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# Cranio-cervical Junction Malignant Extrarenal Rhabdoid Tumor: A Case Report

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## *Abstract*

***Case Report:*** A 2-year-old girl was referred with the chief complaint of limb weakness following a mild trauma. She had been suffering from restlessness and neck pain for a month. Laboratory findings were normal. In MRI, there was evidence of craniocervical junction extra-axial mass lesion arising from the posterior aspect of the dense process ligamentous complex extending from the foramen magnum to the posterior fossa with engulfment of the right vertebral artery. Regarding the compressive effect of the tumor, a right trans-condylar suboccipital surgical approach was used to resection the mass, near totally, and decompress the brain stem. Immune-Histo-Chemical Staining (IHC) showed a grade 2 meningioma. Low-dose radiotherapy was applied; but the pathology result corroborated the tumor's radiologic features. Due to the follow-up MRI evidence of aggressive tumor recurrence the clinical behavior of the tumor and the patient's progression, there was a possibility that the first diagnosis was not correct; hence, a second operation was performed during which a smaller portion of the tumor could be resected compared with the first operation. Pathological study and IHC staining reported MRT and tumor markers, including pan-cytokeratin (CK), epithelial membrane antigen (EMA), and vimentin, were strongly positive. So, a chemotherapy regimen was added to radiotherapy. Unfortunately, the patient did not respond well to the follow-up treatment, and she expired after one year.

***Conclusion:*** In similar cases, where the radiological and pathological features of the tumor are atypical, the histological examination should include molecular examination, as meningioma in this age group is extremely rare. And, confirming the pathological and molecular characteristics of the tumor by different experts is strongly recommended.

***Key Words:*** Atypical Teratoid/Rhabdoid Tumor (AT/RT), Intra-Axial Tumors, Malignant Pediatric Neoplasm, Rhabdoid Tumor (MRT).

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## 1- INTRODUCTION

Rhabdoid Tumor (RT) is a poorly differentiated pediatric neoplasm that often affects children under three years of age (1-4). This tumor usually involves the Central Nervous System (CNS), kidney, and soft tissue (5-7). The RT that arises from the extra CNS tissues is an uncommon neoplasm identified as malignant rhabdoid tumor (MRT). The most frequent location of MRT is the kidney (8-10). In contrast to MRT, the intracranial RT is a common intra-axial CNS neoplasm of childhood categorized as atypical teratoid/rhabdoid tumor (AT/RT) (11, 12).

Because of its location and imaging characteristics, the AT/RT should be considered a differential diagnosis for intra-axial tumors such as medulloblastoma, primitive neuro-ectodermal tumors (PNET), and malignant gliomas. Extra-axial RT is extremely rare, and despite its intracranial or spinal canal location, it cannot be categorized as AT/RT (13, 14).

This paper presented a radiologically and histo-pathologically challenging case of extra-axial craniocervical junction MRT.

## 2- CASE PRESENTATION

A 2-year-old girl was referred to our department with the chief complaint of limb weakness following a trauma. During playing, she suffered a mild trauma in the form of the same-level falling down. She had been suffering from restlessness and neck pain for a month, but no follow-up was performed on her. She had no history of past medical problems. There was no cancer history in her family. Significant findings on her examination included left-side torticollis, quadriplegia, and limb weakness. Muscle force in her upper and lower limbs on the right side was $\frac{1}{5}$ and on the left side was $\frac{3}{5}$, and no cranial nerve defects were found.

Laboratory findings were normal. As for quadriplegia, cervical and brain magnetic resonance imaging (MRI) was done. In the imaging, there was evidence of craniocervical junction extra-axial mass lesion arising from the posterior aspect of the dense process ligamentous complex extending from the foramen magnum to the posterior fossa with engulfment of the right vertebral artery. The tumor had a severe compressive effect on the upper cervical cord and the medulla oblongata **(Fig. 1** and **2**).

Regarding the compressive effect of the tumor, a right trans-condylar suboccipital surgical approach was used to resection the mass near totally, and decompress the brain stem. On post-operative physical examination, the patient had no neurological deficits, and her muscle force was increased. The histological findings **(Table 1)** were suggestive of meningioma; and immune-histo-chemical staining (IHC) was performed to reach a definitive diagnosis, which was a grade 2 meningioma. The oncologist recommended low-dose radiotherapy. Since the pathology result corroborated the tumor's radiologic features, the treatment was finished only by considering periodic follow-up imaging.

Six months after the operation, in the follow-up MRIs, there was evidence of aggressive tumor recurrence at the site of previous surgery. Because the clinical behavior of the tumor and the patient's progression were disproportionate to grade 2 meningioma, there was a possibility that the first diagnosis was not correct, so the tumor specimen had to be re-examined. Hence, a second operation for brain stem decompression and pathological assessment was considered. During the second surgery, a smaller portion of the tumor could be resected compared with the first operation. Pathological study and IHC staining reported MRT and tumor markers, including pan-cytokeratin (CK), epithelial

membrane antigen (EMA), and vimentin, were strongly positive **(Table 1** and **fig. 3** and **4**). Based on these findings, the oncologist added a chemotherapy regimen to radiotherapy. Genetic evaluation was performed, and absence of expression of SMARCB1/INI1 was detected. Unfortunately, the patient did not respond well to the treatment, and she expired after one year.

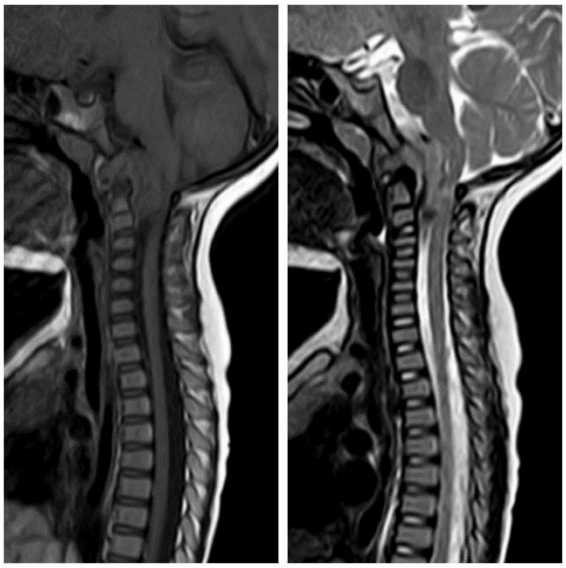

**Fig. 1:** Craniocervical junction extra-axial mass lesion arising from the posterior aspect of the dense process ligamentous complex extending from the foramen magnum to the posterior fossa with engulfment of the right vertebrobasilar system/ In sagittal T2 sequence, the tumor was hyperintense (right), and in T1 sagittal sequence (left), it was to hyperintense in comparison with the brain stem.

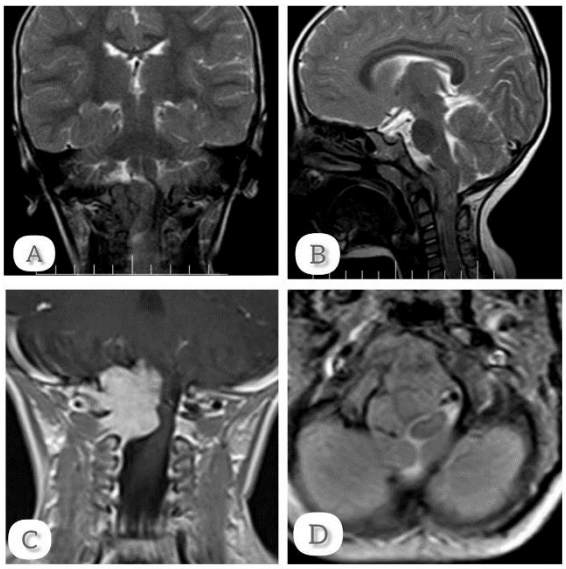


**Fig. 2:** In coronal T2 sequence (A), there is a right side extra-axial craniocervical junction tumor with a compressive effect on the brain stem. In sagittal T2 (B), the involvement of vertebrobasilar arteries is apparent. In coronal T1(C), after gadolinium injection, the tumor has a vivid enhancement. In axial T2 Sequence (D), the compressive effect of the tumor on the brain stem was evident.

**Table-1:** Pathology description of tumor samples

| Diagnosis | Pathology description |
|---|---|
| First sample: Meningioma | Macroscopic features:<br>- Size: 2.5×2.5×1 cm<br>- Soft consistency in cream gray color<br>Microscopic examination:<br>- Proliferation of neoplastic cells arranged as tight whorls with delicate rounded to oval nuclei, inconspicuous nucleoli, lightly eosinophilic, cytoplasm and indistinct cytoplasmic border<br>- Foci of myxoid change<br>- Brain invasion, necrosis, and mitosis were not detected. |
| Second sample: MRT | Microscopic features:<br>- Proliferation of rhabdoid cells and polygonal cells with eccentric vesicular nuclei, prominent nucleoli, and abundant cytoplasm containing juxta-nuclear eosinophilic |

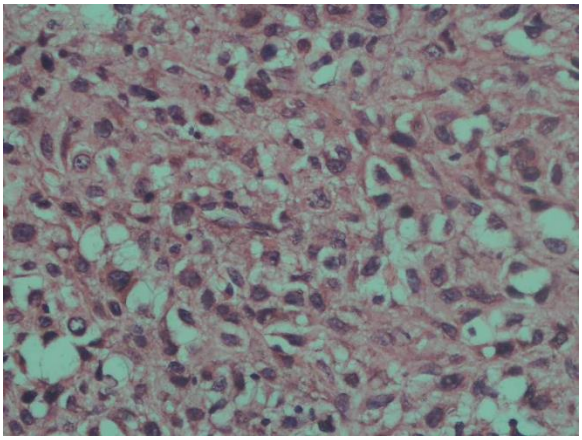

**Fig. 3:** Sheets of large epithelioid cells with abundant eosinophilic cytoplasm in the malignant extrarenal rhabdoid tumor. Some tumor cells have eccentric nuclei with macronuclei.

## 3- DISCUSSION

RTs such as the MRT or either AT/RT are rare embryonal tumors of childhood (15). As in the presented case, RTs have the highest incidence in children under three years of age (1). RTs were first described as a rhabdomyosarcomatous variant of Wilms tumor of the kidney in the pediatric population, however, it can also originate from extrarenal structure, specifically the CNS (16). Its CNS counterpart, i.e., the AT/RT, also is predominantly found in pediatric patients (1). Similar to our case, most intracranial RTs are located in the posterior fossa (17); nevertheless, the unique point of our case is its extradural presentation. In our case, the tumor originated from the posterior aspect of the ligamentous structure of the C2 dens process and the occipital clivus extending from the craniocervical junction to the posterior fossa. The mentioned features correspond with the foramen magnum meningioma or clivus chordoma as the principal differential diagnosis (18, 19). Hence the diagnosis of primary MRT of the brain can be made only pathologically. Nonspecific image findings may not help reach the diagnosis. But the differential diagnosis may be considered in

cases of large invasive pediatric intracranial neoplasms (20, 21).

MRTs of the neck and extradural sites were formerly introduced in limited case studies. Wolfe et al. (2018) reviewed cervical MRTs cases, and found poorer outcomes and more variable ages of presentation and progression times in these cases, as compared to the MRTs at other locations. The histologic diagnosis of MRT is according to the identification of characteristic rhabdoid cells, i.e., large cells with eccentrically located nuclei and abundant eosinophilic cytoplasm, and positive vimentin, CK, and EMA markers in IHC staining. Because of the complex histopathologic appearance of the RT, it can be mistaken for intra-axial, poorly differentiated tumors such as medulloblastoma and choroid plexus carcinoma. However, in our case, in the first pathological investigations, the presence of epithelioid cells together with the tumor's extra-axial origin led to the diagnosis of meningioma. In this case, both the pathology and radiologic characteristics were atypical, and due to an aggressive clinical course, reassessment of the tumor was essential. The histological examination should have included molecular examination, as meningioma in this age group is extremely rare. In the second evaluation, CK, EMA, and vimentin were detected **(Fig. 4)**. EMA can be shared between meningioma and RTs markers **(Table 2)**. Absence of SMARCB1/INI1 expression in our case was confirmed. Usually, 33% of new cases with RTs have a genetic predisposition to tumors because of a germline SMARCB1 alteration, and the patient's family may manifest gonadal mosaicism. Therefore, genetic consultation with other family members is important (22-27).

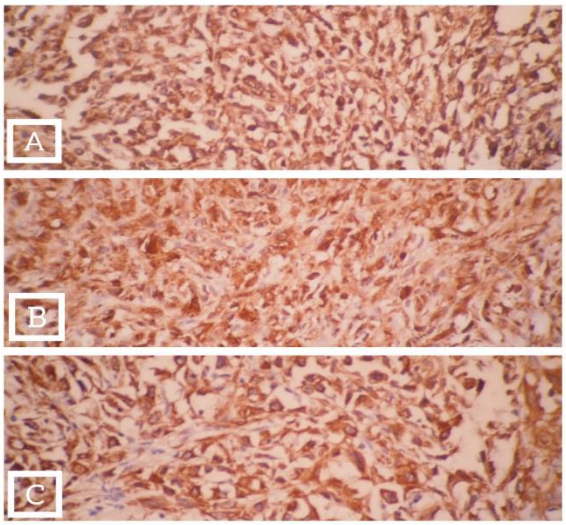


**Fig. 4:** A= strongly positive CK, B= strongly positive EMA, C= strongly positive vimentin

**Table-2:** Positive stains of RTs/ meningioma

| Tumor | Positive stains |
|---|---|
| RTs | Keratin (particularly CK8), vimentin, EMA, desmin and neurofilament |
| Meningioma | Somatostatin receptor 2a (SSTR2a) is a specific meningioma marker in CNS tumors<br>EMA: usually patchy, not diffuse<br>Progesterone receptor: diffuse strong nuclear in low-grade meningiomas and diminished in high-grade meningiomas |

Treatment approaches to CNS RTs incorporate multi-drug chemotherapy, radiation therapy, and surgery. Complete surgical resection is recommended if the vital structures are not involved, and in the cases where complete resection is not feasible, an initial biopsy followed by adjuvant chemotherapy and definitive local control measures is appropriate (28). High-dose chemotherapy regimens with autologous stem cell rescue (HDC-ASCR) as consolidative therapies for MRTs are controversial (23). Our treatment plans were a combination of surgical and chemo-radiotherapy methods. Although, the patient did not respond well to the treatment, and she expired after one year.

## 4- CONCLUSION

MRT should be a differential diagnosis of craniocervical junction extra-axial tumors. Meningioma should also be on the list of differential diagnoses of MRTs. The molecular evaluation should be included in histological examination given that meningioma in this age group is extremely rare. In similar cases, where the radiological and pathological features of the tumor are atypical, confirming the pathological and molecular characteristics of the tumor by different experts, as the mainstays of diagnosis and selection of appropriate treatment strategy, is strongly recommended.

## 5- ETHICAL CONSIDERATIONS

Ethical approval was waived by the local Ethics Committee of Isfahan University of Medical Sciences, in view of the retrospective nature of the study and all the procedures being performed were part of the routine care. The study was conducted in accordance with the declaration of Helsinki. Parental consent for publication was also obtained.

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## 7- REFERENCES

1. Adesina AM, Tihan T, Fuller CE, Poussaint TY. Atlas of pediatric brain tumors: Springer; 2016.

2. Buscariollo DL, Park HS, Roberts KB, Yu JB. Survival outcomes in atypical teratoid rhabdoid tumor for patients undergoing radiotherapy in a Surveillance, Epidemiology, and End Results analysis. Cancer. 2012; 118(17):4212-9.

3. Geller JI, Roth JJ, Biegel JA. Biology and Treatment of Rhabdoid Tumor. Crit Rev Oncog. 2015; 20 (3-4):199-216.

4. Li D, Heiferman DM, Syed HR, Santos JG, Bowman RM, DiPatri AJ, Tomita T, Wadhwani NR, Alden TD. Pediatric primary spinal atypical teratoid rhabdoid tumor: a case series and review of the literature. Journal of neurosurgery Pediatrics. 2019:1-17.

5. Abu Arja MH, Patel P, Shah SH, Auletta JJ, Meyer EK, Conley SE, Aldrink JH, Pindrik JA, AbdelBaki MS. Synchronous Central Nervous System Atypical Teratoid/Rhabdoid Tumor and Malignant Rhabdoid Tumor of the Kidney: Case Report of a Long-Term Survivor and Review of the Literature. World neurosurgery. 2018; 111:6-15.

6. Liu Y-C, Chang Y-S, Liang W-X, Wan K-S. A newborn with malignant Rhabdoid tumors: A visual diagnosis case. IP International Journal of Medical Paediatrics and Oncology. 2018; 4(4).

7. Saunders J, Ingley K, Wang XQ, Harvey M, Armstrong L, Ng T, Dunham C, Bush J. Loss of BRG1 (SMARCA4) Immunoexpression in a Pediatric Non-Central Nervous System Tumor Cohort. Pediatric and developmental pathology: the official journal of the Society for Pediatric Pathology and the Pediatric Pathology Society. 2020; 23(2):132-8.

8. Baker TG, Lyons MJ, Leddy L, Parham DM, Welsh CT. Epithelioid Sarcoma Arising in a Long-Term Survivor of an Atypical

Teratoid/Rhabdoid Tumor in a Patient With Rhabdoid Tumor Predisposition Syndrome. Pediatric and developmental pathology: the official journal of the Society for Pediatric Pathology and the Pediatric Pathology Society. 2021; 24(2):164-8.

9. Li J, Zhang W, Hu H, Zhang Y, Wang Y, Gu H, Huang D. Case Analysis of 14 Children with Malignant Rhabdoid Tumor of the Kidney. Cancer Manag Res. 2021; 13:4865-72.

10. Tsipou H, Roka K, Gavra M, Glentis S, Stefanaki K, Kattamis A. Congenital extracranial extrarenal rhabdoid tumor: a rare clinicopathologic entity and diagnostic challenge. Liver. 2020; 4:5.

11. Benesch M, Bartelheim K, Fleischhack G, Gruhn B, Schlegel PG, Witt O, Stachel KD, Hauch H, Urban C, Quehenberger F, Massimino M, Pietsch T, Hasselblatt M, Giangaspero F, Kordes U, Schneppenheim R, Hauser P, Klingebiel T, Frühwald MC. High-dose chemotherapy (HDCT) with auto-SCT in children with atypical teratoid/rhabdoid tumors (AT/RT): a report from the European Rhabdoid Registry (EU-RHAB). Bone Marrow Transplant. 2014; 49(3):370-5.

12. Dardis C, Yeo J, Milton K, Ashby LS, Smith KA, Mehta S, Youssef E, Eschbacher J, Tucker K, Dawes L, Lambie N, Algar E, Hovey E. Atypical Teratoid Rhabdoid Tumor: Two Case Reports and an Analysis of Adult Cases with Implications for Pathophysiology and Treatment. Front Neurol. 2017; 8:247.

13. Ahmeda H, Darwisha EA, Abo-bakrkhattabb OM. Role of Diffusion Mri In Differentiation Between The Common Pediatric Posterior Fossa Brain Tumors. The Egyptian Journal of Hospital Medicine. 2018; 73(2):6090-6.

14. Sali AP, Epari S, Nagaraj TS, Sahay A, Chinnaswamy G, Shetty P, Moiyadi A, Gupta T. Atypical Teratoid/Rhabdoid Tumor: Revisiting Histomorphology and Immunohistochemistry With Analysis of Cyclin D1 Overexpression and MYC Amplification. Int J Surg Pathol. 2021; 29(2):155-64.

15. Krishnan C, Vogel H, Perry A. Atypical teratoid/rhabdoid tumor with ganglioglioma-like differentiation: case report and review of the literature. Hum Pathol. 2014; 45(1):185-8.

16. Tahir F, Majid Z, Qadar LT, Abbas A, Raza M. Co-existent Rhabdoid Tumor of The Kidney and Brain in a Male Infant: A Rare Case. Cureus. 2019; 11(8):e5423.

17. Shiflett JM, Herrington BL, Joyner DA, Saad AG. Atypical teratoid rhabdoid tumor of the cauda equina in a child: report of a very unusual case. Applied Immunohistochemistry & Molecular Morphology. 2020; 28(7):e58-e62.

18. Menezes AH. Craniovertebral junction neoplasms in the pediatric population. Childs Nerv Syst. 2008; 24(10):1173-86.

19. Mocco J, Laufer I, Mack WJ, Winfree CJ, Libien J, Connolly ES, Jr. An extramedullary foramen magnum cavernous malformation presenting with acute subarachnoid hemorrhage: case report and literature review. Neurosurgery. 2005; 56(2):E410; discussion E.

20. Kumar R. Primary malignant rhabdoid tumors of the brain, clinicoradiological findings of two cases. Neurology India. 1999; 47(4):314-7.

21. Rahmat K, Kua CH, Ramli N. A child with atypical teratoid/rhabdoid tumor of the posterior cranial fossa. Singapore medical journal. 2008; 49(12):e365-8.

22. Abolfotoh M, Tavanaiepour D, Hong C, Dunn IF, Lidov H, Al-Mefty O. Primary calcified rhabdoid meningioma of the cranio-cervical junction: A case report and review of literature. J Craniovertebral Junction Spine. 2012; 3(1):32-7.

23. Wolfe AD, Capitini CM, Salamat SM, DeSantes K, Bradley KA, Kennedy T, Dehner LP, Patel NJ. Neck Rhabdoid Tumors: Clinical Features and Consideration of Autologous Stem Cell Transplant. Journal of pediatric hematology/oncology. 2018; 40(1):e50-e4.

24. Shih RY, Koeller KK. Embryonal Tumors of the Central Nervous System: From the Radiologic Pathology Archives. Radiographics. 2018; 8(2):525-41.

25. Sigauke E, Rakheja D, Maddox DL, Hladik CL, White CL, Timmons CF, Raisanen J. Absence of expression of SMARCB1/INI1 in malignant rhabdoid tumors of the central nervous system, kidneys and soft tissue: an immunohistochemical study with implications for diagnosis. Mod Pathol. 2006; 19(5):717-25.

26. Menke JR, Raleigh DR, Gown AM, Thomas S, Perry A, Tihan T. Somatostatin receptor 2a is a more sensitive diagnostic marker of meningioma than epithelial membrane antigen. Acta neuropathologica. 2015; 130(3):441-3.

27. Eaton KW, Tooke LS, Wainwright LM, Judkins AR, Biegel JA. Spectrum of SMARCB1/INI1 mutations in familial and sporadic rhabdoid tumors. Pediatr Blood Cancer. 2011; 56(1):7-15.

28. Stabouli S. Pediatric Atypical Teratoid/Rhabdoid Tumor in the Spine: Diagnosis and Treatment. Pediatric Cancer, Volume 3: Springer; 2012. p. 55-62.