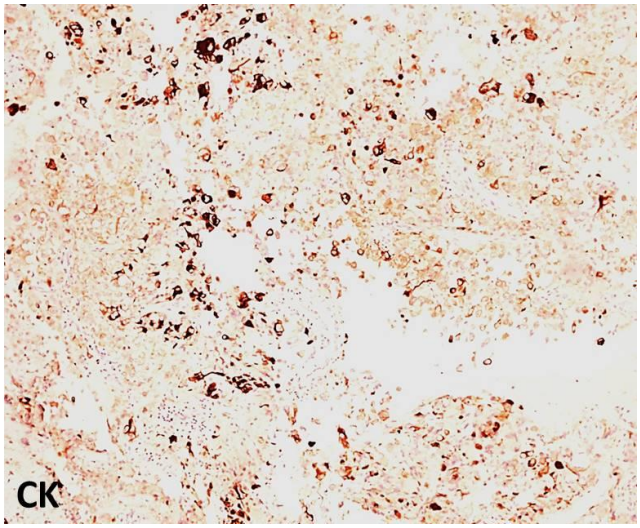

FIG. 3. **IHC with Cytokeratin show focal strong positivity.**

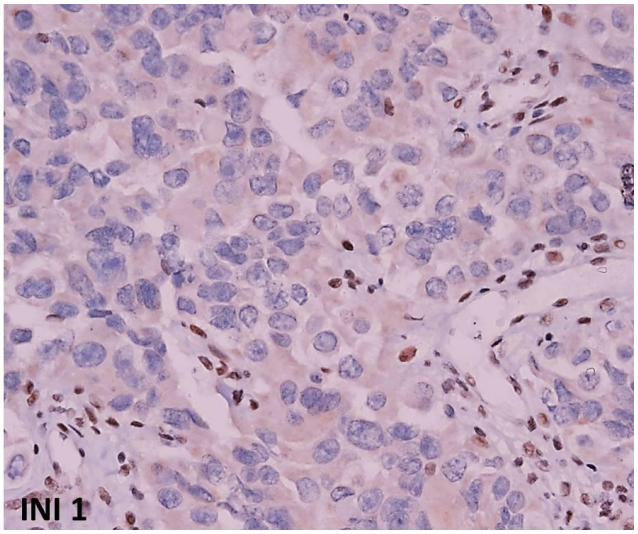

FIG. 4. **IHC with INI-1 staining shows abnormal loss of nuclear staining within the rhabdoid lesional cells with preserved nuclear staining of internal control (capillary endothelial cells).**

4. Discussion

ATRT is rare and aggressive form embryonal cancer predominantly found in CNS. AT/RT is seen in children <2 years of age chiefly arising in the cerebellum, followed by the ventricles, frontal lobe, and brainstem [6]. However rare cases of Adult ATRT s have been documented [7]. The prognosis of adult ATRT is poor with early metastatic disease and relapses.

The spinal location of Atypical Teratoid Rhabdoid Tumor (ATRT) is exceptionally rare and aggressive malignancy usually seen in paediatric population with 45 cases reported till date [8-10]. More exceptionally rare is adult onset spinal ATRTs with only ten cases have been published in literature [11-20].

Patients with spinal ATRT typically present with axial neck or back pain, radiculopathy, neurological deficits and paralysis in severe cases. Depending on the location and size of the tumor, patients can present with sensory changes, motor weakness with bowel and bladder involvement. The present Case also had weakness and paresthesisas of both lower limbs with bladder involvement.

ATRT is characterized by the loss of function of the SMARCB1 (INI1) gene, which plays a role in the regulation of cell growth. The loss of this gene's function al locus 22q11.2 is a hallmark feature of ATRT and also diagnostic. Inactivation of SMARCB1 is caused by structural variants and mutations (insertion/deletion, point mutations, frame shift mutations).

ATRT is histopathologically characterised by the presence of rhabdoid cells which are large cells with eccentric nuclei and prominent eosinophilic cytoplasm. The tumor may also display a heterogeneous histological pattern with areas of primitive neuroepithelial cells, mesenchymal elements, and sometimes, true teratoid features. Immunohistochemical staining for INI1 is a key diagnostic tool for ATRT. Loss of nuclear expression of INI1 in tumor cells is a consistent finding in ATRT. Other markers such as epithelial membrane antigen (EMA), vimentin, and cytokeratin may also be used to aid in the diagnosis. ATRT in adults, including spinal ATRT, may exhibit molecular heterogeneity. While alterations in the SMARCB1 gene are a common feature, other genetic mutations or alterations may also be present. Next-generation sequencing and other molecular profiling techniques can provide a more detailed understanding of the genetic landscape of adult spinal ATRT.

The pathological differential diagnosis of spinal Atypical Teratoid Rhabdoid Tumor (ATRT) involves distinguishing it from other spinal tumors or lesions that may share some histological features. Ependymomas are glial tumors that can occur in the spinal cord. They may share some histological features with ATRT, such as cellular atypia, but typically lack the rhabdoid cells seen in ATRT. Immunohistochemistry for INI1 can help differentiate ATRT from ependymoma, as loss of INI1 expression is characteristic of ATRT. Medulloblastomas are embryonal tumors that primarily occur in the cerebellum but can occasionally involve the spinal cord. They may exhibit small, blue, undifferentiated cells, but lack the rhabdoid morphology seen in ATRT. Immunohistochemistry and genetic profiling can help differentiate between medulloblastoma and ATRT. Schwannomas are benign tumors arising from Schwann cells and are common in the spinal cord. They usually present with spindle cells and are typically benign. The presence of rhabdoid cells and the loss of INI1 expression can help differentiate ATRT from schwannoma. Meningiomas are often benign tumors arising from the meninges. They can occur in the spinal cord and may exhibit variable histological patterns. It is essential to distinguish from Rhabdoid meningioma. Immunohistochemistry and detailed histological examination are essential for distinguishing meningiomas from ATRT. Metastatic lesions in the spine, particularly from carcinomas, can mimic primary spinal tumors. They may present with a variety of histological patterns. Clinical history, imaging, and additional immunohistochemical stains can aid in distinguishing metastatic carcinoma from ATRT Germ cell tumors, including germinomas, may occur in the spinal cord. They often exhibit primitive neuroepithelial features. Distinction may require immunohistochemistry and, in some cases, molecular studies.

Accurate diagnosis of spinal ATRT requires a comprehensive approach, combining clinical, radiological, histopathological, immunohistochemical, and molecular analyses. Collaboration among pathologists, oncologists, and other specialists is crucial in ensuring an accurate diagnosis and appropriate management for patients with spinal tumors.

The pathological features of ATRT, including the extent of tumor invasion, mitotic activity, and molecular profile, may have implications for prognosis and treatment planning. High-grade histology and the presence of certain molecular alterations may indicate a more aggressive clinical course [21-22]. Pathological findings play a crucial role in guiding treatment decisions. The extent of surgical resection, the need for adjuvant therapies such as radiation and chemotherapy, and the choice of specific agents may be influenced by the pathological characteristics of the tumor. The underlying molecular genetics, pathophysiology, advancements in research and clinical understanding continue to evolve of such rare tumors. Case reports highlight patients being treated with aggressive therapy including surgery, radiation therapy and multi-agent chemotherapy using the Intergroup Rhabdomyosarcoma III (IRS III) designed for parameningeal Rhabdomyosarcoma (Regimen 36) can significantly alter the course of the disease [23]. Additionally, considering the rarity of adult ATRT, collaboration between clinicians, pathologists, and researchers is vital to improve diagnostic accuracy and develop effective treatment strategies tailored to this specific population.

5. Conclusion

ATRTs are aggressive neoplasms and Adult Spinal ATRTs are extremely rare with only a few handful cases published in literature. These tumors are characterised by loss of function of the SMARCB1 (INI1) gene which is considered pathognomic hallmark. Characteristic histomorphology composed of high-grade cells with rhabdoid morphology supported by immunochemistry and genetic analysis are essential in making the final diagnosis. There have been some encouraging results of aggressive multimodality treatments including combination surgery, chemotherapy followed by radiotherapy.

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