



Patient's Life Ability With Malignant Astrocytoma Grade IV

Lilik Widodo^{a*}, Andi Asadul Islam^{b*}, Djoko Widodo^{c*}, Joni Wahyuhadi^{d*}

^aBhayangkara Hospital, Surabaya, Indonesia

^{b,c}Departement of Surgery, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia

^dDepartement of Neurosurgery, Faculty of Medicine, Airlangga University, Surabaya Indonesia

Abstract

Grade IV astrocytoma is a primary brain tumor with a high mortality rate. The survival time for astrocytoma grade IV is about 6-12 months. Conventional therapies that exist to date in the form of surgery, radiation and chemotherapy. The main problem with malignant astrocytoma is that tumor cells grow infiltratively into the surrounding brain tissue and are always recurrent despite conventional therapy. This condition results from a complex gliomagenesis process involving the role of neural cancer stem cells (NCSC). The lack of an efficient immune response and the micro-invasive nature of malignant astrocytoma cells has been explained by many immune surveillance mechanisms in brain malignancies. The survival ability of these tumors results in a complex interaction between the tumor and the body's immune system. The aim of this study was to evaluate the survival time of malignant astrocytoma grade IV patients treated with surgery, radiotherapy with or without chemotherapy. A retrospective study of the survival time of patients with malignant astrocytoma grade IV treated by us during the period 2005 - 2015 was 12 patients. All patients postoperative craniotomy resection of tumors undergoing radiation with 42 Gy. Among these 6 patients received chemotherapy as well. Sexually male proportion more than female with ratio 1.6 : 1. Most were over 50 years old (83%), 2 patients under the age of 50 years. Four patients (33%) survived for one year, survived for two years found 5 patients (41%), survived more than 3 years 3 patients (25%) and none survived more than 5 years .. This study suggests that chemotherapy have no effect on the survival time of the patient.

Keywords: astrocytoma grade IV; survival; conventional therapy.

* Corresponding author.

1. Introduction

Highly malignant astrocytoma or high grade astrocytoma are tumors of the central nervous system (CNS). They are solid tumours arising from transformed cells of the brain and/or the spinal cord. Since they directly originate from the CNS, they are also called primary CNS tumours. High grade astrocytoma is a term encompassing various histologically defined brain tumors linked by glial origin. Until recently, standard treatment consisted of maximum safe surgical debulking followed by external beam radiotherapy. Chemotherapy with temozolamide has also become for newly-presenting patients [1,4,6,11]. Prognosis remains extremely poor, with a median survival of 14.6 months. Commonly radiotherapy starts 2 – 4 weeks post-operatively but the optimum timing is not known. The length of life and its quality are the basic parameters through which one can determine the outcome. Observing this aspect high grade astrocytoma represents a strikingly important neurosurgical and oncological problem. New diagnostic methods as well as the microsurgical technique in several studies did not significantly improve the survival rate, and 5 – year survival is still sporadic [1,3,7,10]. The objective of this study is to analyse the survival time of patients with malignant astrocytoma grade IV operatively treated, radiotherapy with/without chemotherapy, to discuss factors which influence the survival.

2. Patient and Methods

Patients were identified from medical reports at Bhayangkara Hospital and Siloam Hospital Surabaya. Any equivocal histopathology reports were reviewed by a pathologist to confirm a diagnosis of WHO grade IV astrocytoma.

3. Result

Twelve patients with malignant astrocytoma grade IV who were operated on in a ten-year period (2005 – 2015) had their survival time evaluated. All patients were treated postoperatively by radiation therapy, according to oncological protocol, while a small number of patients was also treated by chemotherapy with temozolamide. Time to radiotherapy after surgery varied from two weeks to over 8 weeks.

Table 1: Survival time of postoperative 4th grade Astrocytoma patients with radiation therapy + chemotherapy and without chemotherapy

Variable		Survival Time (month)		P
		Min - Max	Mean ± SD	
Age (Years)	≤60 years (n=4)	23 – 38	33.0 ± 6.9	.023*
	>60 years (n=8)	11 – 40	17.6 ± 10.2	
Gender	Male (n=7)	11- 40	20.9 ± 11.9	.533**
	Female (n=5)	13 - 38	25.4 ± 12.3	
Chemotherapy	Yes (n=5)	11 - 37	23.6 ± 11.8	.432**
	No (n=7)	12 - 40	22.1 ± 12.5	

*independent t test ** MannWhitney test

Table2: The difference of survival time of postoperative malignant astrocytoma grade IV patient based on chemotherapy and patient age

Age	Chemotherapy	Survival Time (month		P
		Min - Max	Mean ± SD	
≤60 Years	Yes (n=3	23 – 37	31.3 ± 7.4	.500**
	No(n=1)	38 – 38	38.0	
≤60 Years	Yes(n=2	11 – 13	12.0 ± 1.4	.286**
	No(n=6	12 – 40	19.5 ± 11.36	

** MannWhitney test

The summary of the results of the analysis in Table 1 showed that no survival difference was observed although there was a tendency for survival time in female (25.4 months) to be longer than male (20.9 months) and no significant difference ($p > 0.05$) between those who underwent chemotherapy and those who did not, although the mean survival time in those undergoing chemotherapy (23.6 months) was longer than that for no chemotherapy (22.1 months), indicating that the chemotherapy action was not proven to prolong survival time for patients with malignant astrocytoma grade IV ,

While the survival time of patients were actually affected by age. A younger patient (≤ 60 years) had a mean survival time (33.0) longer than the elderly (> 60 years) .This means the age of potentially confounding patients chemotherapy. To ensure this is done by certifying the sample by age group, then analyzed a chemotherapy effect in each age group. The results can be seen in table 2.

Summary of chemotherapeutic effect analysis results through comparison of survival time between chemotherapy and no chemotherapy in each age group showed no significant difference ($p > 0.005$), even the average survival time of astrocytoma patients was longer in the non-chemotherapy group (38.0 months) than those who received chemotherapy (31.3 months) for age group ≤ 60 years and similarly for age group > 60 years, mean of non-chemotherapy survival time (19.5 months) than chemotherapy (12.0 months). This suggests that chemotherapy have no effect on the survival time of the patient.

4. Discussion

If high-grade astrocytoma has been diagnosed, treatment should be started as soon as possible. The most effective treatment high-grade astrocytoma is a combination of neurosurgery, radiotherapy, and chemotherapy [2,5,11]. Among these treatment modalities, neurosurgery is of highest impact, since the extent of tumour removal significantly determines the further course of the disease. The more radical the tumour can be resected,

the higher are the chances of survival [1,5].

Debulking surgery is beneficial in reducing the tumour load and thus the side effects of raised intracranial pressure and providing a more representative histological sample. Whether it provides an improvement in survival is controversial [7]. Retrospective studies have suggested that gross total resection as defined by post operative MRI findings of more than 98% tumour resection, has shown better quality of life and progression free survival. The problem with gross total resection remains balancing maximal resection against potential neurological deficits [5].

Radiotherapy has been the mainstay of adjuvant therapy for high grade astrocytoma since multiple studies from the 1970s showed a survival benefit. However, attempts to improve on the initial benefits by increasing dosage of radiation has failed to have any success. Unfortunately the therapeutic window for radiotherapy to the brain is narrow and there is an increased incidence of radiation necrosis with increased radiation dose [2,4]. Part of the reason for this is the inability of conventional imaging to identify infiltrating tumour. As a result radiotherapy planning outlines the obvious tumour as the Gross Tumour Volume (GTV). A 2.5cm margin is then applied to form the Clinical Target Volume (CTV). A 0.5cm margin is added to account for set up errors and patient movement to form the Planning Target Volume (PTV). In other words, a 3cm margin is applied around the tumour that will contain normal brain. To reduce the risk of radiation necrosis the dose is therefore limited [7].

The introduction of temozolomide has provided some improvement in survival. It is given orally over five consecutive days within a 28 day cycle. Leucopenia and thrombocytopenia are commonly associated side effects of this treatment. The combination of radical radiotherapy and daily, concomitant temozolomide followed by six cycles of adjuvant temozolomide has significantly altered the prognosis of astrocytoma grade IV. (3,4,5,8)

Although the current standard treatment for high grade astrocytoma are maximal resection followed by radiotherapy with concomitant and adjuvant concomitant chemotherapy including temozolamide [3,5,6], median survival of high grade astrocytoma only <2 years and 2.5 years, respectively [6,7].

The insignificant effect of chemotherapy on survival time in my study was probably due to: 1/ small number of patients (n = 12). 2/ Karnofsky Performance Scores were not evaluated. 3/ no evaluation of gross / non gross total resection of the tumor mass. 4/ initial neurological status are not the same. 5/ time to radiotherapy, 6/ time to introduce chemotherapy, 7/ possibility of comorbidities that are not included in the evaluation. 8/ not all MGMT tests are performed.

5. Conclusion

This study suggests that chemotherapy have no effect on the survival time of the patient.

6. Recommendations

Further research is needed with large sample, more stringent inclusion and exclusion criteria and include other

variables such as Karnofsky Score, initial neurologic status, gross/non gross total resection , and other comorbid diseases.

7. Confits of Interest Disclosure

The authors report no conflict of interest. The authors have no personal, financial, or institutional interest in any of the drugs, materials or devices used in the article.

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