Interdisciplinary Neurosurgery: Advanced Techniques and Case Management xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Interdisciplinary Neurosurgery: Advanced Techniques and Case Management

journal homepage: www.inat-journal.com

Neuroanatomical Studies

Survival patterns of oligoastrocytoma patients: A surveillance, epidemiology and end results (SEER) based analysis☆,☆☆

Tyler A. Lanman, BS [a], Jason N. Compton, BS [a], Kate T. Carroll, BA [a], Brian R. Hirshman, MD [b], Mir A. Ali, BS [a], Bryson Lochte, BA [a], Bob Carter, MD PhD [b], Clark C. Chen, MD PhD [c,*]

[a] School of Medicine, University of California, San Diego, 9500 Gilman Drive, La Jolla, CA 92093, United States
[b] Division of Neurological Surgery, University of California, San Diego, 200 West Arbor Drive #8893, San Diego, CA 92103, United States
[c] Department of Neurosurgery, University of Minnesota, Minneapolis, D429 Mayo Memorial Building, 420 Delaware Street S.E., MMC 96MN 55455, United States

ARTICLE INFO

Article history:
Received 25 April 2017
Revised 24 June 2017
Accepted 30 July 2017
Available online xxxx

ABSTRACT

Objective: The 2016 update to the World Health Organization (WHO) states that oligoastrocytoma (OA) should be classified as either oligodendroglioma or astrocytoma based on molecular biomarkers. We examined the survival patterns of patients diagnosed with OA in the Surveillance, Epidemiology and End Results (SEER) registry in the context of this revised scheme.
Methods: We used data from the SEER database (1999–2010) to identify patients diagnosed with WHO grade II astrocytoma (A2, $n = 4113$), WHO grade II oligodendroglioma (O2, $n = 2378$), and oligoastrocytoma (OA, $n = 1505$). Survival comparison was performed using Kaplan-Meier analysis and multivariate Cox proportional hazards analysis.
Results: Similar to O2 patients, gross total resection (GTR) was not associated with improved survival in OA patients. In contrast, GTR is associated with improved survival in A2 patients. For OA patients who did not undergo surgery or radiation therapy (RT), those with tumors < 5 cm in maximal diameter exhibited survival patterns similar to O2 patients, while those with tumors ≥ 5 cm exhibited survival patterns similar to A2 patients.
Conclusions: Distinct survival patterns were observed in SEER OA patients with tumors < or ≥ 5 cm in maximal diameter.

1. Introduction

Certain pathologic diagnoses are adopted to overcome challenges associated with histologic ambiguity. A case-in-point involves oligoastrocytoma (OA), a diagnosis historically used when glioma specimens contain histological features of both oligodendroglioma and astrocytoma [1]. The 2016 update to the World Health Organization (WHO) states that now OA should be classified as oligodendroglioma or astrocytoma based on their molecular profiles [2]. Oligodendrogliomas are characterized by mutations in the Isocitrate Dehydrogenase (IDH) gene and 1p/19q deletion [3–6]. In contrast, astrocytomas are characterized by mutations in the a-thalassemia/mental retardation syndrome X-linked (ATRX) gene, over-expression of p53, and the lack of 1p/19q deletion [7–11]. When reclassified based on these molecular criteria, most oligoastrocytoma (approximately 75%) are diagnosed as WHO grade II oligodendrogliomas (O2) [12].

WHO grade II astrocytomas (A2) and O2 exhibit distinct clinical survival patterns. For instance, A2 tend to be more chemo-resistant and derive survival benefit from gross total resection (GTR) [13–16]. In contrast, O2, like primary central nervous system lymphomas (PCNSL), are more chemo-sensitive [17–19], and improved survival is associated with chemotherapy more than extent of surgical resection [20–22]. The 2016 WHO classification revision is based on the observation that patients previously diagnosed with OA with molecular features of O2 (e.g. 1p/19q deletion and IDH mutation) exhibit survival patterns that resemble O2. Similarly, patients previously diagnosed with OA with molecular features of A2 (e.g. ATRX and p53 mutations) exhibit survival patterns resembling A2. Here we determined whether similar

Abbreviations: A2, WHO grade II astrocytoma; ATRX, a-thalassemia/mental retardation syndrome X-linked; GTR, gross total resection; ICD-O-3, International Classification of Disease for Oncology, 3rd Edition; IDH, isocitrate dehydrogenase; O2, WHO grade II oligodendroglioma; OA, oligoastrocytoma; NCI, National Cancer Institute; PCNSL, central nervous system lymphomas; RT, radiation therapy; SEER, Surveillance, Epidemiology and End Results; STR, subtotal resection; WHO, World Health Organization.

☆ Funding: None declared.
☆☆ Conflict of interest: None declared.

* Corresponding author at: Department of Neurosurgery, University of California, San Diego, 3855 Health Sciences Drive #0987, La Jolla, CA 92093, United States.
E-mail address: ccchen@umn.edu (C.C. Chen).

http://dx.doi.org/10.1016/j.inat.2017.07.017

stratification can be made using clinical variables. Using the Surveillance, Epidemiology, and End Results (SEER) registry, we showed that for OA patients who did not undergo surgery or radiation therapy (RT), patients with OA < 5 cm in maximal diameter exhibit survival patterns similar to O2 patients, while those with tumors ≥5 cm exhibit survival patterns similar to A2 patients.

2. Materials & methods

2.1. Data source and population

The SEER Program was established by the National Cancer Institute (NCI) to collect cancer incidence and survival data from 18 population-based cancer registries that cover about 28% of the total U.S. population (SEER Research Data 1973–2010). This study employed data released in April 2013 that was based on November 2012 submissions. Data was downloaded as an ASCII text file [23].

We chose to examine the oligoastrocytoma tumor type in relation to WHO grade II astrocytoma and oligodendroglioma [24]. This study included patients who were diagnosed between 1999 and 2010 with OA, A2, or O2 as the only cancer diagnosis. The following International Classification of Disease for Oncology, 3rd Edition (ICD-O-3) histology codes were used: 9382 (oligoastrocytoma, WHO grade II), 9400, 9410, 9411, 9420 (diffuse astrocytoma, WHO grade II), and 9450 (oligodendroglioma, WHO grade II). Brain tumors were selected with ICD-O-3 topologic site codes C71.0–C71.9. These codes were cross-referenced and validated with Table 1 of the Central Brain Tumor Registry of the United States Statistical Report [25]. Patients were excluded from the study if the surgical status was coded as unknown or if the histology did not have microscopic confirmation. Using these criteria, patients were grouped into three diagnostic categories: OA ($n = 1505$), A2 ($n = 4113$), and O2 ($n = 2378$).

2.2. Extent of resection and covariates

The following surgery codes from SEER were used to define extent of surgical resection: no surgery (code 00), excisional biopsy (code 20), subtotal resection (codes 21, 40), or GTR (codes 30, 55). Despite minor modifications of codes in each edition of SEER Program Coding and Staging Manual, the general definition has remained constant during the time period we have selected [26,27]. Historical definitions can be found on the SEER website [28].

Survival time was defined as the number of months from diagnosis to the date of death due to any cause or the date of last known follow-up. The following demographic variables were used in the analysis: age (<18, 18–44, 45–49, 50–54, 55–59, 60–74, or >75 years), race/ethnicity (white, black, Asian/Pacific Islander, Hispanic, American Indian/Alaskan Native, or other/unknown), marital status (single, married, or [separated, divorced or widowed]), and sex (male or female). The following clinical variables were also included in the analysis: tumor size (<5 cm or ≥5 cm), tumor location (based on ICD-O-3 topologic site codes C71.0–C71.9), RT status (radiation or no radiation), and surgical treatment (no surgery, biopsy, STR, or GTR).

2.3. Statistical analysis

All analyses were conducted using Stata version 11.2 [29], and the level of statistical significance was set at $p < 0.05$. We performed comparisons of overall survival between OA, A2, and O2 patients. Analyses were performed to determine the impact on survival of GTR relative to biopsy only. This GTR/biopsy hazard ratio was then compared in each tumor type relative to OA. Similarly, we analyzed the effect of RT on survival relative to no RT and further compared hazard ratios in each tumor type to OA. We performed post-hoc analyses in a subset of patients with no surgery and no radiation to explore the effect of tumor size (segregated into tumors <5 cm and ≥5 cm) on survival.

Table 1
Demographic and clinical characteristic of OA cases, SEER 1999–2010.

Number of patients, n	1505
Age, median (IQR)	40 (31–52)
Surgery, n (%)	
Gross total resection	555 (36.88)
Partial resection	452 (30.03)
Local excision/biopsy	280 (18.60)
No surgery	218 (14.49)
Radiotherapy, n (%)	
No	608 (41.36)
Yes	862 (58.64)
Age category, years, n (%)	
<18	72 (4.78)
18–45	831 (55.22)
45–60	399 (26.51)
60–75	160 (10.63)
>75	43 (2.86)
Race, n (%)	
White	1049 (69.70)
Black	90 (5.98)
Asian/Pacific Islander	107 (7.11)
Hispanic	243 (16.15)
American Indian/Alaskan Native	11 (0.73)
Other/Unknown, Non-Hispanic	5 (0.33)
Marital status, n (%)	
Single	456 (31.08)
Married	836 (56.99)
Separated, divorced, widowed	175 (11.93)
Sex, n (%)	
Male	853 (56.68)
Female	652 (43.32)
Tumor size, cm, n (%)	
<5	554 (52.41)
≥5	503 (47.59)
Tumor site, n (%)	
Cerebrum	43 (2.86)
Frontal lobe	725 (48.17)
Temporal lobe	317 (21.06)
Parietal lobe	165 (10.96)
Occipital lobe	20 (1.33)
Ventricle, NOS	7 (0.47)
Cerebellum, NOS	11 (0.73)
Brain stem	10 (0.66)
Overlapping lesion of brain	168 (11.16)
Brain, NOS	39 (2.59)
Year of diagnosis, n (%)	
1999	56 (3.72)
2000	80 (5.32)
2001	112 (7.44)
2002	112 (7.44)
2003	137 (9.10)
2004	126 (8.37)
2005	141 (9.37)
2006	166 (11.03)
2007	151 (10.03)
2008	132 (8.77)
2009	139 (9.24)
2010	153 (10.17)
Overall mortality, n (%)	
Living	969 (64.39)
Deceased	536 (35.61)

We used the Kaplan-Meier method to generate unadjusted survival curves for the overall population and specific subsets. Statistical significance was determined using log-rank tests across survival functions. To calculate the multivariate adjusted hazard ratios of death, we performed Cox proportional hazard analysis adjusting for all aforementioned demographic and clinical covariates. To compare the effect of treatment by tumor type, we used the Wald test.

Please cite this article as: T.A. Lanman, et al., Survival patterns of oligoastrocytoma patients: A surveillance, epidemiology..., Interdisciplinary Neurosurgery: Advanced Techniques and Case Management (2017), http://dx.doi.org/10.1016/j.inat.2017.07.017