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Epilepsy associated with neoplastic brain tumours. A clinical study

Padaczka w przebiegu nowotworów ośrodkowego układu nerwowego.
Analiza kliniczna

Primary neoplastic tumours of the brain, accounting for 2% of malignant neoplasms in man as well as metastases to the brain occurring in the course of 1/3 systemic neoplasms are associated with severe neurological functional disturbances and high death risk (6, 9). That is why the earliest possible diagnosis is essential for treatment and prognosis. The classical triad of clinical symptoms of the brain tumour including focal symptoms, increased intracranial pressure and epileptic seizures is now found in less than 15% of the patients due to, among others, neuroimaging enabling the recognition of tumours at an early, oligosymptomatic stage of development (3). Epileptic incidences occur in about 30–60% cerebral neoplasms incidence depending on the localisation and histopathologic characteristics as well as the age of patients (6, 9). There is also emphasised the importance of neoplastic brain tumours in the epidemiology of late epilepsy. According to Dam about 10–20% of epilepsies of adults are symptomatic cases associated with brain tumour (4). In 8% patients over 15 years of age the first epileptic seizure is associated with brain tumour which constituted the fourth most frequent etiologic factor of the disease after stroke, consequences of alcoholism and neuroinfections and the risk of tumour associated with epilepsy increased with age: in patients over 45 years, in 12% cases the first epileptic seizure was caused by brain tumour, as the second commonest cause of disease after stroke (13).

OBJECTIVE

The aim of the study was to analyse clinical characteristics of primary and metastatic brain tumours in adult patients in whom epileptic seizures determined taking up diagnostic procedures.

MATERIAL AND RESULTS

In 1990–1996 the Department of Neurology hospitalised 172 patients aged from 15 – 88 years (mean age 57.02) with brain tumours recognised according to diagnostic criteria and the picture of pathologic changes in CT neuroimaging and/or MRI of the head. In 124 patients (72.1%) a primary neoplastic tumour was found and the remaining 48 (27.9%) metastatic process to the brain was observed. In 39 patients (23%; 17 women, 22 men, mean age 51.5) in the pre–diagnostic period epileptic seizures occurred. In this group of patients CT examination revealed a primary neoplastic tumour in 22 patients (56.4%), metastatic process in 12 patients (30,8%) and hypodensic pathological area which did not meet neuroimaging criteria of the proliferative process in 5 patients (12.8%). Repeated CT examinations after sometime or direct MRI scans confirmed in 3 doubtful cases the suspicion of the primary tumour and in 2 patients metastatic changes which were the first detected localisation of the neoplastic process. The final ratio of primary to metastatic tumours with epileptic seizures amounted to 25:14 (64.1%:35.9%). Neoplastic changes were always localised in the supratentorial area. In patients with primary process meningioma in the sella region was recognised in one case, in all the remaining cases tumours of glial origin growing infiltrating way in the brain hemispheres with (n = 9) or without (n = 15) penetration of corpus callosum.

In 172 of the analysed patients epileptic seizures preceding diagnosis occurred in 20.2% patients with a primary tumour and in 29.2% with metastases to the brain mean age was 45.1 and 66.1 years respectively. The ratio of women to men in the compared groups was 12:13 and 5:9. In primary tumours with accompanying epilepsy the prevailing localisation was in the right (n = 14; 56%) over the left hemisphere (n = 7; 28%) or in the middle cerebral area (n = 4; 16%; in 3 patients infiltration of the structures in both hemispheres and of the corpus callosum). In most patients (n = 15; 60%) the lesion area involved one lobe: frontal (n = 6), parietal (n = 5), temporal (n = 3) or occipital (n = 1). In the remaining patients (n = 9; 36%) the tumour was localised between the temporal and parietal (n = 3), temporal and frontal (n = 2), temporo–parieto–occipital (n = 1) or in deep structures of both hemispheres (n = 3). Neoplastic metastases were localised subcortically; a change was visualised in 5 patients, in 5 – two, in 4 – three metastatic foci. Most changes were found in the left hemisphere (n–16 out of 27) and in frontal lobes (n = 10) or temporal (n = 8), more rarely in parietal ones (n = 6) and occipital (n = 3). In 6 out of 14 patients (42.9%) with metastases to the brain primary localisation of the tumour was not known and neurological symptoms preceded other symptoms of the disease. In the remaining 8 patients (57.1%), the previously recognised process involved the lungs (micro–cellular cancer – 4 patients – 28.6%), breast cancer (2 patients – 14.3%), renal cancer (1 patient – 7.1%) or it was melanoma of the eye–ball (1 patient – 7.1%).

In EEG examination the most frequently observed was abnormal recording without characteristic features – generalised deceleration of medium degree (14 patients – 35.9%) or disseminated acute waves (8 patients – 20.5%). In 11 patients (28%) there was found a focal recording of free theta–delta waves and 6 patients (15.4%) a focal recording exhibiting deceleration type to the delta frequency with seizure profile of high voltage acute waves.

In 20 out of 39 patients (51.3%) epileptic seizure was the first symptom of the pathologic process in the brain. In 17 of them (44%) physical examination did not reveal any other abnormal symptoms and in 3 remaining patients (8%) elements of psychooorganic syndrome or hemiparesis were found. In 19 patients (48.7%) the following findings were previously observed: focal symptoms (n = 6; 15.4%), psychoorganic syndrome or intracranial hypertension (2 patients each – 5.1%) or two or three abnor-

mal symptoms at the same time (n = 9; 23.1%). Additional epileptic seizures were the disorder deciding about taking up the diagnostic procedures. In 5 patients in whom preliminary CT examination did not allow to recognise the tumour epileptic seizures were the first and only disturbance of CNS functioning.

Epileptic seizures were observed between the first day to 13 months before hospitalisation except one patient with meningioma picture in CT in whom sporadic seizures lasted up to 10 years. A single seizure occurred in 6 patients (15.4%), two in 12 patients (30.8%), three – in 8 patients (20.5%) and more than three in 13 patients (33.3%). In patients with the primary tumour the most frequent seizures were partial simple ones (focal) of the motor type (less frequently sensoric ones) or generalised convulsive primary seizures (9 patients each – 36%). Focal seizures with secondary generalisation or partially complex were found in 3 patients each – 12%. In one case epileptic state of generalised convulsive seizures occurred (4%). In patients with metastases partial simple seizures prevailed (7 patients – 50%). Primary generalised seizures were found in 4 patients (28.5%) and secondary generalised ones in one patient (7.1%). Epileptic state was found in 2 patients (14.3%).

DISCUSSION

In our study epileptic seizures occurred in 23% patients with neoplastic process in the CNS. Constituting an early clinical symptom, which is consistent with findings of other authors (12, 14). In nearly half of patients sporadic epileptic seizures in the preceding year were still the only symptom of cerebral neoplasm at the moment of its detection by neuroimaging. More frequently they accompanied metastases, which was found in 29% patients, than primary brain tumours. In 43% patients with metastases to the brain epileptic seizure was also the first symptom of neoplastic process of unknown primary localisation. Primary tumours associated with epilepsy were found equally often in women and men, usually in the fifth decade of life and metastases to the brain, mainly of lung cancer, more, frequently occur in men (64.3%) and older patients. Observations of Delarive and others (5) are comparable with our material as for the frequency of metastases changes in the brain with accompanying epilepsy, i.e. 31%, mainly as complications of lung cancer, also similar commonest localisation of changes in frontal lobe mostly in men (71%).

Metastases to the brain are most common in the course of lung cancer, breast cancer and melanoma. These neoplasms are more likely to give multiple metastases, which has been confirmed by this study (10). The earliest metastases to the brain, within 6 to 9 months are given by lung cancer but clinical symptoms of metastases can occur side by side with the primary focus or even precede them which has also been confirmed by our observations (5).

Clinical symptomatology of brain tumours in patients in the study group with epileptic seizures which were sometimes preceding or even the only symptoms could result from the localisation and type of recognised neoplasms. Primary tumours were most often localised in the frontal, parietal, temporal lobe or at the edge of the temporal lobe of the right brain hemisphere, which is in most people functionally subsidiary, and in neuroimaging had features of gliomas with slow developmental dynamics. Metastatic lesions, though with distinctly smaller volume had similar localisation in subcortical structures of individual lobes but more often in the left hemisphere. Gliomas make up over 50% of brain tumours occurring in adults and in 90% cases they grow in deep parts of frontal, temporal lobe or temporal edge (2). Convulsions occur in over half of patients with all kinds of gliomas, more often than focal symptoms of psychoorganic syndrome, usually being the first symptom of this

Table 1. Primary and metastatic neoplastic tumors in CNS in investigated population (n = 172)

Type of neoplasms:	N		%	
	total	with epilepsy	total	with epilepsy
Primary	124	25	72.1	14.5
Metastatic	48	14	27.9	8.5
Total	172	39	100	23

Table 2. Localisation of primary neoplastic tumors with epileptic fits in CNS (n = 25)

Localisation of tumors:	% of cases
Right hemisphere	56
Left hemisphere	28
Both right and left	16
Total	100
Frontal lobe	24
Parietal lobe	20
Temporal lobe	12
Occipital lobe	4
Total	60
Subcortical profound structures	16
Fronto-temporo-occipital joint	24
Total	40

Table 3. Derivation of metastases in CNS
(total n = 14)

Primary location of neoplasms with meta in CNS	N	%
Unknown	6	42.9
Lungs	4	28.6
Breast	2	14.3
Melanoma	1	7.1
Kidney	1	7.1

pathologic process. The highest risk of epileptic seizures concerns gliomas with a high degree of histologic differentiation, slowly growing in the case of which epileptic seizures are the commonest symptom in 86.5% patients. However, in multiform gliomas with fart development convulsive attacks are found in about 29% patients (1). Besides convulsions are more likely in the case of tumours growing in the so–called epileptogenic areas, i.e. in the fronto–parietal region or temporal lobe (7). This localisation also affects the morphology of seizures; in most patients focal, mainly motoric seizures occur, sometimes secondarily generalised in the so–called Jackson march and epileptic state as the first manifestation is a complication found in only 11.5% patients but characteristically difficult for controlling with drugs (11, 12). Similar types and frequency of epileptic seizures were observed in our material.

In 12% patients CT examinations assessing the brain in thin 4 mm layers and using contrast enhancement was not sufficient for differential diagnosis at the lesion. However single hypodensic changes found in CT pictures had at the same time typical features of neoplastic process. In MRI about 6% brain tumours are incorrectly recognised in CT imaging, usually as vasculogenic lesions, ischaemic, less frequently haemorrhagic ones (8, 15). In patients with an earlier neoplastic disease of extracerebral localisation a single supratentorial hypodensic area in 90% cases turns out to be a metastasis while in patients without neoplasm in past history, confirmation of neoplastic aetiology is obtained in 15% of such changes (8). Moreover, in patients with a single metastatic focus in CT imaging, NMR examination reveals at the same time numerous metastases in the brain (14). In EEG only in 15% epileptic seizures associated with neoplastic lesions in the brain we found focal recordings to be consistent with CT/MRI pictures. In studies comparing the usefulness of various diagnostic methods only about 10–20% tumours in CNS coursing with epileptic seizures were accompanied by paroxysmal activity in EEG examinations and neuroimaging was considerably more useful for localising the epileptogenic focus (2, 15, 16). In our material every fifth patient with brain tumour had sporadic focal or generalised convulsive seizures as an early and sometimes the only symptom of the primary process which was localised more frequently in the right cerebral hemisphere or of

metastases to the brain despite the lack of data about earlier neoplastic disease. Patients with the fast epileptic seizures in adult life, especially, if they do not belong to the risk group for cerebro-vascular diseases should undergo a very thorough CT examinations, and in doubtful cases also early MRI of the head.

CONCLUSIONS

1. In every fifth adult patient with neoplastic process in CNS epileptic seizure were an early and often the only symptom of the organic process.

2. Epileptic seizures, usually focal or generalised convulsive ones accompanied supratentorial tumours: gliomas in the right cerebral hemisphere and single or multiple metastases of Jung or breast cancer.

3. Epileptic seizures were sometimes the first clinical symptom in the so far asymptomatic neoplastic process of unknown primary localisation.

4. MRI examination had conclusive diagnostic value in cases of symptomatic epilepsy at an early stage of tumour growth in CNS, where no characteristic CT pictures and EEG changes were found.

REFERENCES

1. Berger M.S., Keles E.: Epilepsy associated with brain tumors. [In:] Brain Tumors – An Encyclopedic Approach. Red.: A.H. Kaye, E.R. Laws Jr., Churchill, Livingstone, 239, 1995.
2. Black P.M.: Brain tumors, II. N. Engl. J. Med., 32, 1555, 1991.
3. Brody A.S.: New perspectives in CT and MRI imaging. Neurol. Clin., 9, 273, 1991.
4. Dam A.M. et al.: Late onset epilepsy: Etiologies, type of seizures and value of clinical investigation, EEG and computerized tomography scan. Epilepsia, 26, 227, 1985.
5. Delarive J., de-Tribolet N.: Cerebral metastases: a study of the surgical series of 81 cases. Neurochir., 38, 89, 1992.
6. Ettinger A.B.: Structural causes of epilepsy: tumors, cysts, stroke and vascular malformations. Neurol. Clin., 12, 41, 1994.
7. Morris H.H. et al.: Chronic intractable epilepsy as the only symptom of primary brain tumor. Epilepsia, 34, 1038, 1993.
8. Patchel R. et al.: A randomised trial of surgery in the treatment of single metastases. N. Engl. J. Med., 322, 494, 1990.
9. Salcman M.: Malignant glioma management. Neurosurg. Clin. North Amer., 1, 49, 1990.
10. Sawaya R., Bindal R.K.: Metastatic brain tumors. [In:] Brain Tumors – An Encyclopedic Approach. Red.: A.H. Kaye, E.R. Laws Jr., Churchill, Livingstone 1995, 923, 1995.
11. Sanders K.M., Murray G.B.: Geriatric epilepsy: a review. J. Geriatr. Psychiatry Neurol., 4, 98, 1991.
12. Scheuer M.L., Cohen J.: Seizures and epilepsy in the elderly. Neurol. Clin., 11, 78, 1993.
13. Sempere A.P. et al.: First seizures in adults : a prospective study from the Emergency Department. Acta Neurol. Scand., 12, 41, 1982.

14. Thomas R.J.: Seizures and epilepsy in elderly. Arch. Int. Med., 157, 605, 1997.
15. Yue N.C.: Advances in brain tumors imaging. Curr. Opin. Neurol., 6, 831, 1993.
16. Quesney L.F. et al.: Presurgical EEG investigation in frontal lobe epilepsy. Epilepsy Res., 5 (Suppl.), 55, 1992.

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STRESZCZENIE

U 23% spośród kolejnych 172 dorosłych pacjentów z nowotworem w ośrodkowym układzie nerwowym wystąpiły napady padaczkowe jako objaw wczesny, częściej w przerzutach (29,2%) niż w guzach nowotworowych pierwotnych (20,2%). U 44% chorych sporadyczne napady padaczkowe stanowiły objaw wyłączny, w pozostałych przypadkach poprzedzone były innymi objawami osiowymi guza mózgu. Najczęściej występowały napady ogniskowe ruchowe lub uogólnione drgawkowe; stan padaczkowy stanowił rzadkie zaburzenie. Guzy pierwotne z padaczką ,stwierdzano równie często u kobiet i mężczyzn młodszych (śr. 45,1 l), a przerzuty, głównie z płuc lub sutka, częściej u starszych mężczyzn (śr. 66,1 l). Lokalizacja zmian nowotworowych dotyczyła struktur nadnamiotowych. W neuroobrazowaniu guzy pierwotne miały cechy glejaków, najczęściej umiejscowionych w płacie czołowym lub ciemieniowym półkuli prawej. U 12% chorych obrazy KT były niejasne, a badanie MRI miało wartość rozstrzygającą w rozpoznaniu nowotworu. Ogniskowy zapis EEG z cechami drażnienia stwierdzono zaledwie u 15% chorych. W ustalaniu przyczyny pierwszego napadu padaczkowego w wieku dojrzałym, przy braku czynników ryzyka dla chorób naczyniowych mózgu, należy uwzględnić przede wszystkim nowotwór mózgu; wczesne badanie MRI jest rozstrzygające wobec wątpliwości diagnostycznych.