Factors associated with five-year survival in children with cerebral astrocytoma

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Abstract

Introduction: The second cause of children's death is cancer, with leukemia and central nervous system tumors being the most common, among which astrocytomas account for 40%. **Objective:** To find out the factors associated with 5-year survival in children with cerebral astrocytoma. **Method:** Case-control study nested in a retrospective cohort of patients diagnosed with cerebral astrocytoma who received treatment from December 2006 to January 2010. Descriptive statistics and the chi-square test were carried out; the Kaplan-Meier method was used to assess survival. **Results:** Twenty-one patients diagnosed with cerebral astrocytoma were included; survival was 76% at 5 years; with pilocytic astrocytoma being the most common (61%); mean age was 7 years, and male gender was predominant; age at death ranged from 8 to 12 years ($p = 0.022$), with 80% of deceased patients having infratentorial localization (OR = 17.3; 95% CI = 1-622; $p = 0.01$). There was no treatment-attributable survival difference. **Conclusions:** Five-year survival was 76%; the limiting risk factor is tumor infratentorial localization.

KEY WORDS: Pediatric cancer. Cerebral astrocytoma. Surveillance.

Introduction

The leading cause of death at pediatric age is accidents, followed by childhood cancer, which accounts for 0.5 to 5.7 % of total malignancies in the general population.¹ Leukemia constitutes the most common malignancy in children, and central nervous system (CNS) tumors the second. In Mexico, brain tumors are reported at a frequency of 10.9 to 12 % and have an incidence of 3.3 to 3.5 cases per 100 000 children in tertiary care medical centers, and are more common in children younger than 10 years of age, with a peak at between 4 and 6 years of age.¹⁻³ Astrocytomas comprise the group of tumors originating in the glia; according to the American Cancer Society, these tumors account for 40 % of CNS neoplasms^{4,5} and are the most common type. To assess treatment success, establishing survival is necessary; patients with astrocytomas have been documented to have a 5-year survival of 85 %.

In the treatment of childhood cancer, risks and benefits are assessed for each patient; notwithstanding, 20 % of children die and survivors have negative effects on their quality of life.⁶ Surgical resection is curative if fully achieved, with up to 25 years of survival, conversely to what occurs in patients in whom it is not achieved,⁷⁻⁹ which is influenced by the lesion anatomical localization. Patients with supratentorial tumors have been shown to have better survival when surgery is added chemotherapy and radiotherapy, with the latter being somehow controverted as regards the ideal timing to be started and the recommended dose; nevertheless, radiotherapy early initiation has been shown to prevent tumor progression, by means of which higher survival is achieved.^{10,11}

Astrocytomas are divided in 4 grades depending on the histologic type: the pilocytic type is the most common and the one with the best prognosis; the most aggressive types are anaplastic and glioblastoma.

Currently, brain tumors are more promptly diagnosed thanks to the available imaging studies;

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however, an increase in CNS tumors-associated mortality has been documented in recent years, especially within the first 6 years after diagnosis.^{12,13}

With the advance of diagnostic tests and different treatment modalities for brain tumors, it is necessary for expectable survival time and influencing factors to be known, particularly in cerebral astrocytomas in children. The purpose of our study was to assess the factors associated with 5-year survival in this group of patients.

Method

This was a longitudinal, retrospective, observational, analytical study that included all patients diagnosed with CNS astrocytoma in a 5-year period from January 2006 to December 2010 at Specialty Hospital 25 in Monterrey, Nuevo León. Patient charts were used to obtain the following data: gender, age at diagnosis, anatomical region of tumor site, histopathologic study, administered treatment, time elapsed since diagnosis, chemotherapy and number of sessions, surgical treatment and whether radiotherapy was administered or not, as well as months elapsed until death. Analyses were carried out using the SPSS software, version 17.0. The chi-square test and Fischer's exact probability test were used; the Kaplan-Meier method was used to assess survival and, to assess the magnitude of association of the different risk factors, the odds ratio (OR) with its 95 % confidence interval (CI) was measured, with a p-value < 0.05 being regarded as significant.

Results

Twenty-one patients diagnosed with cerebral astrocytoma between January 2006 and December 2010 were included, out of which 16 were alive at 5 years of follow-up and 5 had died, which represented 75 % of survival (Fig. 1). Of total patients, 11 (52 %) were males; the population had an age range of 2 to 12 years, with a mean of 7 years; the patients who survived had a mean age of 6 years, with a range of 2 to 11 years; those who died had a mean age of 9 years, ranging from 8 to 12 years ($p = 0.02$).

Of the 21 patients diagnosed with cerebral astrocytoma, 13 (61 %) were found to correspond to the pilocytic astrocytoma diagnosis, 4 (19 %) to the diffuse type, 2 (9.5 %) to anaplastic and 2 (9.5 %) to glioblastoma. As for anatomical site, 14 (66 %) had supratentorial localization and 7 (33 %) infratentorial. Of the patients who survived, 13 (81%) had supratentorial localization

Figure 1. Five-year survival of 21 pediatric patients diagnosed with astrocytoma.

and 3 (18 %) infratentorial; of those who died, one (20 %) had supratentorial localization and 4 (80 %) infratentorial (OR = 17.3; 95% CI = 1-622, $p = 0.01$).

Seventeen patients (80 %) received treatment with chemotherapy, out of which 12 (75%) survived and 5 (100 %) died ($p = 0.22$); 20 patients underwent a surgical procedure, out of which 12 (57%) had partial resection and 8 (38 %), complete resection (Table 1).

Discussion

In this study, among all tumors that were diagnosed in the CNS, astrocytoma was found to remain with 30 % and to be the most common in the male gender.

Astrocytomas are diagnosed in 20 % of patients with ages ranging from 0 to 14 years, but the most common age range is from 4 to 6 years.^{1,3,14} According to Bandopadhyay et al.,¹⁵ one factor of poor prognosis is age at diagnosis: mortality is higher in children < 2 years of age. We found that average age at diagnosis was 7 years and that patients who died were < 9 years' old.

According to the World Health Organization, astrocytoma is histologically classified in 4 degrees, with the pilocytic type being the most common and the one with the best prognosis;¹⁶ our findings were consistent with those described in the world literature. Pilocytic astrocytoma was the most common histological variety in the patients who died: 13 of the 21 patients had this histological variety (61 %), and of the 5 who died, 3 had a histological diagnosis of pilocytic astrocytoma

Table 1. Clinical characteristics and treatment of 21 astrocytoma-diagnosed pediatric patients according to 5-year survival

	Total		Alive		Dead		p
	(n = 21)		(n = 16)		(n = 5)		
	n	%	n	%	n	%	
Gender							
Male	11	5	8	50	3	60	0.702
Female	10	48	8	50	2	40	
Histopathologic study							
Pilocytic	13	61	10	62.5	3	60	0.429
Diffuse	4	19	4	25	0	0	
Anaplastic	2	9.5	1	6.2	1	20	
Glioblastoma	2	9.5	1	6.2	1	20	
Anatomical region							
Supratentorial	14	66	13	81	1	20	0.013
Infratentorial	7	33	3	18	4	80	
Chemotherapy	17	80	12	75	5	100	0.225
Radiotherapy	7	33	5	31.2	2	40	0.723
Surgical resection							
Partial	12	57	8	50	4	80	0.248
Total	8	38	7	43	1	20	
	Median	Min.-max.	Median	Min.-max.	Median	Min.-max.	
Age at diagnosis (years)	7	2-12	6	2-11	9	8-12	0.022
Time on radiotherapy (months)	24	1-48	6	1-48	9	1-17	0.769
Time from diagnosis to surgery (months)	1	0.5-6	1	0.5-3	1	0.5-6	0.420
Chemotherapy sessions	7	1-14	6	1-14	7	1-12	0.980

and localization was infratentorial; as regards the two remaining patients, one showed the anaplastic variety and, the other, glioblastoma. In 2015, Samaan et al.¹³ observed high mortality within the first 2 years after diagnosis owing to tumor aggressiveness.

In 2008, Osorio et al. reported a survival rate of 90 % in patients with complete resection of the lesion; in our population, we found no differences between different therapeutic modalities (chemotherapy, radiotherapy and surgical resection) in terms of survival; however, supratentorial tumor location was found to be a factor of good prognosis; it might be that there is surgical benefit associated with a more accessible surgical procedure in the supratentorial than in the infratentorial region. Bandopadhyay et al.¹⁵ found that the type of astrocytoma resection (partial or complete) did not influence on survival, a situation that was observed in our population.

The different treatment modalities in our study, such as chemotherapy, radiotherapy or surgical resection, showed no relevance for survival as independent variables; however, Bandopadhyay et al.¹⁵ analyzed the databases of children diagnosed with low-grade

astrocytoma who survived, and observed that when resection was partial and the children received radiotherapy the results were poor; they concluded that probably this result was due to radiotherapy side effects.¹⁵

Our population showed a survival of 76 %, with higher probability to die in the first 2 years after diagnosis; once the 2 years had elapsed, the likelihood for staying alive was extended to more than 5 years. In a multi-center study carried out in 1994, Geyer et al.⁷ compared anaplastic tumors and glioblastomas during the first 2 years after diagnosis and observed a survival of 75 %; in their research conducted in 2013, Bandopadhyay et al.¹⁵ observed that patients with low-grade astrocytoma achieved a survival of 85 %; in turn, the American Cancer Society attributes a probability of survival of 85 % in children with cerebral astrocytoma.¹⁸ In view of the above, we concluded that 5-year survival in our population was slightly lower than that reported in the world literature.

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