Pediatric Supratentorial Ependymoma: Clinical, Radiographic and Molecular Analysis

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Learning Objectives

1. Understanding ependymomas
2. Appreciating the complexity of these tumors based on different locations and molecular subtypes
3. Analyzing prognostic indicators to guide future treatment

Introduction

Recent molecular analyses support a behavioral and clinical distinction between supratentorial and infratentorial ependymomas, with supratentorial tumors, in general, having a more favorable prognosis. The goal of this study was to describe our experience managing supratentorial ependymoma in children.

Methods

Two separate databases from two pediatric institutions were queried to identify cases of supratentorial ependymoma from January 1990 through December 31, 2014. Children enrolled in an ongoing clinical trial were excluded. Clinical, operative and radiographic information was abstracted retrospectively. The two primary outcomes were progression free survival (PFS) and overall survival (OS). Detection of the C11orf95RELA fusion and C11orf95 gene rearrangement was performed using iFISH in those patients whose tumor tissue was still available.

Results

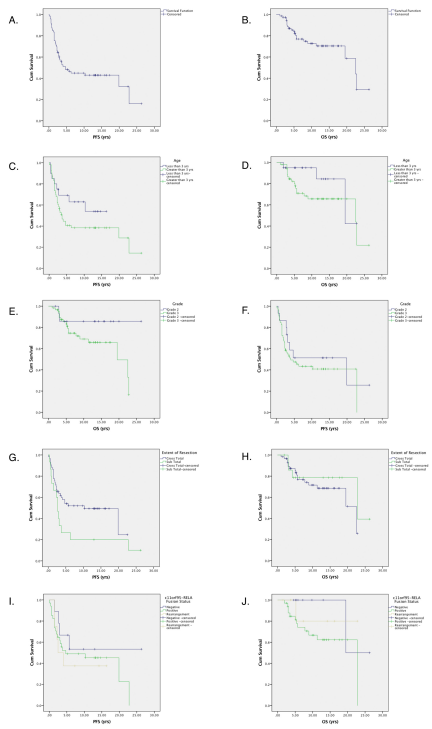
Seventy-three cases of supratentorial ependymoma were identified. There were 41 female and 32 male patients, with a median age at diagnosis of 6.7 years (range, 1 month to 18.8 years). Median follow up was 8.3 years (range, 1.0-26.3). Fifty-eight (79.5%) of 73 patients underwent gross total resection (GTR). Forty-two patients (57.5%) experienced subsequent disease progression, with 17 patients ultimately dying of their disease, and an additional 4 succumbing for reasons other than their cancer. Median PFS was 3.7 years. Eighty-seven percent of children with subtotal resection (STR) developed disease progression compared to 50% with GTR. For those patients with tumor recurrence, 36 of 42 (86%) underwent further treatment such as surgery, chemotherapy, radiation or some combination thereof. Molecular analysis was available for 51 patients (70%). On bivariate analysis, PFS and OS were not statistically affected by age, tumor grade or extent of resection, although there was a significant trend for the latter in favor of aggressive resection. Children with RELA fusion had no significant difference in PFS or OS when compared to those with C11orf95 gene rearrangement.

Bivariate Analysis

	PFS		OS		
	Median* (range)	5-year (95% CI)	Median (range)	5-year (95% CI)	10-year (95% CI)
Overall	3.7 (0.1-26.3)	43% (26-60)	8.3 (1.0-26.3)	73% (61-85)	43% (26-60)
Age					
< 3 years	6.5	60 (32-87)	9.05	80% (60-99)	45% (13-78)
≥ 3 years	3.5	38% (17-59)	7.8	70% (55-85)	43% (23-64)
p-value	0.185		0.166		
WHO grade					
Grade II	4.7	47% (10-84)	13.2	73% (47-99)	60% (29-92)
Grade III	3.5	43% (23-63)	7.3	72% (59-86)	40% (20-60)
p-value	0.418		0.137		
Extent of Resection					
GTR	10.3	48% (30-67)	8.35	74% (61-87)	45%(26-64)
STR	2.7	27% (0-70)	7.3	66% (37-96)	47% (10-84)
p-value	0.061		0.533		
C11orf95RELA fusion vs C11orf95 rearrangement**					
Fusion	4.7		9.4		
Rearrangement	2.7		6.25		
p-value	0.545		0.207		

* years; ** 5 and 10 year estimates not calculated because of incomplete data

Survival Data



PFS (A) and OS (B) for the entire cohort. Bivariate analysis for age (C,D), grade (E,F), extent of resection (G,H), and molecular profile (I,J).

Conclusions

In our series, GTR was not significantly superior to STR statistically but was clinically. Additionally, there are viable salvage therapies such that OS is not altered by extent of resection. Age and tumor grade did not impact PFS or OS. Surprisingly, RELA fusion was not found to be a negative prognostic factor as suggested by other studies, suggesting that GTR may overcome any deleterious effects of RELA as described previously.

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