Non-enhancing Medulloblastomas: Differences in VEGF Expression, Postoperative Complications, and Outcomes

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CONGRESS OF NEUROLOGICAL SURGEONS
2011 ANNUAL MEETING
WASHINGTON, DC
OCTOBER 1-6, 2011

Introduction

In most cases medulloblastomas enhance on MRI scans with the administration of gadolinium contrast. However an estimated 30% of medulloblastomas do not show significant enhancement. The goal of this study was to compare gadolinium enhancing to non-enhancing medulloblastomas on MRI to evaluate differences in surgical complication rates, outcome, tumor histopathology, and Vascular endothelial growth factor (VEGF) expression.

Methods

We retrospectively reviewed the records of children that underwent surgical resection of medulloblastoma at a single institution over a 18-year period. 58 patients were identified. Enhancement was graded as "enhancing", "partially enhancing", or "non-enhancing" based on greater than 50% tumor enhancement, less than 50% enhancement, or the complete absence of enhancement, based on the consensus opinion of 3-blinded pediatric neurosurgeons. Pearson 2-way contingency table analysis and Kaplan Meier progression free and overall survival were used for analysis. Select patient tumors graded as "enhancing" and "non- enhancing" were analyzed for VEGF and VEGF-R expression by RT PCR and western blot.

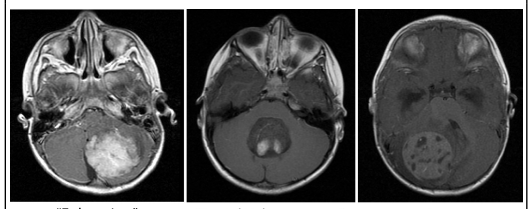
Results

There were 24 girls and 34 boys with a mean age of 6.6 years at the time of diagnosis. 34 (59%) were considered gadolinium enhancing and 24 (41%) partially or non-enhancing. The mean age at diagnosis for enhancing and non-enhancing patients was 6.4 and 6.9 years respectively. Tumor size and histology did not differ significantly between the groups. 15 of 34 patients (44%) in the enhancing group experienced post-operative neurologic complications in comparison to 4 of 24 (17%) in the tumor non-enhancing group. Cerebellar mutism was seen in 21% of enhancing and 29% of non-enhancing tumors. Gross total resection was achieved in 28 of 34 (82%) enhancing and 16 of 24 (67%) non-enhancing patients. The rate of tumor progression did not differ significantly between the two groups. A trend towards significance was noted in VEGF expression between "enhancing" and "non-enhancing" tumors.

Summary of "Enhancing" vs "Non-Enhancing" Medulloblastoma patient data

	Enhancing Group $n = 46$	Non-Enhancing Group $n = 12$	p-value
Sex			0.74
Male	26 (57%)	8 (67%)	
Female	20 (43%)	4 (33%)	
Race			0.51
Caucasian	29 (63%)	8 (66%)	
Black	4 (9%)	2 (17%)	
Hispanic	1 (2%)	1 (8.5%)	
Bi-racial	2 (4%)	1 (8.5%)	
Other	10 (22%)	0 (0%)	
Mean age at diagnosis	77 months	88 months	0.56
Risk[a]			0.73
High	20 (44%)	6 (50%)	
Standard	25 (56%)	6 (50%)	
Tumor Histology			0.94
Classic	38 (83%)	11 (92%)	
Desmoplastic	5 (11%)	1 (8%)	
Large cell	2 (4%)	0 (0%)	
Nodular	1 (2%)	0 (0%)	
Tumor volume[b]	39 cc	27 cc	0.45
Metastasis at diagnosis	8 (17%)	5 (42%)	0.12
Hydrocephalus at diagnosis	41 (89%)	8 (67%)	0.06
Extent of resection			0.25
Gross total (>80%)	38 (83%)	6 (60%)	
Partial (50-80%)	3 (6.5%)	1 (10%)	
Subtotal (<50%)	5 (10.5%)	3 (30%)	
Post op EVD	40 (87%)	10 (83%)	0.67
Post op complications[c]	32 (70%)	5 (42%)	0.10
Cerebellar mutism	12 (26%)	1 (8.5%)	0.27
Post op shunt or 3rd ventriculostomy	19 (41%)	6 (50%)	0.62
Early reoperation (<30 days)	17 (40%)	4 (33%)	0.99
Late reoperation (30 day- 3 months)	9 (20%)	3 (25%)	0.69
Post op chemotherapy	44 (96%)	11 (92%)	0.38
Post op brain radiation	35 (76%)	10 (83%)	0.99
Tumor recurrence	11 (24%)	2 (17%)	0.99
Survival	110 (months)	147 (months)	0.60

Medulloblastoma Enhancement Grades



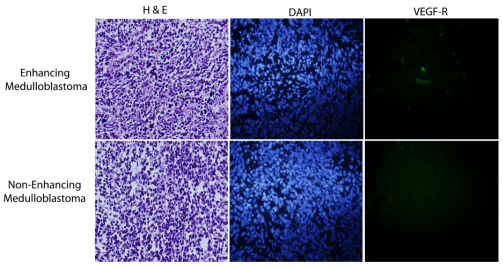
"Enhancing" "Partial Enhancement" "Non Enhancing"

Tumor enhancement was graded as " enhancing", "partially enhancing" or "non-enhancing" based on greater than 50% tumor enhancement, less than 50% enhancement, or complete absence of enhancement. Grading results were based on the concensus opinion of 3 blinded pediatric neurosurgeons.

Conclusions

Patients with non-enhancing exhibit a trend towards less VEGF expression and may be less likely to have postoperative neurologic complications after resection, but may receive less aggressive initial surgical resections.

VEGF-R Immunoflourescence



Non-Enhancing Medulloblastoma tumor exhibit diminished VEFR-R immunoreactivity by immunoflourescence.

VEGF-R Expression