

SURVIVAL OF BRAIN ASTROCYTOMA PATIENTS CONSIDERING PREOPERATIVE TUMOR SIZE

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Actual neuroradiological diagnostics of the brain tumors, including astrocytomas, is of great influence on successful planning and realization of the tumor resection, considering the fact that it is oftentimes preoperative. CT diagnostics is the most frequently used method of the brain tumor visualization in Serbia, due to height reliability, short time of the exposition, lower costs, and wide using even in smaller health centers, compared to concurrent methods. In our study we examined 63 adult patients, which have been operated for a brain tumor at the Clinic of Neurosurgery in Nis. In all of the cases tumors were supratentorial, without cysts and complete resection was confirmed after control CT scan has been done. In all of the patents, pathohistological analysis of the tumor specimen revealed astrocytoma. The features of astrocytoma grade IV are: hypercellularity, pleomorphism, endovascular proliferation and necrosis were dominant.

All patients had maximal reduction of the tumor bulk and were postoperatively treated according to current oncological protocols. The preoperative CT parameter-tumor size was correlated to survival.

The most frequent tumor bulk was presented as medium sized, average diameter between 25 and 50 mm (34 patients). Large tumor bulks, with average diameter over 50mm were found in 17 patients, and rarely, the tumors were small, with average diameter less then 25 mm, which was found in 12 patients. Patients that had large tumor masses lived significantly shorter (24 weeks) compared to patients that had medium sized or small tumors (97 and 84 weeks, respectively). *Acta Medica Medianae 2007;46(1):17-20.*

Key words: *brain astrocytoma, tumour size, survival.*

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Introduction

More than a half of the primary brain tumors are astrocytomas, or little less than a quarter of the all cases of the brain tumors. Death occurs usually due to the effects of terminal evolution of astrocytomas (1).

Modern neuroradiological techniques are of great importance in successful preoperative planning and realization of the tumor resection. Intraoperative techniques are also of considerable benefit, when available, especially for precise location of the tumor, and therefore more precise resection. Postoperative evaluation is essentially of control significance, and should be practiced without exceptions.

Routine neuroradiological evaluation procedures as computed tomography (CT) or magnet resonance imaging (MRI) have speed up attaining the correct diagnosis of the brain tumors. The

latest diagnostic procedures, as positron emission tomography (PET) and single photon emission computed tomography (SPECT), give new qualities in estimating their type and grade and histological, biological and biochemical characteristics of brain tumors (2).

Before starting an operation of the brain astrocytoma, neurosurgeant considers CT and MRI findings. Cerebral angiography is rarely performed, usually when localizing the tumor in relation to cerebral vascularisation. Skull x-ray is of no importance as a diagnostic procedure for brain astrocytoma.

In Serbia and Montenegro, CT is most frequently used for brain tumor visualisation, because of its high reliability (98% sensitivity) (3), short duration of the procedure, lower costs, and its high accesability in regional medical centers.

MRI is obtained when differential dilemmas are to be solved concerning cerebrovascular insults, haematomas during resorption process, low-grade astrocytomas, brain abscess, cerebral metastases or when precise location regarding other endocranial neurovascular elements is needed. Also, MRI is a procedure of choice in post-operative evaluation of extension of glioma resection (4).

Aims

The aim of the study was to find connection between survival and tumor dimensions visualized by preoperative CT.

Material and methods

The study group consisted of 63 adult patients that had been operated at the Clinic of Neurosurgery in Nis, in the period from May 16, 1995 until December 12, 2001. Their medical condition was followed until March 1, 2003. In all of the cases tumors were supratentorial, without cysts and complete resection was confirmed after control CT scan was performed. In all of the patients pathohistology analysis of the tumor specimen revealed astrocytoma. The features of astrocytoma grade IV: hypercellularity, pleomorphism, endovascular proliferation and necrosis were dominant.

We obtained preoperative CT in all of the cases, due to technical reasons preoperative MRI was performed in two patients only. The patients were divided in 3 groups according to the tumor size: small tumor mass (average tumor diameter less than 25 mm), medium (average tumor diameter from 25 to 50 mm) and large (average tumor diameter wider than 50 mm). Average tumor diameter ($D_{1-3 \max}$) was calculated as a quotient between addition of the maximal tumor diameters (a,b,c) in all dimensions and number 3: $D_{1-3 \max} = (a+b+c)/3$. Date of the patients' death was partly available from medical records, but mostly after telephone interview with the members of the patients' family.

In statistical analysis we performed "long-rank" test, Kaplan-Meier survival curve, and we presented the results by graphs and tables.

Results

Large tumors are associated with shorter postoperative survival (Graph 1). Most of the patients had medium-sized tumors (34 patients), large and small tumor masses were present in 17 and 12 patients, respectively (Table 1).

Table 1 shows minimal difference in survival between medium and small-sized tumors, 83 and 97 weeks, respectively, which is of no significance. However, after comparing survival in these two groups with survival of patients with large tumors (24 weeks), we found the significance (Log Rank test=8,81; $p=0,0122 < 0,05$).

Discussion

There is a clear connection between symptoms and location of the brain astrocytoma, but tumor biology (growth rate, infiltration, peritumor edema) and patient individuality (senile brain atrophy) also has some impact on clinical presentation. Biology of the astrocytoma is firmly linked to its histological grade, and a kind of its expression is the tumor size.

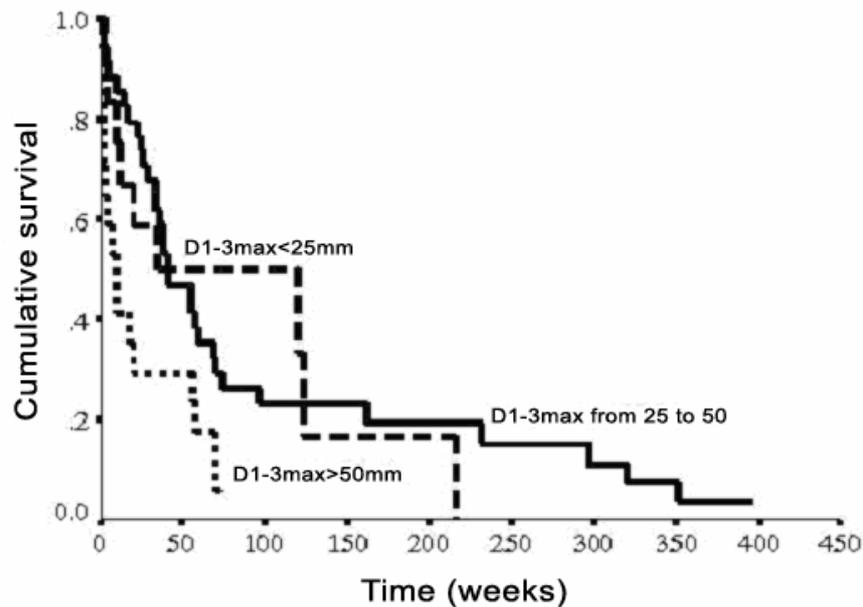
The volume of the tumor mass is proportional to the tumor growth rate and tumor coefficient of diffusion, which is $0,0013\text{cm}^3/\text{day}$ in GBM. Therefore, the volume of GBM duplicates every 60 days. Brain CT scan, after application of contrast, shows some parts of the tumor with increased tumor cell concentration, up to 8000 tumor cells/ mm^3 , while periphery parts with 100 tumor cells/ mm^3 presents as healthy or edematous brain tissue (5). This is a very essence of relative failure in surgical treatment of the high-grade astrocytoma.

Table 1. Survival (weeks) of the patients operated from brain astrocytoma compared to preoperative size of the tumor mass

$D_{1-3 \max}$	N	Xsr	95 % CI	Median	95 % CI
< 25mm	12	83,42	33,61-133,22	35,00	0,0 - 148,16
25 mm - 50 mm	34	96,64	56,52-136,75	41,00	22,94 - 59,06
> 50 mm	17	23,76	10,76-36,77	9,00	0,93-17,07

Table 2. Relation of deceased and censored patients operated from brain astrocytoma with preoperative size of the tumors

$D_{1-3 \max}$	N	Deceased	Censored	% censored
< 25mm	12	9	3	25,00
25mm - 50 mm	34	31	3	8,82
> 50 mm	17	16	1	5,88
Ukupno	63	56	7	11,11



Graphic 1. Relation of survival of patients operated from brain astrocytoma with preoperative size of the tumors

Connection between tumor volume and survival of the astrocytoma patients is clearly emphasized by Swanson (5), who defines survival time as the time needed for the volume A tumor (tumor volume found at initial CT scan) to reach the volume B (tumor volume at autopsy). Mathematical model that considers both tumor growth rate and tumor coefficient of diffusion gives us survival of 158 days for patients with GBM that grows from white matter, or 256 days for patients with GBM that grows from grey matter.

Correlation between tumor volume and survival also has been a matter of interest of other authors. Thus, Wood et al. in their study group of 510 glioma patients (6) showed that tumor size is of great prognostic importance, apart from other prognostic variables. Similar, other authors found this kind of correlation in their studies (7,8). According to results from his study, Scerrati (9) has found 3 groups of low-grade astrocytoma according to maximal diameters of the tumor mass: less than 3, 3-5, and more than 5 cm. Significantly, the survival was the shortest in group with the largest tumor masses ($p=0.0193$). In Wurschmidt's study (10), the patients with maximal tumor diameter wider than 5 cm, also live significantly shorter ($p=0,04$). In our study, the patients that had large tumor masses ($D_{1-3 \max} > 5\text{cm}$) lived significantly shorter compared to patients that had medium- sized or small tumors ($p=0,0122$).

In the Nwokedija (11) study, the average volume of GBM was 29 cm^3 , which correlates with our results where, according to Pinski formula, 60% of GBM had the same volume, with $2,5\text{cm} < D_{1-3 \max} < 5\text{cm}$.

MRI is a superior method on morphological diagnosis of brain tumor. Thanks to MRI it is possible to see relation of tumor to the basis of the skull and also the structure elements of brain stem. Advantage of MRI, when compared to CT, is high contrast scan resolution, ability of image reconstruction in several planes, absence of artifacts caused by bones, good vessel presentation, absence of x-ray. MRI is more sensitive for brain astrocytomas than CT. T2WI MR show that abnormalities spread well outside Ct zone of low attenuation. MRI findings were confirmed by stereotaxic biopsy, when tumor cells had been found also outside hypodense area presented on CT scan.

The latest generation of MRI (with magnetic field of 3 Tesla), can produce high resolution images in quality much closer to classic photo, and shorten the time of imaging to 6 minutes. Thus, importance of MRI as a descriptive diagnostic tool, capable of displaying even minor parameters that correlates with survival, significantly grows.

Conclusion

The larger preoperative brain astrocytoma correlates with shorter patient survival.

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ODNOS PREOPERATIVNE VELIČINE TUMORA I PREŽIVLJAVANJA KOD OBOLELIH OD ASTROCITOMA MOZGA

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Savremena neuroradiološka dijagnoza tumora mozga, samim tim i astrocitoma, je od ogromnog značaja za uspešno planiranje i realizaciju resekcije tumora, obzirom da je kao metoda, i najčešće, preoperativna. CT-dijagnostika, na teritoriji Srbije, predstavlja najzastupljeniju metodu vizuelizacije tumora mozga, zbog svoje visoke pouzdanosti, kratkog vremena i nižih troškova snimanja, kao i zbog veće zastupljenosti po regionalnim centrima u odnosu na konkurentne metode. U našoj studiji, obuhvaćeno je 63 adultnih bolesnika operisanih na Neurohirurškoj klinici u Nišu. U svim slučajevima se radilo o supratentorijalno lociranim tumorima, bez cistične komponente, koji su maksimalno ekscirpirani, što je potvrđeno kontrolnim CT-om mozga. Radi se o bolesnicima kod kojih je patohistološkim pregledom operativno ekscirpiranog materijala na Institutu za patologiju kliničkog centra u Nišu, postavljena dijagnoza astrocitoma mozga. Prilikom patohistološkog pregleda dominantno su nalažene karakteristike gradusa IV astrocitoma: naglašena hipercelularnost, pleomorfizam, endovaskularna proliferacija i nekroze. Kod svih bolesnika preduzeta je maksimalna resekcija tumorske mase, a postoperativno lečenje je nastavljeno u skladu sa aktuelnim onkološkim protokolima. Razmatran je odnos preoperativne CT prezentacije veličine tumora i dužine preživljavanja bolesnika. Najčešće su se tumorske mase prezentovale kao one srednjih veličina, sa srednjim dijametrom od 25 do 50 mm, i to kod 34 bolesnika. Velikih tumorskih masa, sa srednjim dijametrom od preko 50 mm, bilo je kod 17 bolesnika, a najređe su se tumorske mase ispoljavale kao one malih veličina, sa srednjim dijametrom manjim od 25 mm, i to kod 12 bolesnika. Bolesnici sa velikim tumorskim masama značajno su kraće živeli (24 nedelje) u odnosu na bolesnike sa srednje velikim, odnosno malim tumorima (97 odnosno 84 nedelje). *Acta Medica Medianae* 2007;46(1):17-20.

Ključne reči: astrocitomi mozga, veličina tumora, preživljavanje