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

INTRODUCTION

Atypical teratoid/rhabdoid tumor (AT/RT) is an aggressive neoplasm that constitutes approximately 6% of pediatric central nervous system (CNS) tumors. Primary spinal AT/RT, especially within an adult patient, is rare. This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

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...
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. 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. 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. Imaging characteristics in spinal AT/RT have been nonspecific. Lesions are heterogeneous. 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. 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. The median survival is 6–18 months for pediatric patients. 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. Better prognoses correlate with older age, localized disease, and adequate resection.

**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 [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. Early relapse was common in all patients, and two demonstrated delayed intracranial disease (e.g., exhibiting hydrocephalus and
| Literature          | Year | Age | Gender | Initial/Relapse | Symptoms                          | Disease level | Surgery          | Chemotherapy                                                                 | Radiotherapy | Survival          |
|---------------------|------|-----|--------|----------------|-----------------------------------|---------------|-----------------|-------------------------------------------------------------------------------|--------------|------------------|
| Bruch et al. [3]    | 2001 | 21  | Female | ***           | ***                               | ***           | ***             | Induction: Alternating doxorubicin; ifosfamide/cisplatin/etoposide; vincristine/cyclophosphamide/actinomycin | ***          | 6 months         |
| Gotti et al. [5]    | 2015 | 19  | Female | ***           | Back, left leg pain               | L4-L5         | Yes             | Induction: Alternating doxorubicin; ifosfamide/cisplatin/etoposide; vincristine/cyclophosphamide/actinomycin | 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         | ***             | **Consolidation:** Carboplatin, thiopeta                                       | ***          | 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 craniocervical axis, 20 Gy to lumbar region | 12 months |
|                     |      |     |        | 2             | Left arm weakness                 | C7-T1         | No              | Oral metronomic therapy (thalidomide, celebrex, fenofibrate, cyclophosphamide, etoposide); bevacizumab | None |                  |

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 punctate 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 |             | No, palliative |

**REFERENCES**

1. André N, Abed S, Orbach D, Alla CA, Padovani L, Pasquier E, et al. Pilot study of a pediatric metronomic 4-drug regimen. Oncotarget 2011;2:960-5.
2. Beckwith JB, Palmer NF. Histopathology and prognosis of Wilms tumors: Results from the First National Wilms’ Tumor Study. Cancer 1978;41:1937-48.
3. Bruch LA, Hill DA, Cai DX, Levy BK, Dehner LP, Perry A. A role for fluorescence in situ hybridization detection of chromosome 22q dosage in distinguishing atypical teratoid/rhabdoid tumors from medulloblastoma/central primitive neuroectodermal tumors. Hum Pathol 2001;32:156-62.
4. Gnoni A, Silvestris N, Licchetta A, Santini D, Scarotti M, Ria R, et al. Metronomic chemotherapy from rationale to clinical studies: A dream or reality? Crit Rev Oncol Hematol 2015;95:46-61.
5. Gotti G, Biassoni V, Schiavello E, Spreatico F, Antonelli M, Calareso G, et al. A case of relapsing spinal atypical teratoid/rhabdoid tumor (AT/RT) responding to vinorelbine, cyclophosphamide, and celecoxib. Childs Nerv Syst 2015;31:1621-3.
6. Kanoto M, Toyoguchi Y, Hosoya T, Kuciki M, Sugai Y. Radiological image features of the atypical teratoid/rhabdoid tumor in adults: A systematic review. Clin Neuroradiol 2015;25:55-60.
7. Lau CS, Mahendraraj K, Chamberlain RS. Atypical teratoid rhabdoid tumors: A population-based clinical outcomes study involving 174 patients from the surveillance, epidemiology, and end results database (1973-2010). Cancer Manag Res 2015;7:301-9.
8. Moeller KK, Coventry S, Empgen S, Moriarty TM. Atypical teratoid/rhabdoid tumor of the spine. AJNR Am J Neuroradiol 2007;28:593-5.
9. Rickert CH, Paulus W. Epidemiology of central nervous system tumors in childhood and adolescence based on the new WHO classification. Childs Nerv Syst 2001;17:503-11.
10. Ronke LB, Packer RJ, Biegel JA. Central nervous system atypical teratoid/rhabdoid tumors of infancy and childhood: Definition of an entity. J Neurosurg 1999;85:56-65.
11. Schrey D, Carceller Lechón F, Maleitizis G, Moreno L, Dufour C, Chi S, et al. Multimodal therapy in children and adolescents with newly diagnosed atypical teratoid rhabdoid tumor: Individual pooled data analysis and review of the literature. J Neurooncol 2016;126:81-90.
12. Sinha P, Ahmad M, Varghese A, Parekh T, Ismail A, Chakrabarty A, et al. Atypical teratoid rhabdoid tumour of the spine: Report of a case and literature review. Eur Spine J 2015;24 Suppl 4:5472-84.
13. Wetmore C, Boyett J, Li S, Lin T, Bendel A, Gajjar A, et al. Alisertib is active as single agent in recurrent atypical teratoid rhabdoid tumors in 4 children. Neuro Oncol 2015;17:882-8.
14. Zarovnaya EL, Pallatroni HF, Hug EB, Ball PA, Cromwell LD, Pipas JM, et al. Atypical teratoid/rhabdoid tumor of the spine in an adult: Case report and review of the literature. J Neurooncol 2007;84:49-55.

**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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Nil.

**Conflicts of interest**

There are no conflicts of interest.

**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. 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). Gotti et al. 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. Wetmore et al. documented four pediatric patients who all had disease stabilization/regression after 3 cycles of therapy; two patients demonstrated stable disease regression for at least 1 year on therapy.