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Case Report

Primary atypical teratoid/rhabdoid tumor of the spine in an adult patient

Luyuan Li, Mohit Patel, Ha Son Nguyen, Ninh Doan, Abhishiek Sharma, Dennis Maiman

Department of Neurosurgery, Medical College of Wisconsin, Milwaukee, WI 53226, USA

E-mail: Luyuan Li - luli@mcw.edu; Mohit Patel - patelm@mcw.edu; *Ha Son Nguyen - hsnguyen@mcw.edu; Ninh Doan - ndoan@mcw.edu; Abhishiek Sharma - absharma@mcw.edu; Dennis Maiman - dmaiman@mcw.edu
*Corresponding author

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Abstract

Background: Atypical teratoid/rhabdoid tumor (AT/RT) is an aggressive neoplasm of the central nervous system that generally arises intracranially in patients under 2 years of age. Primary spinal AT/RT in an adult is rare.

Case Description: A 23-year-old female presented with left lower extremity sciatica attributed to a magnetic resonance imaging (MRI)-documented intradural mass between L2 and L4. The lesion was biopsied (was unresectable) and treated with high-dose chemotherapy (methotrexate, vincristine, cyclophosphamide, etoposide, and cisplatin) with autologous hematopoietic stem cells rescue, followed by 2 months of radiation therapy (36 Gy to craniospinal axis, 20 Gy to lumbar region) with concurrent temozolomide; the latter was discontinued after 3 weeks due to myelosuppression. Tumor relapsed 1 year later at C7–T1 level. She was started on oral metronomic therapy, and bevacizumab was added 2 months later. Three months later, a cervical MRI showed progression of the tumor, along with new lesions in the thoracic/lumbar spine plus intracranial punctate nodular tumors. Following resection of the C7/T1 lesion, she was started on palliative alisertib; a month later, a cranial computed tomography showed progression of her disease with hydrocephalus. Treatment was discontinued, and she expired 12 months after initial diagnosis.

Conclusion: Primary spinal AT/RT in the adult patient is rare. The pathology is associated with early recurrence and a poor prognosis. Although potential benefits of metronomic chemotherapy and alisertib have been reported, the patient in this study did not favorably respond to these modalities.

Key Words: Adult spine tumor, alisertib, atypical teratoid/rhabdoid tumor, metronomic therapy, primary spine tumor

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INTRODUCTION

Atypical teratoid/rhabdoid tumor (AT/RT) is an aggressive neoplasm that constitutes approximately 6% of pediatric central nervous system (CNS) tumors.[5,9] Primary spinal AT/RT, especially within an adult patient, is rare.[3,5,6,12,14]

CASE PRESENTATION

Clinical presentation

A 23-year-old female presented with left lower extremity sciatica accompanied by numbness and weakness in her left leg and foot plus right leg paresthesias. A magnetic resonance imaging (MRI) of the lumbar spine showed

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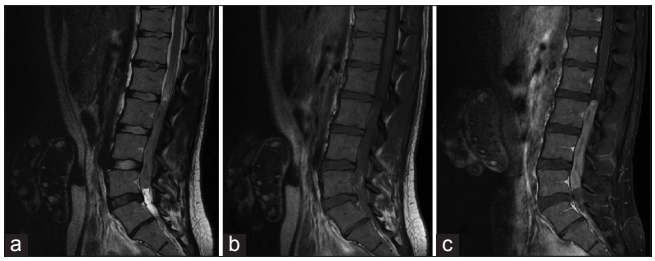

Figure 1: Magnetic resonance imaging L spine. Sagittal slices demonstrates lesion on T2 (a), T1 (b), and T1 with contrast (c)

an intradural mass from L2 to L4 [Figure 1]; there were no other lesions in the neuraxis on MR/computed tomography (CT). At surgery, the lesion could not be resected as it had encased the nerve roots of the cauda equina. The biopsy, however, demonstrated spinal AT/RT.

Treatment with radiation and chemotherapy

First, she received chemotherapy (high-dose methotrexate, vincristine, cyclophosphamide, etoposide, and cisplatin) with autologous hematopoietic stem cells rescue. This was followed by 2 months of radiation therapy (36 Gy to craniospinal axis, 20 Gy to lumbar region) with concurrent temozolomide; the latter was discontinued after 3 weeks due to myelosuppression. She underwent disease reevaluation 4 weeks after the completion of radiation, which showed improvement in the spinal tumor and no new metastatic lesions.

Relapse 1 year later

The patient relapsed 1 year later, demonstrating a metastasis on the left at the C7–T1 level [Figure 2]. She was started on oral metronomic therapy (thalidomide, celebrex, fenofibrate, cyclophosphamide, and etoposide); bevacizumab was added 2 months later. Three months later, however, an MRI of the cervical spine demonstrated progression of her cervical lesion. In addition, MR studies now showed new intradural, extramedullary small nodules at T3, T10, L1, L2, and possibly at L4. In addition, an MRI of the brain revealed multiple punctate, nodular enhancing lesions in the subarachnoid space. At this point, the patient had mild weakness in the left finger (e.g., abduction and grip); metronomic therapy was discontinued, and she underwent repeated resection of the lesion at C7/T1. She was next started on palliative alisertib. A month later, she was admitted for leg pain, progressive headaches, and altered mental status; CT head showed progression of her disease with hydrocephalus. She transitioned to comfort care and expired a total of 12 months after the initial diagnosis.

DISCUSSION

History

In the 1970s, AT/RT was formerly labeled as a malignant RT due to similarities to Wilms' tumor.[2] Rorke *et al.*[10]

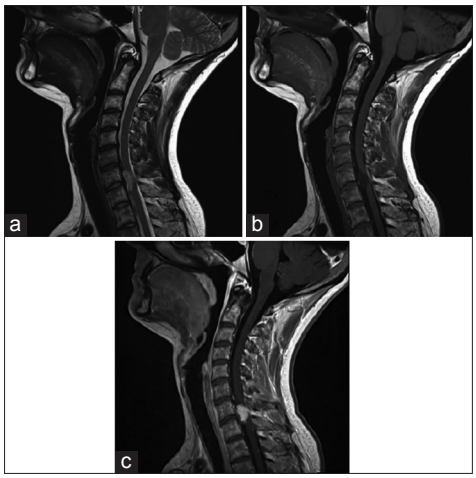

Figure 2: Magnetic resonance imaging C spine. Sagittal slices demonstrates lesion on T2 (a), T1 (b), and T1 with contrast (c)

further characterized the pathology as a definite CNS tumor, coining the term AT/RT, where "teratoid" refers to the divers cell types as seen in teratoma while "rhabdoid" refers to the resemblance to rhabdomyosarcoma.[8] Histologically, AT/RT lacks germ cell markers, and may be comprised solely with rhabdoid cells or variegated with primitive neuroepithelial, mesenchymal, and/or epithelial tissue.[8] Imaging characteristics in spinal AT/RT have been nonspecific.[8] Lesions are heterogeneous.[8] Other features include contrast enhancement, varying intensities on T2 sequences, presence of hemorrhage, signs of cerebrospinal fluid dissemination, and findings of a syrinx or edema along the cord adjacent to the tumor.[8] In our patient, the lumbar and cervical lesions were isointense to hyperintense relative to cord, and avidly enhanced with contrast.

Epidemiology of atypical teratoid/rhabdoid tumor

AT/RT largely develops in children <2 years of age arising in the cerebellum, followed by the ventricles, frontal lobe, and brainstem.[7] The median survival is 6–18 months for pediatric patients.[7,10-12] Poor prognoses for patients under two years of age correlate with the early presence of metastatic disease. In older children and adults, the tumor largely appears in the cerebral hemispheres, followed by the sellar region and cerebellum.[7,10-12] Better prognoses correlate with older age, localized disease, and adequate resection.[5]

Rare spinal cord lesions

Findings within the spinal cord are rare. In particular, there have been only five prior cases of primary spinal AT/RT in adult patients[3,5,6,12,14] [Table 1]. Patients typically present with axial neck or back pain and radiculopathy; only one exhibited cauda equina syndrome requiring acute surgical resection and decompression.[12] Early relapse was common in all patients, and two demonstrated delayed intracranial disease (e.g., exhibiting hydrocephalus and

Table 1: Review of literature

Literature	Year	Age	Gender	Initial/ Relapse	Symptoms	Disease level	Surgery	Chemotherapy	Radiotherapy	Survival
Bruch *et al*.[3]	2001	21	Female	***	***	***	***	***	***	6 months
Gotti *et al*.[5]	2015	19	Female	1	Back, left leg pain	L4-L5	Yes	Induction: Alternating doxorubicin; ifosfamide/ carboplatinum/ etoposide; vincristine/ cyclophosphamide/ actinomycin Consolidation: Carboplatinum, thiopeta	54 Gy	Alive up to 36 months
				2	Back pain, gait issues	L2-L3	Yes	Vinorelbine, cyclophosphamide, celecoxib	None	
				3	Routine imaging	T12-L5	***	***	***	
Kanoto *et al*.[6]	2015	60	Male	***	***	C5-T1		***	***	18 months
Sinha *et al*.[12]	2015	65	Male	1	5w pain/ acute cauda equina syndrome	T12	Yes	No	50 Gy	2 years
				2	Back pain and weakness	T4	Yes	No	Yes, no more info	
				3	Confusion/ worsen mobility	Hydrocephalus, sacrum, pelvis	Yes, VPS	No, palliative	No, palliative	
Zarovnaya *et al*.[14]	2007	43	Female	1	Neck, left arm pain	C4-C6	Yes	No	50 Gy to local area	2.5 years
				2	Back pain, right leg weakness	L1	Yes	No	50 Gy to local area	
				3	Left abducens palsy	Left prepontine mass	No	No	46 Gy whole brain radiation	
				4	Leg weakness	T9-T10	Yes	Phase 1 trial interferon, temozolomide	37.5 Gy to local area	
				5	Back pain and right leg weakness	L2-L3	Yes	No	38 Gy to local area	
				6	Routine imaging	Anterior foramen magnum, L1	No	Temozolomide, doxorubicin, gemcitabine, docetaxel	Some radiation for posterior fossa, but no info; received 12 Gy to L1 lesion	
Our case	2015	23	Female	1	Left leg pain, weakness; right leg paresthesias	L2-L4	Yes	Methotrexate, vincristine, cyclophosphamide, etoposide, and cisplatin Temodar	36 Gy to craniospinal axis, 20 Gy to lumbar region	12 months
				2	Left arm weakness	C7-T1	No	Oral metronomic therapy (thalidomide, celebrex, fenofibrate, cyclophosphamide, etoposide); bevacizumab	No	

Contd...

Table 1: Contd...

Literature	Year	Age	Gender	Initial/ Relapse	Symptoms	Disease level	Surgery	Chemotherapy	Radiotherapy	Survival
				3	Routine imaging	Larger C7-T1 lesion, MRI brain with puntate nodules; lesions at T3, T10, L1, L2 and possibly at L4	Yes	Alisertib	No	
				4	Leg pain, headaches, altered mental status	Hydrocephalus	No, palliative	No, palliative	No, palliative	

requiring a shunt).[12,14] Survival intervals ranged from 6 months to 2.5 years.[5]

No standard protocol for treatment atypical teratoid/rhabdoid tumor (primary/relapsing)

There is no standard protocol for the treatment of primary and relapsing AT/RT. Immediate multimodal treatment has been advocated, including gross tumor resection, followed by high-dose chemotherapy with autologous hematopoietic stem cells rescue and radiotherapy.[5,11] Metronomic chemotherapy has also been utilized in pediatric patients with recurrent and refractory solid tumors (e.g., treatment with drugs for an extended period, targeting tumor vasculature instead of tumor cells).[1,4] Gotti *et al.*[5] reported a patient with good clinico-radiological response while on metronomic therapy. Moreover, alisertib has been recently used for recurrent AT/RT; this medication inhibits aurora kinase A, a protein that regulates the formation and stability of the mitotic spindle.[13] Wetmore *et al.*[13] documented four pediatric patients who all had disease stabilization/regression after three cycles of therapy; two patients demonstrated stable disease regression for at least 1 year on therapy.

CONCLUSION

There is no standardized treatment for primary spinal AT/RT in adults. Most of the treatment protocols are derived from the pediatric population where data are inadequate. Primary spinal AT/RT in adults is rare and is associated with early recurrence and a poor prognosis. Although potential benefits of metronomic chemotherapy and alisertib have been reported, the patient in this study did not favorably respond to these modalities.

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Conflicts of interest

There are no conflicts of interest.

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