Outcomes of Atypical Teratoid Rhabdoid Tumors (ATRT) Treated with Proton Therapy

J.Y. Shin[1], S. Mayekar[1], W. Hartsell[2], C. Vargas[3], G. Larson[4], H. Tsai[5], G. Laramore[6], J.H. Chang[2]

1) Rush University Medical Center, Chicago, IL – Radiation Oncology 2) Northwestern Medicine Chicago Proton Center, Warrenville, IL – Radiation Oncology 3) Mayo Clinic, Scottsdale, AZ – Radiation Oncology 4) Procure Oklahoma City, OK – Radiaton Oncology 5) Procure New Jersey, Princeton, NJ– Radiation Oncology 6) University of Washington, Seattle, WA – Radiation Oncology.

Introduction:

Atypical teratoid rhabdoid tumors (ATRT) are highly malignant tumors of the central nervous system diagnosed predominately in pediatric patients. Treatment of these tumors usually involves multimodality treatment including surgery, chemotherapy and radiation. Outcomes have historically been poor. The Dana Farber Cancer Institute (DFCI) ATRT intensive chemotherapy regimen has been implemented with hopes to improve disease outcome, and we evaluated the use of the DFCI regimen in conjunction with proton beam radiotherapy (PRT).

Methods :

We identified and retrospectively analyzed 14 ATRT patients treated at our institution with curative intent using the DFCI regimen/PRT and prospectively enrolled in a nationwide registry (PCG RGE 0119). The patients were treated between March 2010 and November 2016. The endpoints analyzed were incidence and severity of treatment-related acute toxicity and overall survival (OS). Acute treatment-related toxicities were assessed according to the CTCAE v4.0. All data analyses were performed using SPSS 22.0. Kaplan-Meier estimates were used to analyze OS rates.

Clinical and treatment characteristics

Characteristic	Number (%)
Age	
Median (range)	3.7 years (9 months - 15.5 years)
Gender	
Female	7 (50.0%)
Male	7 (50.0%)
Site of disease	
Cerebrum	5 (35.7%)
Cerebellum	3 (21.4%)
Ventricular system	3 (21.4%)
Spinal cord	2 (14.3%)
Brainstem	1 (7.1%)
Type of lesion	
Solitary	10 (71.4%)
Multifocal	4 (28.6%)
Resection	
Yes	12 (85.7%)
Gross total resection	9 (64.3%)
Subtotal resection/debulking	3 (35.7%)
No	2 (14.3%)
Proton beam radiotherapy dose	
Median (RBE) (range)	47.8 Gy (14.43-54.13)
Chemotherapy	
Concurrent	8 (57.1%)
Sequential	6 (42.9%)

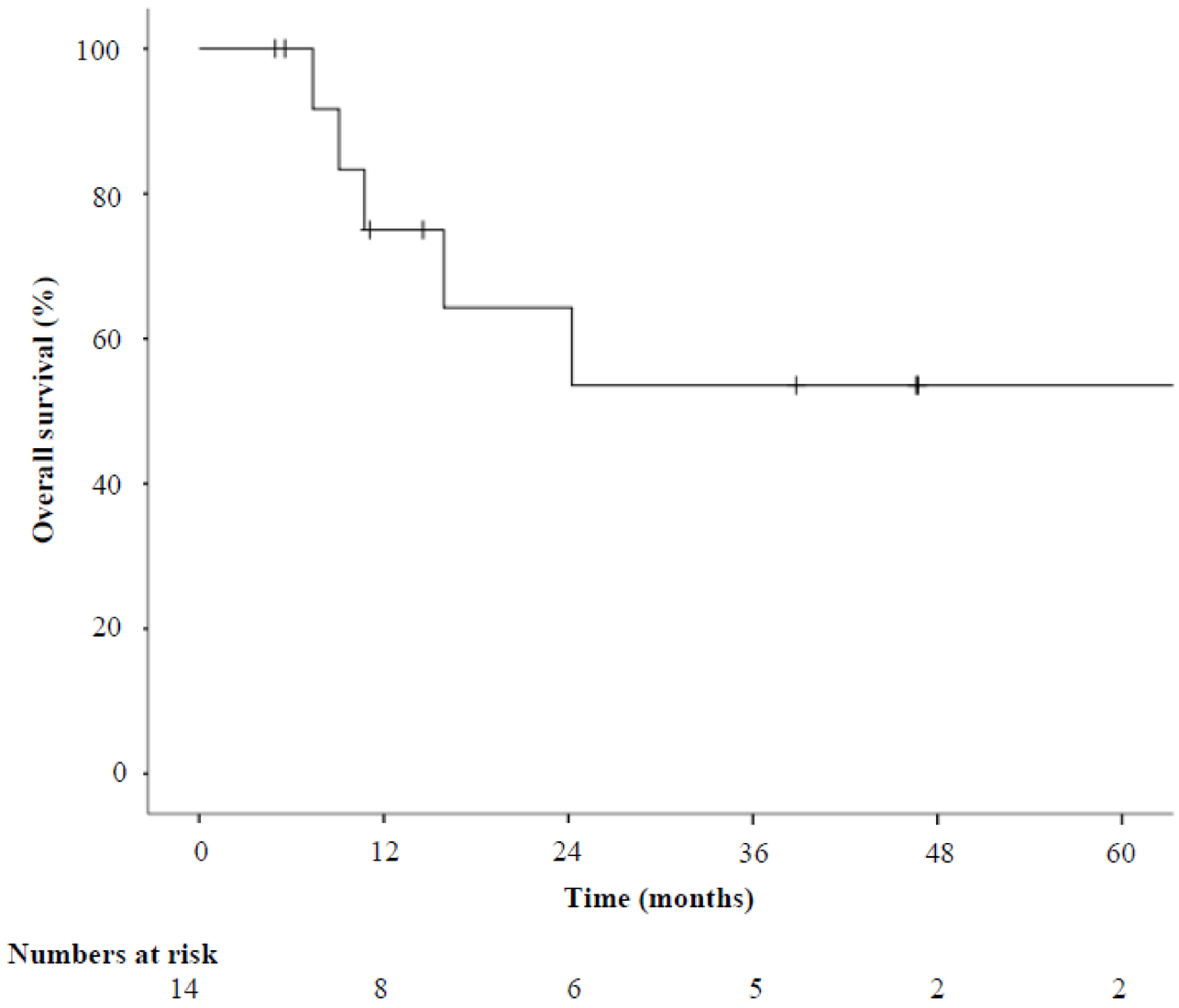
Acute toxicity by grade

	0	1	2	3	4	5
Alopecia	1 (7.1%)	1 (7.1%)	12 (85.7%)	0	0	0
Radiation dermatitis	3 (21.4%)	6 (42.8%)	5 (35.7%)	0	0	0
Nausea	6 (42.8%)	2 (14.3%)	2 (14.3%)	4 (28.6%)	0	0
Vomiting	9 (64.3%)	3 (21.4%)	2 (14.3%)	0	0	0
Weight loss/anorexia	8 (57.1%)	1 (7.1%)	1 (7.1%)	4 (28.6%)	0	0
Fatigue	6 (42.8%)	4 (28.6%)	4 (28.6%)	0	0	0
Headache	11 (78.6%)	3 (21.4%)	0	0	0	0
Blurred vision	12 (85.7%)	1 (7.1%)	1 (7.1%)	0	0	0
Insomnia	11 (78.6%)	2 (14.3%)	1 (7.1%)	0	0	0
Ataxia	8 (57.1%)	4 (28.6%)	2 (14.3%)	0	0	
Dysarthria	10 (71.4%)	3 (21.4%)	1 (7.1%)	0	0	
Muscle weakness	9 (64.3%)	1 (7.1%)	4 (28.6%)	0	0	0
Thrombocytopenia	0	0	0	1 (7.1%)	0	0

Results :

Median age at time of treatment was 3.7 years (9 months - 15.5 years). Ten patients (71.4%) had solitary lesions and four (28.6%) were multifocal. Twelve patients (85.7%) underwent resection prior to radiation. Nine patients (64.3%) underwent gross total resection and three (35.7%) underwent subtotal resection/debulking. Five tumors (35.7%) were located in the cerebrum, three (21.4%) in the cerebellum, three (21.4%) in the ventricular system, two (14.3%) in the spinal cord and one (7.1%) in the brainstem. The median radiation dose of 47.8 Gy (RBE) (range 14.43 – 54.13) at 1.8 Gy (RBE) per fraction. Eight patients (57.1%) were treated with concurrent chemotherapy while the remaining six (42.9%) received PRT sequentially following chemotherapy. With a median follow up of 9.5 months (range: 1-70 months), seven of the 14 patients were alive. The 1-year and 5-year OS were 75.0% and 53.6%, respectively. The most common acute toxicity was grade 2 alopecia (n=12, 85.7%) and grade 2 dermatitis (n=5, 35.7%). Four patients (28.6%) experienced grade 3 nausea and anorexia, and 1 patient had grade 3 thrombocytopenia. There were no grade 4 or 5 toxicities reported.

Kaplan-Meier overall survival



Conclusion:

Trimodality with the incorporation of proton beam radiotherapy is a safe and effective treatment for ATRT. Further follow up is needed to evaluate for long-term survival and quality of life in this patient cohort.