Proliferative activity of chosen central nervous system (CNS) neoplasms

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Abstract

Gliomas are the most common neoplastic tumours of the central nervous system. The aim of the study was to evaluate the proliferative activity of chosen types of gliomas and to analyse their correlation with histological type, malignancy grade, location, size and clinical symptoms. The study involved patients with astrocytoma, anaplastic astrocytoma, glioblastoma, oligodendroglioma, anaplastic oligodendroglioma. The proliferative activity (the labelling index - LI) of glial cells was estimated, using immunohistochemistry. In studied groups, a positive correlation was noted between the proliferative activity and tumour size, but not between the proliferative activity and tumour location. The clinical symptoms were conditioned mainly by tumour location and, to a smaller extent, by its size

Key words: proliferative activity, glioma, Ki-67, PCNA.

Introduction

Gliomas constitute approximately 50% of all brain tumours, showing a varied clinical course, depending on their histological type, grade and location. In case of many gliomas, the basic histopathological investigation requires the use of accessory diagnostic methods. One of them is the immunohistochemical examination which detects the presence of cycle phase-specific nuclear antigens to indicate the proliferative activity of tumours [1].

The aim of the study was to evaluate the proliferative activity of chosen brain gliomas and to analyse its correlation with histological type, grade, location, size and clinical symptoms.

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Material and Methods

The study involved 99 patients, aged 18-80 (54 women and 45 men) with clinically diagnosed brain tumour. Prior to surgery, all the patients had neurological examinations, revealing either symptomatic or asymptomatic focal CNS damage or intracranial hypertension. CT and/or MRI examination allowed determination of the location and size of the tumour. Group I consisted of patients with astrocytoma (22 patients), Group II - patients with anaplastic astrocytoma (31), Group III - patients with glioblastoma (23), Group IV - patients with oligodendroglioma (12) and Group V - patients with anaplastic oligodendroglioma (11). Ki-67 (clone MIB-1, DAKO): working dilution 1:50 and PCNA (clone PC 10, DAKO): working dilution 1:100 antibodies were used for immunohistochemical examinations. The proliferative activity was determined, based on the labelling index (LI), expressing the percentage of cells with Ki-67 and PCNA nuclear immunoreactivity, compared to the total cell count. The Statistica PL program with StatSoft was used for statistical analysis. For comparison of means, Student's 't' test was performed.

Results

In the presented study, the mean LI values differed among the groups, depending on the tumour histological grade. The highest proliferative activity, expressed by LI, was found in glioblastoma cells. Lower LI values were noted in anaplastic astrocytomas and oligodendrogliomas. Statistically significantly lower LI values were observed in astrocytomas and oligodendrogliomas. Detailed data are shown in Table 1.

Discussion and Conclusion

LI values in neoplastic glial cells, presented by other authors, show evident variations. Compared to the present study, lower Ki-67 LI values in anaplastic astrocytoma and glioblastoma were found

Group	Histological type grading (G)	number of cases	Ki-67 – LI x (SD)	PCNA – LI x (SD)	diameter (cm)	Location of tumors (%)					Focal CNS damage of patients (%)				Intracranial hypertension of patients (%)			
						frontal lobe	temporal lobe	parietal lobe	motor and sensory area	area of posterior contact	aphasia	paresis	psychiatric disturbance	epilepsy	headache	vomiting	papilloedema	consciousness disturbance
I	Astrocytoma G2	22	1.52	2.42	4.96	18.2	40.9	9.1	18.2	13.6	9.1	50	13.6	27.3	63.6	9.1	18.2	4.5
II	Anaplastic astrocytoma G3	31	18.98	20.47	5.27	32.3	25.8	12.9	12.9	16.1	19.3	45.2	6.45	29	58.1	9.7	16.1	16.1
Ш	Glioblastoma G4	23	31.34	34.18	3.75	13	43.5	17.4	8.7	17.4	34.8	65.2	8.7	21.7	69.6	8.7	26.1	13
IV	Oligodendroglioma G2	12	2.25	3.14	3.63	50	25	0	25	0	8.3	33.3	25	50	25	0	8.3	0
v	Anaplastic G3 oligodendroglioma	11	14.72	17.02	4.69	45.5	27.3	18.2	9.1	0	0	36.4	18.2	54.5	63.6	0	18.2	9.1

Table 1. Proliferative activity, size, location and clinical symptoms in the respective study groups.

by Eneström et al. [2] (13.3 and 24.3 respectively). However, LI values, detected in glioblastomas, are consistent with those, reported by Kayaselcuk et al. [3]. Considerably higher PCNA LI values, reaching 67 in glioblastoma and 48.57 in anaplastic astrocytoma, were noted by Korkolopoulou et al. [4]. The differences in LI values, presented by various authors, may have resulted from the use of different fixation methods and research procedures [5, 6]. However, despite LI variations, in all the reports, the proliferative activity of gliomas shows a correlation with tumour grade [1, 3, 7]. This seems to indicate that the proliferation index can be used as an accessory parameter to differentiate between border grades [8]. Many authors believe that LI value is a significant survival index [9, 10, 11] and can be used to assess the risk of recurrence [3]. The present analysis showed a positive correlation between the proliferative activity of the tumours and their diameters within respective histological types. The activity was most enhanced in glioblastomas, which demonstrated the highest LI level but were the smallest in diameter. No correlation was found between the proliferative activity and tumour location.

We observed that the clinical symptoms and their severity varied among patients. The prevailing symptoms were conditioned mainly by tumour location and concomitant swelling, rather than by glioma size. When tumour location was the same, the clinical symptoms, especially intracranial hypertension, were more enhanced in patients with higher proliferative activity of the neoplastic cells.

References

- 1. Zimnoch L, Kozielec Z, Lewko J, Cylwik B, Mariak Z. Badania aktywności proliferacyjnej glejowych nowotworów mózgu. Neur Neurochir Pol, 1999; 33: 89-96.
- 2. Eneström S, Vavruch L, Franlund B, Nordenskjöld B. Ki-67 antigen expression as a prognostic factor in primary and recurrent astrocytomas. Neurochirurgie, 1998; 44: 25-30.

- 3. Kayaselcuk F, Zorludemir S, Gumurdulu D, Zeren H, Erman T. PCNA and Ki-67 in central nervous system tumors: correlation with the histological type and grade. J Neur Onkol, 2002; 57: 115-21.
- 4. Korkolopoulou PI, Christodoulou P, Papanikolaou A, Thomas-Tsagli E. Proliferating cell nuclear antigen and nucleolar organizer regions in CNS tumors. Correlation with histological type and tumor grade. Am J Surg Pathol, 1993; 17: 912-9.
- 5. Sallinen PK, Haapasalo HK, Visakorpi T, Helen PT, Rantala IS, Helin HJ. Prognostication of astrocytoma patient survival by Ki-67 (MIB-1), PCNA, and S-phase fraction using archival paraffin-embedded samples. J Pathol, 1994; 174: 275-82.
- 6. Torp SH. Diagnostic and prognostic role of Ki67 immunostaining in human astrocytomas using four different antibodies. Clin Neuropathol, 2002; 21: 252-7.
- 7. Kordek R, Biernat W, Alwasiak J, Liberski P. Proliferating cell nuclear antigen PCNA and Ki-67 immunopositivity in human astrocytic tumors. Acta Neurochir, 1996; 138: 509-13.
- 8. Stupp R, Janzer RC, Hegi ME, Villemure JG, Mirimanoff RO. Prognostic factors for low-grade gliomas. Semin Oncol, 2003; 30: 23-8.
- 9. Ang LC, Plewes M, Tan L, Begley H, Agranovich A, Shul D. Proliferating cell nuclear antigen expression in the survival of astrocytoma patients. Can J Neurol Sci, 1994; 21: 306-10.
- 10. McKeever PE, Strawderman MS, Bakhtiar Y, Mikhail AA, Mila B. MIB-1 proliferation index predicts survival among patients with grade II astrocytoma. J Neuropathol Exp Neurol, 1998; 57: 931-6.
- 11. Zagzag D, Blanco C, Friedlander DR, Miller DC, Newcomb EW. Expression of p27KIP1 in human gliomas: relationship between tumor grade, proliferation index, and patient survival. Hum Pathol, 2003; 34: 4448-53.