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BRAIN TUMORS AND EPILEPSY

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SUMMARY – Brain tumors are a common cause of epilepsy. Tumor type and location are determining factors that significantly influence seizure frequency. The aim of this study was to analyze clinical data of patients diagnosed with brain tumors and epilepsy. Data for this study were obtained from patient medical records over a 6-year period (2000-2005). Patient history and findings obtained by diagnostic methods such as electroencephalography, computerized tomography and magnetic resonance were analyzed. Data were analyzed by appropriate statistical methods and the structure, prevalence, mean and standard deviation were calculated. The significance of results was tested by use of t-test and χ^2-test. A total of 15 933 patient charts were analyzed. Out of 15 933 patients, 10.8% were diagnosed with epilepsy and 175 (1.09%) patients had brain tumor, 75 (42.86%) of which were significantly associated with epilepsy (P>0.05). Almost forty-three percent (42.86%) of tumors were epileptogenic, with no significant sex difference (confidence level of 95%). Fifty-seven (32.5%) brain tumor patients were aged 51-60. The mean age of all patients with brain tumors was 41.6 years. Focal sensorimotor seizures were dominant in 40 (53.3%) cases. Among epilepsy cases with known etiology, 75 (6.8%) patients had epileptogenic tumors. Types of seizures in patients with epilepsy were different from seizures provoked by brain tumors. The most common tumor site was temporal region (43.4%). There was no significant difference according to epileptogenesis. Focal sensorimotor seizures were common in patients with frontal and parietal region tumors.

Key words: *Brain neoplasms – complications; Brain neoplasms – diagnosis; Epilepsy – diagnosis; Epilepsy – etiology; Epilepsy – statistical and numerical data*

Introduction

The term brain tumor refers to a variety of different neoplasms, each with its own biology, prognosis and treatment. These tumors are better identified as 'intracranial neoplasms', since some do not arise from brain tissue[1]. Brain tumors are a common cause of epilepsy. Intracranial tumors can disrupt normal electrical functional patterns of the brain. Tumor type and location are determining factors that significantly influence seizure frequency. More than one-third of 30,000 patients with newly diagnosed brain tumor *per* year develop epileptic seizures[2]. Seizures occur in at least 50% of cases when the tumor involves the hemispheres.

Developmental tumors, slow growing tumors, hemorrhagic tumors and multiple metastases carry a high risk of seizure occurrence. Genetic factors, as well as multi-drug resistance proteins associated with brain tumors have an important role in epilepsy refractoriness[3].

Seizure frequency is determined by tumor type and location. Benign tumors, as well as tumors with low malignant potential, and tumors with slow progression carry high epileptogenic potential.

Higher epileptogenic potential was observed in supratentorial tumors in the fronto-temporal region

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(80%) and fronto-parietal region (71%). Infratentorially localized tumors had epileptogenic potential in about 2.5% of cases[4]. Tumors that caused seizures were present in all age groups, with a peak incidence between age 35 and 40. The incidence of tumor epileptogenicity significantly declined to 2%-8% at age 65 and older, as well as in childhood where this percentage was even lower (1%-3%)[4].

Complex partial seizures are most commonly triggered by epileptogenic brain tumors.

Patients and Methods

Patient history data and electroencephalography (EEG), computerized tomography (CT) and magnetic resonance (MR) reports were analyzed. Data were collected for the 2000-2005 period and analyzed by staff members of the University Department of Neurology, University Clinical Center of Kosova. Statistical analysis was performed and the structure, prevalence, mean and standard deviation were calculated. Results were tested for significance by t-test and χ^2-test.

Results

We analyzed 15933 patient history charts. All patients were hospitalized during the six-year period, between 2000 and 2005. There were 1725 (10.8%) patients diagnosed with epilepsy (different types) and 175 (1.09%) patients diagnosed with brain tumor. More than forty percent of patients (75 patients; 42.86%) had a brain tumor associated with epilepsy; there was no statistically significant sex difference. The remaining 100 (57.14%) patients with brain tumor were free of seizures (P>0.05) (Table 1, Fig. 1).

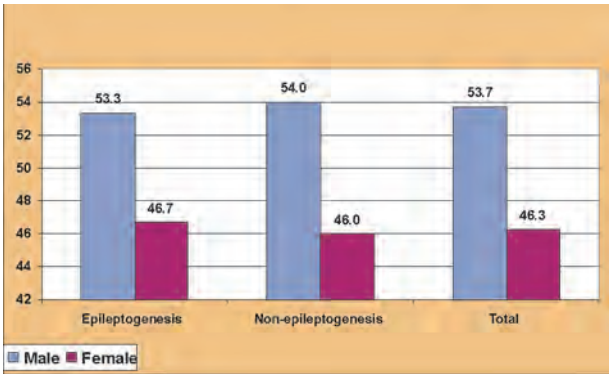

Fig. 1. Brain tumors, epileptogenesis and sex.

Study results pointed to a statistically significantly higher prevalence of brain tumors in the 51-60 and 41-50 age groups, with 57 (32.57%) and 45 (25.71%) cases of brain tumor, respectively, as compared with other age groups. Analysis showed a significantly higher prevalence of epileptogenic tumors in these two age groups (69.33%) as compared with non-epileptogenic tumors in the same age groups (50.00%). Epileptogenic tumors accounted for 58.28% of all brain tumors (Table 2, Fig. 2).

Different types of epileptic seizures were noted in epileptogenic tumors. The dominant types of seizures were focal sensorimotor seizures, which were present in 40 (53.3%) cases, followed by focal seizures (complex crises) in 15 (20.0%) and generalized seizures in 13 (17.3%) cases. Epileptogenic tumors rarely presented with other types of seizures (Table 3).

Our study included 1108 epilepsy cases of known etiology. Epileptogenic tumors accounted for 6.8% (n=75) of all epilepsy cases of known etiology. This rate varied according to the type of seizures: focal seizures with secondary generalization were present in 13.9%, focal seizures (complex crisis) in 12.2%, and

Table 1. Brain tumors, epileptogenesis and sex

Sex		Brain tumors					
		Epileptogenic		Non-epileptogenic		Total	
		n	%	n	%	n	%
Male		40	53.33	54	54.00	94	53.71
Female		35	46.67	46	46.00	81	46.29
Total	N	75	100.00	100	100.00	175	100.00
	%	42.86*	–	57.14	–	100.00	–

*Less than half (42.86%) were epileptogenic tumors, with no significant sex difference at confidence level of 95%; P>0.05.

Table 2. Brain tumors, epileptogenesis and age

Age group (yrs)	Tumors				Total	
	Epileptogenic		Non-epileptogenic			
	n	%	n	%	n	%
≤10	0	0.00	2	2.00	2	1.14
11-20	2	2.67	3	3.00	5	2.86
21-30	3	4.00	15	15.00	18	10.29
31-40	11	14.67	20	20.00	31	17.71
41-50	25	33.33	20	20.00	45	25.71
51-60	27	36.00	30	30.00	57	32.57
>60	7	9.33	10	10.00	17	9.71
Total	75	100.00	100	100.00	175	100.00
Mean age*	44.1		39.3		41.6	
SD	14		17.1		16	

*The mean age of all patients with brain tumors was 41.6 years, ranging from 39.7 years in non-epileptogenic cases to 44.1 years in epileptogenic cases.

generalized seizures in 3.2% of cases. There was no case associated with generalized form and petit mal seizures (Table 4).

In patients with epileptogenic brain tumors, the types of epileptic seizures differed from those recorded in epilepsy patients. Brain tumor patients showed a higher prevalence (53.3%) of focal sensorimotor seizures as compared with epilepsy patients (46.0%). Focal seizures (complex crisis) were present in 20.0% of patients with epileptogenic brain tumors *versus* 11.1% of epilepsy patients. Generalized seizures were the least common, present in 17.3% of patients with epileptogenic brain tumors, in comparison with 36.2% in epilepsy patients (Table 5).

The most common location of brain tumors was temporal region, recorded in 76 (43.4%) patients, followed by parietal region in 51 (29.1%) and frontal region in 43 (24.0%) patients. Brain tumors were rarely found in occipital region, with only 6 (3.4%) cases. According to epileptogenesis, there were no significant differences between epileptogenic and non-epileptogenic tumors (Table 6).

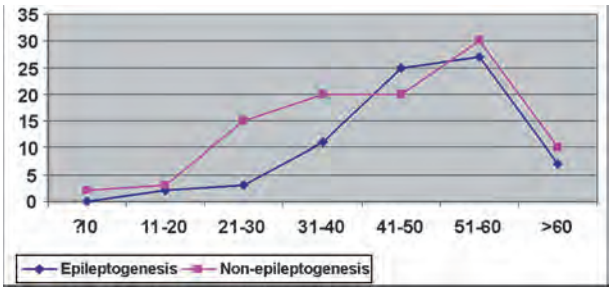

Fig. 2. Brain tumors, epileptogenesis and age (yrs).

Table 3. Structure of epileptic seizures in association with epileptogenic tumors

Types of epileptic seizures	n	%
Focal sensorimotor seizures	40	53.3
Generalized seizures	13	17.3
Focal seizures	15	20.0
Focal seizures with secondary generalization	5	6.7
Association of generalized seizures and psychomotor	2	2.7
Petit mal seizures		0.0
Association of generalized seizures and petit mal		0.0
Total	75	100.0

Table 4. Types of epileptic seizures and prevalence of epileptogenic tumors

Types of epileptic seizures	Total N	Tumors	
		n	%
Focal sensorimotor seizures	510	40	7.8
Generalized seizures	401	13	3.2
Focal seizures (complex crisis)	123	15	12.2
Focal seizures with secondary generalization	36	5	13.9
Association of generalized and psychomotor seizures	22	2	9.1
Petit mal	14		0.0
Association of generalized and petit mal seizures	2		0.0
Total	1108	75	6.8

P<0.01

Table 5. Types of epileptic seizures and comparison of structure between epileptogenic tumors and epilepsy

Types of epileptic seizures	Epilepsy		Tumors	
	n	%	n	%
Focal sensorimotor seizures	510	46.0	40	53.3
Generalized seizures	401	36.2	13	17.3
Focal seizures (complex crisis)	123	11.1	15	20.0
Focal seizures with secondary generalization	36	3.2	5	6.7
Association of generalized and psychomotor seizures	22	2.0	2	2.7
Petit mal seizures	14	1.3		0.0
Association of generalized and petit mal seizures	2	0.2		0.0
Total	1108	100.0	75	100.0

P<0.01

Table 6. Location of brain tumors based on epileptogenesis

Region	Tumors				Total	
	Epileptogenic		Non-epileptogenic			
	n	%	n	%	n	%
Temporal	34	45.3	42	42.0	76	43.4
Frontal	19	25.3	23	23.0	42	24.0
Parietal	20	26.7	31	31.0	51	29.1
Occipital	2	2.7	4	4.0	6	3.4
Total	75	100.0	100	100.0	175	100.0

P>0.05

The types of epileptogenic seizures depend greatly upon tumor location and show considerable differences. Focal sensorimotor seizures were more common in tumors localized in frontal and parietal region, whereas focal seizures (complex crisis) were more common in temporal region (Table 7).

Discussion

Results of our study pointed to a high correlation between brain tumors, their location, and epilepsy seizures. Malignity level and location determine the rhythm and frequency of the onset of crisis. Benign

Table 7. Location of brain tumors and epileptic seizures

	Region				Total
	Temporal	Frontal	Parietal	Occipital	
Focal sensorimotor seizures	10	16	14		40
Generalized seizures	5	2	5	1	14
Focal seizures (complex crisis)	15				15
Focal seizures with secondary generalization	3	1	1		5
Association of generalized and psychomotor seizures	1			1	2
Total	34	19	20	2	75

brain tumors, tumors with low malignity potential, and slowly progressive tumors have high epileptogenic potential[13]. Our study showed that epileptic status and petit mal seizures were a rare manifestation of brain tumors.

The frequency of epileptic seizures in epileptogenic tumors depends on tumor location, especially on tumor penetration into the cortex[13]. Seizures can start either in the localized area of the cortex (partial or focal seizures), or diffusely throughout the brain (generalized seizures)[14].

Out of our 175 patients with brain tumors, 75 (42.86%) patients developed epileptic seizures. Similar results have been presented in fact sheet of a brain tumor society, where 30%-40% of brain tumors are complicated by epilepsy[8].

Globally, brain tumors show a male predominance. In our study, there were 53.7% of male and 46.3% of female patients, also yielding a male predominance, however, without statistical significance. Similar results were obtained by Bromfield, where the range was 10%-20%[15].

According to age groups, epileptogenic and non-epileptogenic brain tumors were more common in the 51-60 age group. The mean age of all patients with brain tumors was 41.6 years, while the mean age of patients with epileptic seizures was 44.1 years. Our results on the patient mean age are generally consistent with literature data[5,10].

Focal sensorimotor seizures were predominant manifestation of epileptogenic tumors in 53.3% of cases. Complex crisis or focal seizures were present in 20.0% of cases. Other types of seizures were very rare. Our results are in concordance with the data shared by epilepsy experts[16,17].

Epileptogenic tumors accounted for 6.8% of all epilepsy cases of known etiology. This rate varied according to the type of seizures, yielding a predominance of focal seizures with secondary generalization (13.9% of cases).

In all brain tumors, the rate of focal sensorimotor seizures was higher in comparison with epilepsy cases (53.3% *vs*. 46%). The rate of focal seizures was 20.0% in comparison to 11.1% in epilepsy cases. Generalized seizures were rarely present. Rosenow and Ludders report on similar data[12]. Brain tumors were rarely localized in occipital region. They were predominantly localized in temporal region (43.4%), parietal region (29.1%) and frontal region (24.0%). These results are consistent with other literature reports[18]. Our study showed the type of epileptogenic seizures to depend on the location of brain tumors. Focal sensorimotor seizures were more common in tumors localized in frontal and parietal regions. Focal seizures (complex crisis) were most common in temporal region. Comparable results have been reported in the literature[3,19].

Conclusion

Study results indicated strong correlation between brain tumors and epilepsy. Brain tumors were equally present in both sexes, without significant difference. Brain tumors were more common in the 51-60 age group. The type of seizures was found to be determined by the location of epileptogenic tumor. The elements of epileptogenesis concerning tumor biology and rate of tumor growth were not analyzed.

Based on the state-of-the-art in the field, our study results on anatomic and morphological changes may be viewed as a new concept of the enigmatic epileptic

crisis pathophysiology caused by the presence of brain tumor. Definitive answer belongs to the future.

We believe that the data presented may aid many general practitioners in patient evaluation, especially in our region, since this is the first paper presenting such data.

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Sažetak

TUMORI MOZGA I EPILEPSIJA

V. Govori, I. Humolli, M. Cepreganov, I. Dedushaj i *B. Gjikolli*

Tumori mozga su čest uzrok epilepsije. Vrst tumora i lokalizacija su odlučujući čimbenici koji značajno utječu na učestalost konvulzija. Cilj ove studije bio je analizirati kliničke podatke bolesnika s dijagnosticiranim tumorom mozga i epilepsijom. Podaci za studiju prikupljeni su iz medicinske dokumentacije bolesnika kroz 6-godišnje razdoblje, od 2000. do 2005. godine. Analizirani su anamnestički podaci i nalazi dobiveni dijagnostičkim metodama poput elektroencefalografije, kompjutorizirane tomografije i magnetske rezonancije. U analizi su se primijenile odgovarajuće statističke metode, te je izračunata struktura, učestalost te srednja vrijednost i standardna devijacija. Značajnost rezultata ispitana je pomoću t-testa i χ^2-testa. Analiza je obuhvatila 15933 bolesničkih kartona. Od 15933 bolesnika epilepsija je bila dijagnosticirana u 10,8%; 175 (1,09%) bolesnika je imalo tumor mozga, od kojih je 75 (42,86%) bilo značajno udruženo s epilepsijom (P>0,05). Gotovo je 43% (točnije, 42,86%) tumora bilo epileptogeno, bez značajne razlike prema spolu, na razini pouzdanosti od 95%. Utvrđeno je 57 (32,5%) slučajeva tumora mozga među bolesnicima u dobi od 51 do 60 godina. Srednja dob svih bolesnika s tumorom mozga bila je 41,6 godina. Žarišni senzomotorni napadaji prevladavali su u 40 (53,3%) bolesnika. Među bolesnicima s epilepsijom poznate etiologije 75 (6,8%) ih je imalo epileptogene tumore. Vrste napadaja u bolesnika s epilepsijom razlikovale su se od napadaja izazvanih tumorom mozga. Najčešće mjesto tumora bilo je temporalno područje (43,4%) i nije bilo značajne razlike u odnosu na epileptogenezu. Žarišni senzomotorni napadaji bili su česti u bolesnika s tumorima frontalnog i parietalnog područja.

Ključne riječi: *Novotvorine mozga – komplikacije; Novotvorine mozga – dijagnostika; Epilepsija – dijagnostika; Epilepsija – etiologija; Epilepsija – statistički i brojčani podaci*