Frontal Lobe Pleomorphic Xanthoastrocytoma are Clinically Aggressive: Evidence from Population-Based Clinical Outcome Study

Evgeniya Tyrtova; Danielle F Miyagishima BA; Isaac G Freedman BPhil, MPH; Anthony K Ma; Kevan Lui Ip BS; Osama Muneer Ahmed BA, BS; Aidan Lee BA; Jennifer A. Moliterno Gunel MD; Joseph M. Piepmeier MD; Jacky Yeung MD

Department of Neurosurgery, Yale School of Medicine, New Haven, CT

Introduction

- Pleomorphic Xanthoastrocytoma (PXA) is a rare primary low-grade astrocytic tumor (~1% of astrocytomas) that usually occurs in children and young adults and typically has favorable prognosis (75-85% overall survival and 30% recurrence with gross total resection at 5 years) [1,2,3]
- Most PXAs are WHO grade II; however, they may undergo anaplastic change and several cases of malignant transformation to anaplastic astrocytoma and GBM were reported [4,5]
- While evidence suggests that anatomic location of various high grade gliomas (ependymomas, oligodendrogliomas, and GBM) has prognostic value for survival, possibly due to its correlation with certain molecular markers, little is known about prognostic significance of anatomic location in PXA
- Our objective was to determine whether PXA location has implications in survival outcomes

Materials and Methods

- We queried the Surveillance, Epidemiology, and End Results (SEER) database from 1973-2014 for all histologically-verified cases of PXA (ICD-O-3:9424/3).
- We obtained and analyzed patient demographic data, tumor characteristics, therapeutic management, and survival data. Chi-squared tests, Student's T-tests and Kruskall-Wallis tests were utilized for comparisons between the groups.
- We performed Kaplan Meier survival analysis followed by Cox proportional hazards regression analysis to identify differences in overall survival between PXAs in different anatomic location and adjust for confounding factors related to survival.

Results

- Among all PXA cases (N=447), frontal lobe PXA (N=89) were associated with decreased survival. Unadjusted median survival from diagnosis was significantly lower in frontal lobe (38 months) versus other locations PXA (62 months) (P=0.026).
- As compared to other location PXA, frontal lobe PXA were significantly enriched in anaplastic/ dedifferentiated grade (28.1% vs. 11.6%, respectively, P=0.007) and were diagnosed at an older age (33yrs vs. 25.8yrs, respectively, P=0.0007)
- Patients with frontal lobe tumors were more likely to have surgery + adjuvant radiation/chemotherapy treatment (P<0.001) and less likely to undergo surgical resection only (P=0.006).
- Multivariate analysis, however, revealed that increased age (HR 1.0372, P<0.0001), anaplastic/dedifferentiated grade (HR 1.7911, P=0.0374), and tumor size (HR 1.7065, P=0.0408) rather than specific tumor location itself were significant predictors of adjusted mortality.

Table 1. Patient Demographics for PXA subdivided by location: frontal lobe vs. other location

	Frontal lobe	Other locations	P
N	89 (19.9%)	358 (80.1%)	
Gender			0.9427
Male	46 (51.7%)	181 (50.6%)	
Mean Age at diagnosis, yrs	33 (SD 18.9)	25.8 (16.3%)	0.0007
Race			0.7821
White	69 (77.5%)	281 (78.5%)	
Non-White	20 (20.5%)	22 (19.5%)	
Unknown	0	7 (2%)	
Grade			0.007
"Well/moderately/poorly differentiated"	17 (19.1%)	76 (21.1%)	
"Anaplastic/dedifferentiated"	25 (28.1%)	41 (11.6%)	
Unknown	47 (52.8%)	241 (67.3%)	
Tumor Size			0.4940
Mean size, mm	33.09 (SD 19.3)	35.78 (SD 21.4)	
Treatment			< 0.001
Surgery only	43 (48.3%)	232 (64.8%)	0.006
Surgery + radiation/chemotherapy	38 (42.7%)	68 (19%)	< 0.001
Radiation/chemotherapy only	2 (2.2%)	8 (2.2%)	
No treatment/unknown	6 (6.8%)	50 (14%)	
*Extend of Surgical resection:			0.085
Gross Total	45 (50.6%)	179 (50%)	0.924
Subtotal/No resection/Unknown	44 (49.4%)	179 (50%)	
Median Overall Survival, yrs	38 (63.6%)	62 (72.1%)	0.026

Conclusions

Frontal lobe PXA location is significantly associated with clinically aggressive features that predict decreased survival and require more complex treatment. These findings have important implications in prognostication and management of these tumors and warrant further investigation into underlying causes.

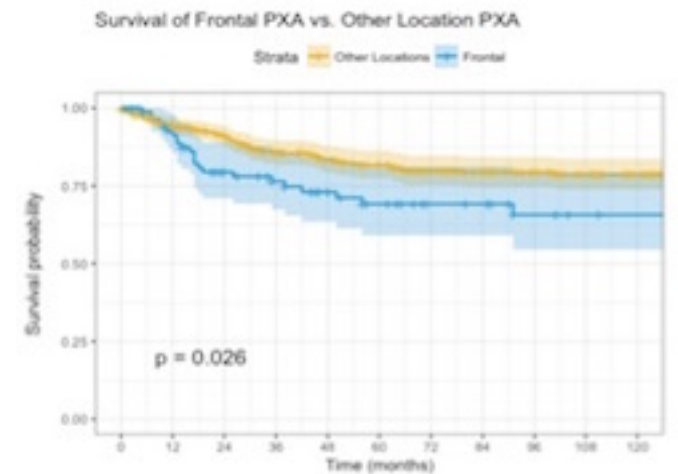## Figure 1. Overall PXA Survival By Location

Survival of Frontal PXA vs. Other Location PXA
Strata — Other Locations — Frontal
p = 0.026

Table 2. Hazard ratios of death among PXA patients by location: frontal lobe vs. other location

Covariate	HR (95% CI)	P
Frontal lobe location	0.9388 (0.5719-1.5424)	0.8031
Male	1.3832 (0.8875-2.1559)	0.1519
Age at diagnosis	1.0369 (1.0241-1.0498)	< 0.0001
Race		
White	1.0500 (0.6203-1.7772)	0.8559
Grade		
WHO grade IV	1.8042 (1.0469-3.1092)	0.0336
Treatment		
Surgery only	0.2680 (0.0979-0.7339)	0.0102
Surgery+radiation/chemotherapy	1.3074 (0.4886-3.4986)	0.5935
No treatment/unknown	0.5653 (0.1946-1.5579)	0.2822
Surgical Resection Extend		
Gross Total	0.5105 (0.1999-0.8379)	0.0078

References 1. Perkins SM, Mitra N, Fei W, Shinohara ET. Patterns of care and outcomes of patients with pleomorphic xanthoastrocytoma: A SEER analysis. J