Risk of Radiotherapy Associated Deterioration in Paediatric Diffuse Intrinsic Pontine Glioma

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Introduction

Palliative radiotherapy (RT) may be associated with tumour oedema and neurological deterioration in patients with DIPG. No tools that guide management currently exist to identify children at greatest risk of this deterioration.

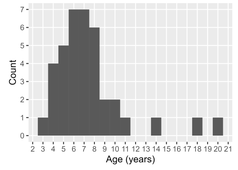
Methods

We performed a retrospective review of patients with DIPG treated at a single UK centre between 28/8/2019- 16/10/2023. Information was collected for demographics, steroid regimen, RT regime, clinical course, and length of inpatient stay.

Wilcoxon rank sum test was used for comparison of steroid dosing and length of inpatient stay between different treatment regimens. Univariate logistic regression with a multiple-testing correction was used to assess for potential predictors of neurological deterioration during RT.

Results

Cohort characteristics: 48 courses of photon RT were given to 38 patients; 37 upfront and 11 relapsed.



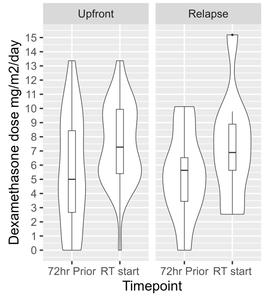
Characteristic	N = 38[1]
Gender	
Female	22 (58%)
Male	16 (42%)
Diagnosis	
DIPG	13 (34%)
DMG H3K27M Mutant	24 (63%)
Pontine Ganglioglioma H3K27M mutant	1 (2.6%)
Biopsy (Y/N)	
Y	25 (66%)
N	13 (34%)
Shunt (Y/N)	
Y	9 (24%)
N	29 (76%)
Number of RT courses	
1	28 (74%)
2	10 (26%)
Age (years) at first RT course	7.0 (5.3, 8.3)

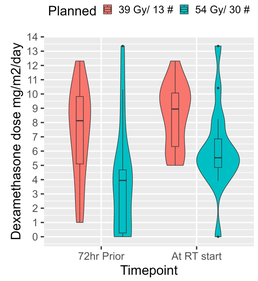
[1] n (%); Median (IQR)

Characteristic	Upfront, N = 37[1]	Relapse, N = 11[1]
Planned		
20 Gy/ 5 #	0 (0%)	2 (18%)
20 Gy/ 10 #	1 (2.7%)	9 (82%)
39 Gy/ 13 #	20 (54%)	0 (0%)
54 Gy/ 30 #	16 (43%)	0 (0%)
Delivered		
4 Gy/ 2 #	0 (0%)	1 (9.1%)
15 Gy/ 5 #	1 (2.7%)	0 (0%)
20 Gy/ 5 #	0 (0%)	2 (18%)
20 Gy/ 10 #	1 (2.7%)	8 (73%)
39 Gy/ 13 #	19 (51%)	0 (0%)
54 Gy/ 30 #	16 (43%)	0 (0%)

[1] n (%)

Steroid dosing: Median dexamethasone dose at the start of RT was 7.1mg/m2/day [5.4-9.8, n = 44]. Patients receiving hypofractionated RT had higher steroid doses

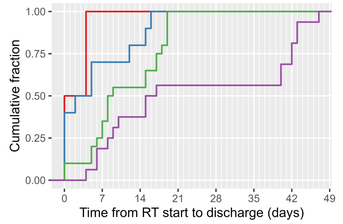




Characteristic	39 Gy/ 13 #, N = 20[1]	54 Gy/ 30 #, N = 16[1]	p-value[2]	q-value[3]
Dexamethasone 72 hr before RT start (mg/m2/d)	8.1 (5.1, 9.8)	3.9 (0.3, 4.7)	0.007	0.007
Dexamethasone at RT start (mg/m2/d)	8.95 (6.32, 10.07)	5.53 (4.85, 6.86)	0.007	0.007

[1] Median (IQR)
[2] Wilcoxon rank sum test; Wilcoxon rank sum exact test
[3] False discovery rate correction for multiple testing

Inpatient stay: Overall median length of inpatient stay from start of RT was 9 days although this varied by RT regimen



Neurological deterioration: Deterioration occurred in 9/48 (19%) RT courses, 6 of which (66%) were in the first week. Treatment was abandoned in 2 cases. There were no acute neurosurgical transfers or deaths during RT. Deteriorations after the 1st week of RT were usually failed steroid weans.

No predictive variable was statistically associated with neurological deterioration in the first week of treatment.

Characteristic	OR[1]	95% CI[1]	p-value	q-value[2]
Shunt (Y/N)	0.55	0.09, 4.38	0.52	0.69
Thickened fluids/unsafe swallow at RT start (Y/N)	0.31	0.04, 1.76	0.20	0.40
Motor dysfunction at RT start (Y/N)	1.25	0.16, 7.33	0.81	0.81
Increasing neurological deficits in week preceding RT start (Y/N)	0.21	0.03, 1.85	0.12	0.40

[1] OR = Odds Ratio, CI = Confidence Interval
[2] False discovery rate correction for multiple testing

Discussion & Conclusions

1 in 5 DIPG patients deteriorate during RT, mostly in the first week. This should inform the design of an adequately powered study to identify patients at greatest risk of deterioration who would benefit from closer surveillance. Further qualitative studies are needed to understand the reasons for differences in steroid dosing and length of stay in those receiving hypofractionated therapy compared with conventional fractionation.