

## The basic morphological characteristics of astrocytomas in Vojvodina in the period 2001-2006

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### Summary

**Purpose:** Astrocytomas are the most common primary intracranial neoplasms. The aim of this investigation was to register the age, sex, tumor localization, frequency and histological types of patients with astrocytomas.

**Methods:** The investigation was carried out from January 2001 to June 2006 and included 490 consecutive patients of both sexes with diagnosed intracranial tumors, who had undergone surgical treatment at the Neurosurgery Clinic of the Clinical Centre of Vojvodina. Tumor histological studies were carried out in the Laboratory of the Centre for Pathology and Histology of the Clinical Centre of Vojvodina. Out of 490 patients with diagnosed intracranial tumors, 139 (28.4%) had astrocytomas.

**Results:** Astrocytomas were more frequent in males (63.3%) and were most common in the 50-59-year age group (39.5%). The most common localization was the frontal region (30.2%), more commonly on the right side (51.8%). In regard to other histological types of intracranial tumors, astrocytomas were more frequent in males (34.8%). Grade III astrocytomas were most common (55.4%). The frequency of hemorrhage and thrombosis showed a positive correlation with the histological grade of astrocytomas.

**Conclusion:** The typical patient with astrocytoma is a male of 50-59 years. The tumor is grade III located in the right frontal region.

**Key words:** astrocytoma, epidemiology

### Introduction

Astrocytic tumors belong to the group of neuroepithelial tumors (gliomas), characterized by infiltrative growth and variable biological behavior. Astrocytic tumors represent the most frequent intracranial tumors, making more than 60% of all primary brain tumors [1-3]. According to World Health Organisation (WHO) data, diffusely infiltrating astrocytomas have an annual incidence of 5-7 per 100,000, and anaplastic astrocytomas 0.17 per 100,000. Diffusely infiltrating astrocytomas are more frequent in males than in females (M:F=1.4-1.5 :1) [4]. Higher frequency in males than in females is also present in anaplastic astrocytomas (M:F=1.8:1) and glioblastomas (M:F=1.5:1) [5].

Astrocytoma grading is determined by 4 well - de-

finer characteristics: nuclear atypia, pathological mitoses, necrosis and proliferation of blood vessels [1,6]. Grade I astrocytoma does not contain any of these characteristics. Grade II astrocytoma contains one, mostly nuclear atypia, grade III astrocytoma shows two, mostly nuclear atypia and pathological mitoses, and grade IV astrocytoma displays 3 or all 4 characteristics [1,5,7].

Astrocytic tumors are characterized by numerous differences related to their localization, growth potential, tendency to progression, level of invasiveness, morphological picture and clinical characteristics (gender, age). These tumors include: diffuse astrocytoma (WHO grade II), anaplastic astrocytoma (WHO grade III), glioblastoma (WHO grade IV) (with subtypes of giant cell glioblastoma - WHO grade IV; and gliosarcoma - WHO grade IV), pilocytic astrocytoma (WHO grade I), pleomorphic

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xanthoastrocytoma (WHO grade II), and subependymal giant cell astrocytoma (WHO grade I) [1,4,5].

Diffuse astrocytoma is the term for a diffusely infiltrative tumor of astrocytic origin. It makes up 10-15% of all astrocytic tumors [3], and occurs mainly in adults aged between 40 and 50 years [4]. It is most frequently localized in the cerebral hemispheres [2,3], where it usually spreads over to the frontal lobe (44%) and temporal lobe (20%), but may occur anywhere within the central nervous system. It shows a special tendency to progress into a more malignant phenotype [1,5,8]. Macroscopically, diffuse astrocytoma may also spread to the white and grey brain matter. Its infiltrative growth often causes an increase of the affected brain structures, not sharply demarcated, and may spread to the opposite side [1,4,5]. The most common localization is supratentorial, both in children and adults, and the second most frequent one is the brain stem [8]. Microscopically, diffuse astrocytoma shows 3 histological characteristics (fibrillary, protoplasmic and gemistocytic subtypes), often occurring within the same tumor [3,7-9]. It is characterized by moderate cellularity and minimal nuclear atypia, with a diffuse, often microcystic pattern. Mitoses are rare or absent. Necrosis or signs of neovascularization are not present [1,4,5].

An important characteristic of astrocytic neoplasms is their progression into a more malignant phenotype, where diffuse astrocytoma (WHO grade II) shows a tendency to progress into anaplastic astrocytoma (WHO grade III) and secondary glioblastoma (WHO grade IV) [4,10,11].

Anaplastic astrocytoma occurs in middle-aged patients, around the age of 40. Glioblastoma is the most malignant and most common astrocytic tumor and, at the same time, the most common primary tumor of the brain in general [1,5]. It makes up 50-60% of all astrocytic neoplasms [4] and occurs mostly in adults between 45 and 60 years of age (primary glioblastoma), or earlier (secondary glioblastoma) [3,8,12].

Immunohistochemically, gliomas show different levels of glial fibrillary acidic protein expression (GFAP). If clearly confined GFAP negative focuses are found within the positive fields of GFAP, they represent new clones of tumor cells. In case of their progression into a malignant phenotype, very high frequency of TP53 gene mutation has been detected [1,4].

## Methods

The investigation covered a period from January 2001 to June 2006 and included a total of 490 consecutive patients of both sexes with diagnosed intracranial

tumors surgically treated at the Neurosurgical Clinic of the Clinical Centre of Vojvodina. Data were obtained from the patients' medical records and included age, gender, tumor localization and histological type. The surgical material was examined macroscopically at the Laboratory of the Centre for Pathology and Histology of the Clinical Centre of Vojvodina, and prepared for microscopic analysis by standard histological techniques used in the daily routine work. All histologic material was reexamined for the purpose of this study.

## Statistical analysis

Descriptive statistics included frequencies and percentages (for attributable parameters). Results were analyzed using the following nonparametric tests: Mann-Whitney test for data collected by ordinal scale, and chi-square test for frequency data. Data were analyzed using the statistical software SPSS for Windows.

## Results

Of 490 patients 253 (51.6%) were males and 237 (48.4%) females. In 139 (28.4%) patients, astrocytoma was histologically diagnosed.

Astrocytoma gender distribution showed 88 (63.3%) males and 51 (36.7%) females ( $p < 0.05$ ).

The patients' age distribution is presented in Table 1.

Regarding disease localization, astrocytomas were situated in the frontal region in 42 (30.2%) patients, in the temporal region in 35 (25.2%) patients, while 12 (8.6%) patients had astrocytomas located in the occipital region ( $p < 0.05$ ).

Concerning the frontal lobe, astrocytomas were found in 26 (29.5%) males and in 16 (31.4%) females.

Supratentorial astrocytomas were found in 124 (89.2%) patients, while 15 (10.8%) had infratentorially localized astrocytomas ( $p < 0.05$ ).

**Table 1.** Age distribution of patients

Age distribution (years)	Male		Female		Total	
	n	%	n	%	n	%
<40	9	10.23	9	17.65	18	12.95
40 - 49	23	26.14	4	7.84	27	19.42
50 - 59	28	31.82	13	25.49	41	29.50
60 - 69	19	21.59	19	37.25	38	27.34
>70	9	10.23	6	11.76	15	10.79
Total	88	100.00	51	100.00	139	100.00
Mean (range)	53.50 (30-77)		50.50 (26-75)		51.50 (26-77)	

Male vs. female,  $p < 0.05$

Astrocytomas were localized on the right side in 72 (51.8%) patients, on the left side in 63 (45.3%) and on both sides in 3 (2.2%) patients. Only 1 (0.7%) patient had astrocytoma localized in the middle line. Statistically highly significant difference was established in the distribution of astrocytomas on the observed sides (right vs. left side  $p < 0.05$ ).

The right cerebral hemisphere was the most common site of the observed astrocytomas in males (46 patients or 52.3%) and in females (26 patients or 51%).

Astrocytomas were more frequently localized on the right side of the temporal (23 patients or 65.7%) and occipital regions (8 patients or 66.7%). In the frontal (23 patients or 54.8%) and parietal regions (5 patients or 62.5%), astrocytomas were more frequent on the left side. Their frequency was even on the right and left sides of the posterior cranial fossa (1 patient or 50%).

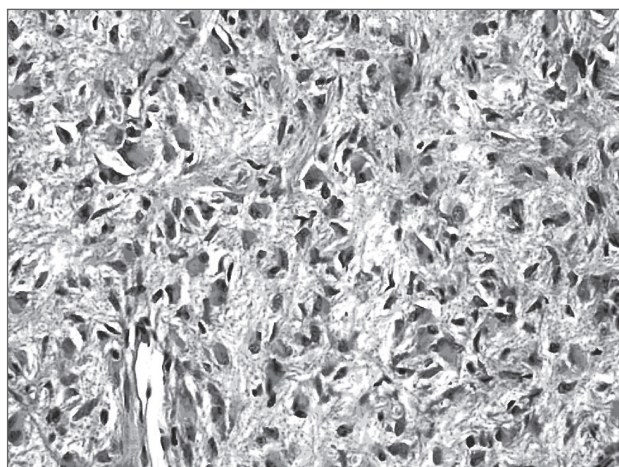
The histological analysis showed that astrocytomas were more frequent in males (88 patients or 34.8%) in comparison with other intracranial tumors. Statistically highly significant difference was established in the distribution of the histological types of intracranial tumors related to the patients' gender ( $p < 0.05$ ; Table 2).

Grade III astrocytomas were found in 77 (55.4%)

**Table 2.** Gender distribution of astrocytoma and other intracranial tumors

Gender	Astrocytoma		Other intracranial tumors		Total n
	n	%	n	%	
Male	88	34.80	165	65.20	253
Female	51	21.50	186	78.50	237
Total	139		351		490

Male vs. female and other intracranial tumors,  $p < 0.05$



**Figure 1.** Grade III astrocytoma.

(Figure 1) and grade IV in 30 (21.6%) cases, while grade I and II were found in 14 (10.1%) and 18 (12.9%) patients, respectively (grade I-II vs. grade III-IV,  $p < 0.05$ ).

It was established that all grades of astrocytomas were more frequent in males, except grade I astrocytomas which were more frequent in females (Table 3).

In all age groups, grade III astrocytomas were the most frequently found, except patients younger than 40 years of age, who mostly had grade I astrocytomas (5 patients or 27.8%).

No statistically significant differences in the distribution of the histological grades of astrocytomas related to the patients' age were established.

Haemorrhage and thrombosis were most frequent in grade III and grade IV astrocytomas.

## Discussion

The gender structure of the examined population with established astrocytoma showed significant differences between males and females ( $m:f=1.7:1$ ). The results of our study are in agreement with the literature data, indicating that astrocytomas occur more frequently in males than in females ( $M:F=1.4-1.5:1$ ) [1,13,14].

The age distribution of the patients with established astrocytomas showed that most of them (29.5%) were 50-59 years old, while patients older than 50 years prevailed (67.6%). In male patients, astrocytomas were most frequently present in the 50-59 age group (31.8%). Among all male patients, 63.6% were older than 50 years of age. Most of the female patients (37.2%) were 60-69 years old, while 74.5% of females were older than 50 years. The oldest patient with established astrocytoma was 77, and the youngest 26 years old. The average age of the patients included in the study was 51.5 years. Literature data indicate that astrocytomas occur after the 3rd decade of life, their number increasing up to the 5th and 6th decades of life, when they are most frequent [14,15].

The results of our study show that the frontal region was the most frequent localization of astrocytomas (30.2%; male: 29.5%; female: 31.4%). In 89.2% of the

**Table 3.** Gender distribution of various grades of astrocytoma

Astrocytoma	Male	Female	Total
Grade I	6	8	14
Grade II	11	7	18
Grade III	47	30	77
Grade IV	24	6	30
Total	88	51	139



cases astrocytomas were localized supratentorially, and only 10.8% of them were localized infratentorially. Our results agree with the literature data stating that astrocytomas are more frequent in the anterior than in the posterior cranial fossa, and that most astrocytomas are found in the frontal (40%) and temporal regions (20%) [16].

The results obtained point out that astrocytomas with temporal (65.7%) and occipital (66.7%) localizations were most frequent on the right side. In the frontal (54.8%) and parietal (62.5%) regions, astrocytomas were more frequent on the left side. The frequency of astrocytomas on the right side was equal to that on the left side of the cerebellum (50%).

The results of histological analysis of the observed astrocytomas showed prevalence of astrocytomas over other histological types of intracranial tumors in males. In the relevant literature, astrocytomas (M:F=1.4-1.5:1) and metastatic intracranial tumors (M:F=1.8:1) are more frequent in males, while meningiomas are twice as frequent in females [1,4].

More than half of the patients in our study had grade III astrocytomas (55.4%), followed by grade IV (21.6%), grade II (12.9%) and grade I (10.1%), in accordance with the results of other authors, indicating that among astrocytomas grades, the most frequent ones are grade III and IV, making about 38% of all primary intracranial tumors [17]. Other studies show that the most frequent astrocytoma is that of grade IV, making 50-60% of all astrocytic tumors [5,7,18,19]. The malignant forms of astrocytomas are more frequent as compared with their benign forms (70 and 30%, respectively) [16].

Analysis of the histological grades of astrocytomas showed that the most frequent astrocytoma, both in males and females, was astrocytoma grade III (53.4% and 58.8%, in males and females, respectively), in accordance with the results of other investigators [16,17].

Grade III astrocytomas were most frequent in all ages, except in patients younger than 40 years of age, in whom grade I astrocytoma was most frequently encountered (27.8%). Several authors have reported that these tumors mostly occur after the 3rd decade of life and that their incidence is increasing up to the 5th and the 6th decades of life, when they are most frequent [14,15].

Like other investigators [1-3,5,20] the results of this study showed that the frequency of haemorrhage and thrombosis was positively correlated with the histological grade.

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