

BRAIN TUMOURS IN SOUTH BRAZIL

A RETROSPECTIVE STUDY OF 438 CASES

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SUMMARY — All brain tumours diagnosed since 1967 in a University Hospital in the Southern region of Brazil were reviewed and clinical information concerning age, sex, symptoms and evolution were analysed. 88.1% of tumours were primary neoplasms and the rest secondary deposits. There was a male predominance and the second and fifth decades of life were the most affected. The main presenting symptoms were headache, vomiting, hemiparesis, loss of vision and epilepsy. The commonest tumour was of astrocytic origin (36.3%) amongst which the malignant ones, including glioblastoma multiforme, predominated. These tumours were frequent in the cerebral hemispheres (31.3%), particularly in the frontal lobes. The time of evolution from the beginning of the clinical manifestations until the first hospital admission was also studied. The authors discuss the clinical and pathological observations in relation to other large series analysed in the literature.

Tumores cerebrais em região sul do Brasil: estudo retrospectivo de 438 casos.

RESUMO — Todos os tumores diagnosticados no Hospital de Clínicas da Universidade Federal do Paraná desde 1967 até o final de 1988 foram revistos e informações clínicas sobre idade, sexo, sintomas e evolução foram comparados aos tipos histológicos. 88,1% dos tumores corresponderam a neoplasias primárias e o restante a metástases. Verificou-se predominância de acometimento no sexo masculino e nas segunda e quinta décadas de vida. Os sintomas principais foram cefaléia, vômitos, hemiparesia, perda de visão e epilepsia. Os tumores mais frequentes corresponderam aos de origem astrocitária (36,3%) destacando-se o glioblastoma multiforme. Estes tumores acometeram hemisférios cerebrais (31,3%), particularmente os lobos frontais. O tempo de evolução desde o início das manifestações clínicas até a primeira admissão hospitalar foi também estudado. Neoplasias malignas, como glioblastoma e meduloblastoma, têm evolução rápida enquanto meningiomas podem levar anos para manifestarem-se clinicamente. Os autores comparam suas observações clínicas e histopatológicas com outras grandes séries estudadas na literatura.

This article presents a review and tabulation of all the central and peripheral nervous system tumours diagnosed in the last twenty-two years in the Department of Pathology, University of Parana, Brazil. This unit examines all the surgical pathology from the largest general hospital in the metropolitan area of Curitiba which is the one and a half million inhabitants capital of the State of Parana in the southern region of Brazil. We aim to compare the present observations with those obtained in other academic centres worldwide. Some care is needed in analysing these epidemiological studies since the methodology, classification and ethnical groups studied vary considerably. In spite of these difficulties such epidemiological analysis seem to contribute for the diagnosis, prevention and management of brain tumours.

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MATERIAL AND METHODS

The files of the Department of Pathology, Federal University of Parana, were reviewed from 1967 onwards. From a total of 8418 surgical biopsies examined in this period 652 corresponded to neurosurgical specimens. From this group (n=652) all tumours involving the central nervous system (CNS) and those affecting cranial and spinal intradural nerves were studied. Pertinent data concerning age, sex, presenting symptoms, clinical diagnosis and previous pathological diagnosis were recorded.

The histological slides were reviewed by a neuropathologist (LFT) and whenever necessary special stainings such as cresyl violet and phosphotungstic acid haematoxylin or immunocytochemical techniques to glial fibrillary acid protein, S-100 and neuron-specific enolase were employed 1,4,18. The tumours were classified according the World Health Organization 25. A few patients (n=13) underwent more than a single surgical procedure but with the same neuropathological diagnosis so that for the purposes of this study they were tabulated only once.

RESULTS

Neurosurgical biopsies represented 0.8% of the total number of specimens received for pathological examination. In this group 66% were brain tumours, 2.0% corresponded to cysticercosis, 5.5% were insufficient for a definitive diagnosis and the rest consisted of arteriovenous malformations, aneurysms, bone and cartilagenous tumours infiltrating CNS and inflammatory processes. The brain tumours (n=438) were primary in 88.1% of the cases and a secondary deposit was found in 11.9%. In the group of primary brain tumours there was a predominance of astrocytic neoplasms including glioblastoma multiforme, followed by meningiomas, schwannomas, ependymomas and primitive neuro-ectodermal tumours (Table 1). There were only three cases of pure oligodendrogliomas and in three other cases there were mixed oligo-astrocytomas as confirmed by immunohistochemical techniques. Meningothelial meningiomas predominated although we were inclined to sub-classify only those with a more aggressive behaviour, i.e. hemangiopericytoma of meninges (n=5) and malignant meningiomas (n=3) 5,11.

The male to female ratio was 1.30 to 1 and the global peak of age incidence is shown in figure 1. Furthermore if age of incidence is directly related to histological types (Fig. 2) it seems clear that the first peak, around 10-25 years, consisted of patients with low grade astrocytomas, medulloblastomas and ependymomas. Older patients were more likely to present with glioblastomas, malignant astrocytomas and secondary deposits. Meningiomas had a peak incidence around the fifth decade of life while schwannomas followed a bimodal distribution. The anatomical sites affected by primary and metastatic tumours were studied in relation to the eight most frequent histopathological types (Table 2). In a small group of patients (n=26) there was no information concerning the topography of the lesions so that they were excluded from this analysis. Low grade astrocytomas, schwannomas and medulloblastomas were common in the posterior fossa. The malignant astrocytomas and glioblastomas affected mainly cerebral hemispheres. Most of the secondary deposits were confined to the spinal cord. The occipital region seemed particularly spared from brain tumours and in only three situations, all metastasis, it was affected.

The main signs and symptoms of patients detected by the time of first admission to hospital are listed in table 3. Some patients presented with more than a single symptom. Intracranial hypertension characterized by headache, vomiting and dizziness was the commonest manifestation. The clinical manifestations with the most frequent histological sub-types are related in table 4. Malignant astrocytomas and glioblastomas presented predominantly with intracranial hypertension, epilepsy was frequent in low grade astrocytomas while chronic headache in meningiomas. Deafness was almost pathognomonic of VIIIth nerve schwannomas. The time of evolution of brain tumours, i.e. the period from the appearance of the first symptoms until the hospital admission, was studied in relation to each of the main histological types (Fig. 3). Malignant tumours had a short evolution while meningiomas may take as long as 2 to 3 years before any clinical disability is detected.

In relation to the previous pathological diagnosis, emitted by general pathologists, there was a 25.3% discordance with those identified by a neuropathologist. Most of the differences were due to inappropriate grading of the astrocytic neoplasms. In 45.2% of discordant cases foci of necrosis were not taken into account and the tumours were low graded. There were some difficulties in establishing the correct histological diagnosis in

| Diagnosis | Number of cases | Percentage |
|----------------------------------|-----------------|------------|
| Low-grade astrocytoma | 67 | 15.3 % |
| Malignant astrocytoma | 44 | 10.0 % |
| Glioblastoma multiforme | 48 | 11.0 % |
| Oligodendroglioma | 3 | 0.7 % |
| Ependymoma | 16 | 3.7 % |
| Myxo-papillary ependymoma | 4 | 0.9 % |
| Mixed glioma | 4 | 0.9 % |
| Choroid plexus papilloma | 3 | 0.7 % |
| Choroid plexus carcinoma | 1 | 0.2 % |
| Colloid cyst | 2 | 0.5 % |
| Meningioma | 74 | 16.9 % |
| Haemangiopericytoma of meninge | 5 | 1.1 % |
| Malignant meningioma | 3 | 0.7 % |
| Pituitary adenoma | 13 | 3.0 % |
| Craniopharyngioma | 9 | 2.1 % |
| Epidermoid cyst | 4 | 0.9 % |
| Dermoid cyst | 4 | 0.9 % |
| Primitive neuroectodermal tumour | 6 | 1.4 % |
| Ganglioneuroma | 3 | 0.7 % |
| Medulloblastoma | 16 | 3.7 % |
| Schwannoma | 43 | 9.8 % |
| Neurofibroma | 1 | 0.2 % |
| Angioma | 4 | 0.9 % |
| Haemangioblastoma | 6 | 1.4 % |
| Haemangiosarcoma | 1 | 0.2 % |
| Undifferentiated neoplasms | 2 | 0.5 % |
| Metastatic deposits | 52 | 11.9 % |
| Total | 438 | 100 % |

Table 1 — Classification of 438 brain tumours diagnosed in the University of Parama, Brazil, from 1967-1988.

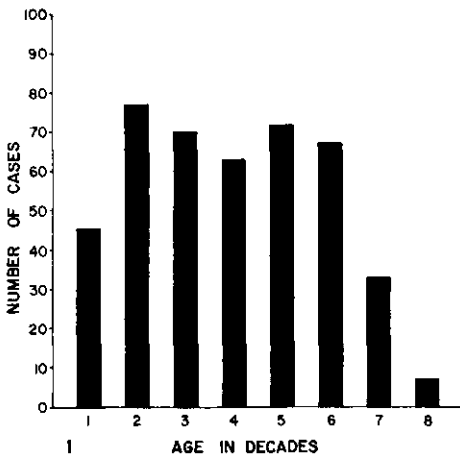


Fig. 1 — Incidence of brain tumours in 438 biopsies reviewed from 1967 to 1988.

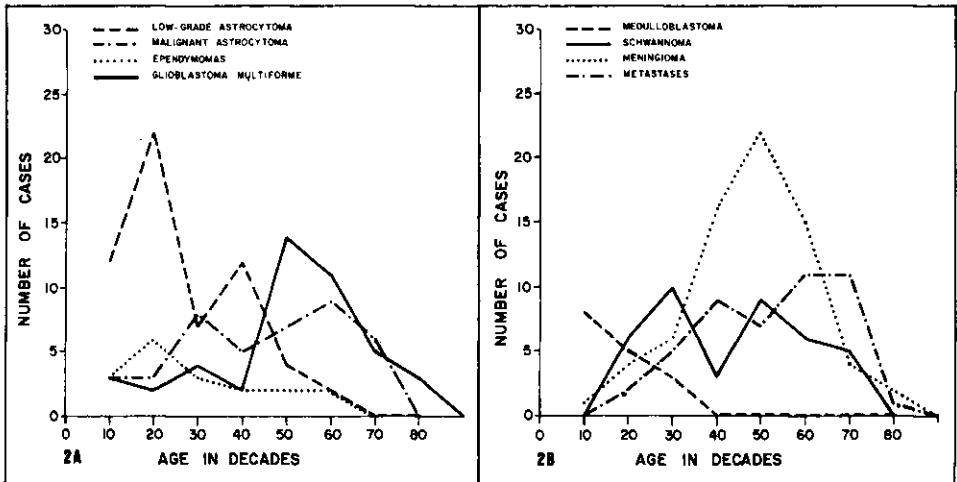


Fig. 2 (A and B) — Distribution of the most frequent histological types of brain tumours according to the age of incidence in 438 biopsies.

| Histopathological diagnosis | Anatomical sites | | | | |
|-----------------------------|------------------|--------|--------|-------|-------|
| | SC | PF | FL | PL | TL |
| Low-grade astrocytoma | 5 | 17 | 7 | 6 | 6 |
| Malignant astrocytoma | 1 | 14 | 13 | 12 | 7 |
| Glioblastoma | — | 1 | 13 | 9 | 15 |
| Ependymoma | 3 | 10 | 1 | — | 1 |
| Medulloblastoma | — | 16 | — | — | — |
| Meningioma | 11 | 5 | 18 | 10 | 8 |
| Schwannoma | 12 | 26 | — | — | 1 |
| Metastatic deposits | 27 | 4 | 4 | 4 | 2 |
| Total of cases | 59 | 93 | 56 | 41 | 40 |
| Percentage | 13.5 % | 21.2 % | 12.8 % | 9.4 % | 9.1 % |

Table 2 — Relationship between the most frequent intradural tumours and the main anatomical sites involved. SC, spinal cord; PF, posterior fossa; FL, frontal lobe; PL, parietal lobe; TL, temporal lobe.

| | |
|---------------------------|-----|
| Intracranial hypertension | 123 |
| Headache | 71 |
| Hemiparesis | 36 |
| Seizures | 35 |
| Loss of vision | 35 |
| Paraparesis | 28 |
| Dementia | 21 |
| Loss of hearing | 17 |
| Lumbar abnormalities | 13 |

Table 3 — Main signs and symptoms of patients presenting with intradural tumours.

| Histological diagnosis | Clinical symptoms | | | | | | |
|------------------------|-------------------|----|----|----|----|----|----|
| | IH | HE | SE | HM | LV | PA | LH |
| Low-grade astrocyt. | 21 | 7 | 10 | 2 | 3 | 3 | 1 |
| Malignant astrocyt. | 18 | 8 | 13 | 7 | 3 | 2 | — |
| Glioblastoma | 17 | 11 | 4 | 5 | 2 | 1 | — |
| Ependymoma | 5 | 1 | 1 | — | — | 2 | — |
| Medulloblastoma | 12 | 1 | — | 1 | 2 | — | — |
| Meningioma | 11 | 16 | 7 | 10 | 6 | 7 | — |
| Schwannoma | 9 | 6 | 1 | — | — | 3 | 16 |
| Metastatic deposit | 10 | 8 | 2 | 4 | 2 | 4 | — |

Table 4 — Relationship between the most frequent tumours and the main clinical symptoms. IH, intracranial hypertension; HE, headache; SE, seizures; HE, hemiparesis; LV, loss of vision; PA, paraparesis; LH, loss of hearing.

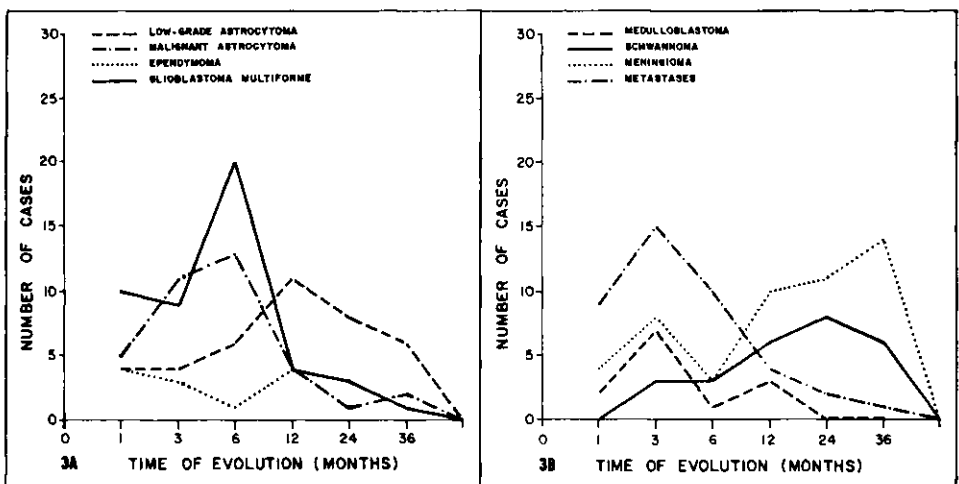


Fig. 3 (A and B) — Distribution of the most frequent histological types of brain tumours according to the time of evolution since the appearance of the first symptoms until the hospital admission.

30.3% of misinterpreted cases, most of which diagnosed before the availability of immunohistochemical techniques⁴. Mixed gliomas and the group of primitive neuro-ectodermal tumours were particularly overlooked.

COMMENTS

Brain tumours correspond to approximately 9.0% of all primary neoplasms¹⁶ but even so there are few epidemiological studies in the world literature analysing large series of patients. The incidence in the general population varies from 1.4 cases per 100000 inhabitants in China²⁴, 4 to 5 cases per 100000 in North America¹⁶ and 12.3 cases per 100000 in Central Finland⁸. In most of the groups studied there is a slight male predominance: 1.30 males to 1 female in the present work, 1.53 to 1 recorded by Wen-ting et al.²⁴, 1.58 to 1 observed in the series described by Kepes et al.¹⁴. However some authors describe a female predominance^{8,15}.

Neuroepithelial tumours are the commonest amongst brain neoplasms with an incidence varying from 32.6% in Japan¹² to 49.8% in western countries^{9,10,21,22}. In the present Brazilian study 49.5% of all tumours belonged to this group. Astrocytic tumours predominated in our results corresponding to 36.3% of all the studied cases; in this group there were low grade astrocytomas (10.1%), cerebellar astrocytomas (2.2%), pilocytic astrocytomas (1.9%), gemistocytic astrocytomas (1.0%), malignant astrocytomas (10.1%) and glioblastoma multiforme (11.0%). These astrocytic predo-

minance is in accordance with previous reported series^{15,24} although Kepes et al.¹⁴ reported a predominance of meningiomas. In the Brazilian population astrocytomas and glioblastomas affected patients in the second and fifth decade of life while in the Chinese series²⁴ both predominated in the fourth decade. In the great majority of published studies these tumours were localized above the tentorium while children suffered from cerebellar astrocytomas and medulloblastomas of posterior fossa^{2,3,7}.

The clinical symptoms of intracranial hypertension predominated in the present work in accordance with the reported literature^{19,24}. The biological behaviour of malignant astrocytomas and glioblastomas followed the observations of Russell and Rubinstein²⁰.

Oligodendrogliomas have a low incidence in our series (0.7%) and in three situations they were concomitant with astrocytomas. They presented with headache and dementia¹⁷. These observations contrast with those reported in the literature which showed these tumours to account for 3.0 to 6.2% of all CNS tumours^{14,20,24}. It is important to notice that in some situations there might be difficulties in the differential diagnosis between oligodendrogliomas and clear cell ependymomas¹³. We could not explain this low incidence of oligodendrogliomas in our Brazilian study. Ependymomas represent between 4.6 to 6.0% of CNS tumours^{19,23} and in the present study they accounted for 4.9%. Some authors described incidences of 10 to 12.0%^{12,15}. The reasons for such differences remain unexplained. Another contradictory finding is the low incidence of pituitary adenomas in the present work (2.0%) well below that by other authors which oscillated from 7 to 17.8%^{6,20}. The incidence of the other brain tumours and metastatic deposits in our series is compared with those

| Author year / country | NET | MEN | SCH | ADE | TER | VAS | MET |
|--|------|------|------|------|-----|------|------|
| Cushing ⁶ 1932 / USA | 43.2 | 13.4 | 8.7 | 17.8 | 5.6 | 2.0 | 4.2 |
| Grant ¹⁰ 1956 / USA | 49.8 | 17.5 | 4.7 | 8.8 | 5.1 | 3.1 | 8.4 |
| Katsura ¹² 1959 / Japan | 32.6 | 15.9 | 12.0 | 11.0 | 9.6 | 3.9 | 4.3 |
| Zulch ²³ 1965 / W. German | 43.1 | 17.2 | 6.8 | 6.8 | 4.3 | 3.4 | 6.1 |
| Sano ²¹ 1969 / Japan | 34.2 | 12.3 | 9.9 | 11.0 | 8.8 | 10.5 | 2.9 |
| Shuangshoti ²² 1974 / Thailand | 42.4 | 15.8 | 5.1 | 4.0 | 9.4 | 5.1 | 16.6 |
| Lana-Peixoto ¹⁵ 1981 / Brazil | 49.7 | 15.6 | 2.8 | 7.8 | 4.2 | 1.7 | 13.9 |
| Wen-ting ²⁴ 1982 / China | 42.8 | 16.5 | 9.5 | 9.5 | 8.4 | 3.8 | 6.8 |
| Fogelholm ⁸ 1984 / Finland | 36.8 | 19.5 | 7.6 | 4.2 | 2.8 | 1.7 | 23.5 |
| Kepes ¹⁴ 1984 / China | 31.7 | 22.3 | — | 16.5 | 4.5 | 3.4 | 4.5 |
| Torres 1988 / Brazil | 49.5 | 16.9 | 9.8 | 3.0 | 3.9 | 2.5 | 11.9 |

Table 5 — Incidence of brain tumours in different countries (%). NET, neuro-epithelial tumours; MEN, meningiomas; SCH, schwannomas; ADE, pituitary adenomas; TER, teratomas; VAS, vascular tumours; MET, metastatic deposits.

observed in the main previous studies (Table 5). It is of notice the high incidence of metastasis in Finland due to lung cancer in males and breast tumours in females⁸.

In our present study neurocysticercosis accounted for one of the highest incidences of infectious diseases which might present as space-occupying lesions (2.0%). This finding strongly suggests that the southern region of Brazil is an endemic area for this type of parasite. This observation is infrequent in other series which described cases of tuberculomas and granulomatous inflammation but with few reports of cysticercosis.

Acknowledgements — We thank the staffs of the Departments of Pathology and Neurosurgery, University of Paraná for their collaboration in this study. This work is in part sponsored by the University of Paraná. Curitiba, Brazil.

REFERENCES

1. Bancroft J, Stevens A — Theory and Practice of Histological Techniques. Churchill Livingstone, Edinburgh, 1982.
2. Becker LE, Hinton D — Primitive neuroectodermal tumors of the central nervous system. *Human Pathol* 14:538, 1983.
3. Becker LE, Yates AJ — Astrocytic tumors in children. In Finegold M (ed): *Pathology of Neoplasia in Children and Adolescents*. WB Saunders, Philadelphia, 1986, pg 373.
4. Bonnin JM, Rubinstein LJ — Immunohistochemistry of central nervous system tumors: its contribution to neurosurgical diagnosis. *J Neurosurg* 60:1121, 1984.
5. Chan RC, Thompson GB — Morbidity, mortality and quality of life following surgery for intracranial meningiomas: a retrospective study in 257 cases. *J Neurosurg* 60:52, 1984.
6. Cushing HW — *Intracranial Tumors: Notes upon a Series of Two Thousand Verified Cases with Surgical-Mortality Percentages Pertaining Thereto*. CC Thomas, Springfield, 1932.
7. Duifner PK, Cohen ME, Myers MH, Heise HW — Survival of children with brain tumors: SEER Program, 1973-1980. *Neurology* 36:597, 1986.
8. Fogelholm R, Uutela T, Murros K — Epidemiology of central nervous system neoplasms: a regional survey in Central Finland. *Acta Neurol Scand* 69:129, 1984.
9. Fulling KH, Nelson JS — Cerebral astrocytic neoplasms in the adult: contribution of histologic examination to the assessment of prognosis. *Seminars in Diagnostic Pathology* 1:152, 1984.
10. Grant FC — A study of the results of surgical treatment in 2326 consecutive patients with brain tumor. *J Neurosurg* 13:479, 1956.
11. Jellinger K, Slowik F — Histological subtypes and prognostic problems in meningiomas. *J Neurol* 208:279, 1975.
12. Katsura S, Suzuki J, Wada T — A statistical study of brain tumors in the neurosurgical clinics in Japan. *J Neurosurg* 16:570, 1959.
13. Kawano N, Yada K, Aihara M, Yashigita S — Oligodendroglioma-like cells (clear cells) in ependymoma. *Acta Neuropathol (Berlin)* 62:141, 1983.
14. Kepes JJ, Chen WYK, Pang LC, Kepes M — Tumors of the central nervous system in Taiwan, Republic of China. *Surgical Neurol* 22:149, 1984.
15. Lana-Peixoto MA, Pittella JEH, Arouca EMG — Primary intracranial tumors: analysis of a series of consecutive autopsies and biopsies. *Arq Neuro-Psiquiat (São Paulo)* 39:13, 1981.
16. Leetsma JE — Brain tumors. *Am J Pathol* 100:243, 1980.
17. Ludwig CL, Smith MT, Godfrey AD, Armbrustmacher VW — A clinicopathological study of 323 patients with oligodendrogliomas. *Ann Neurol* 19:15, 1986.
18. Polak J, van Noorden S — *Immunocytochemistry*. Wright, London, 1986.
19. Rubinstein LJ — *Tumors of the Central Nervous System*. Armed Forces Institute of Pathology, Washington DC, 1972.
20. Russell DS, Rubinstein LJ — *Pathology of the Tumours of the Nervous System*. Williams and Wilkins, Baltimore, 1977.
21. Sano K — Statistics on brain tumors and glioma. *No To Shinkei* 21:463, 1969.
22. Shuangshoti S, Panyathanya R — Neural neoplasms in Thailand: a study of 2897 cases. *Neurology* 24:1127, 1974.
23. Zulch KJ — *Brain Tumors: their Biology and their Pathology*. Ed 2. Springer-Verlag, New York, 1965.
24. Wen-qing H, Shi-ju Z, Quing-sheng T, Jian-qing H, Yu-xia L, Quing-zhong X, Zi-jun L, Wen-cui Z — Statistical analysis of central nervous system tumors in China. *J Neurosurg* 56:555, 1982.
25. World Health Organization — *Classification of Tumours of the Central Nervous System*. WHO, Geneva, 1979.