

## SHORT REPORT

## Histological subtypes of symptomatic central nervous system tumours in Singapore

A Das, C A T Chapman, W M Yap

### Abstract

**The objective was to identify the different subtypes of symptomatic CNS tumours that are encountered in Singapore. Our hospital pathology and operative records from 1994 to 1998 were reviewed and information regarding all patients who underwent biopsy or resection as part of their diagnostic and therapeutic evaluation was extracted. Only histologically confirmed tumours were included in this analysis. Meningiomas made up the largest subgroup of tumours, accounting for 35.1% of all tumours. In order of decreasing frequency, the remaining most often reported histologies were pituitary adenomas (11.8%), secondary neoplasms (10%), tumours of nerve sheath (9.4%), glioblastoma multiforme (9.3%), astrocytomas including anaplastic, diffuse and pilocytic (9.2%), primary CNS lymphomas (2.9%), oligodendrogliomas (2.2%), hemangioblastomas (2.2%), craniopharyngiomas (1.7%), and embryonal tumours (1.2%). Genetic and environmental factors may be responsible for the proportionately higher than expected percentage of meningiomas seen and further study is required to identify these factors.**

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Characterising the different forms and range of CNS neoplasms in different regions may provide aetiological clues to some tumour types. Histological descriptions of CNS tumours as they occur in south east Asia and, in particular, in Singapore are rare. One of the few such studies in Singapore by the National Cancer Registry, which describes trends in cancer incidence from 1968 to 1992, contains information regarding only 594 malignant brain and nervous system tumours over this lengthy period.<sup>1</sup> The limitations of using a cancer registry, particularly the underrepresentation of benign tumours, is immediately apparent. A more recent survey was required to document the current trends in relative frequencies of symptomatic CNS tumours in Singapore. In part these investigations on the relative incidence, age, and sex of

patients with tumours of the CNS are important in providing potential aetiological clues to pathogenesis. Certain cultural and religious beliefs make necropsy studies extremely difficult in Singapore. Given such constraints, our study represents the largest and most recent compilation of data on CNS tumours in Singapore.

### Methods

This study was undertaken at a government hospital, which has the largest neurosurgical unit in Singapore, performing 1200 procedures annually. This hospital serves a predominantly adult patient population within a catchment area of 1 million people. As there are no other hospitals within the vicinity, the distribution of cases is unlikely to be biased by physicians' subspecialty interests. As part of a retrospective survey, 48 001 pathology reports and the neurosurgical records from 1 January 1994 to 31 December 1998 were reviewed and all histologically confirmed CNS tumours were included in this analysis. None of the histopathological data were obtained from necropsy series; all patients underwent biopsy or resection as part of their diagnostic or therapeutic evaluation.

Age, sex, ethnic background, date of diagnosis, and histological diagnosis were recorded for all patients with CNS tumours. The date of diagnosis is the date on which the pathological diagnosis was obtained. All tumours covered by the World Health Organisation (WHO) classification scheme except for cysts were included.<sup>2</sup> Tumours diagnosed on the basis of neuroimaging studies without histological confirmation were excluded.

### Results

During a 5 year period from 1 January 1994 to 31 December 1998, 655 tumours of the CNS were diagnosed and, of this total number, 583 were newly diagnosed. We report only on the 583 newly diagnosed tumours. The remaining 72 were recurrent tumours that occurred in the cohort of 583 patients. No patient had two different CNS neoplasms. The ethnic origin of the 583 patients including Chinese (80.8%), Malays (11.5%), Indians (5.0%), and other groups (2.7%) reflected the percentage distribution of Singapore's population.<sup>3</sup> Patients included 307 women (52.7%) and 276 men

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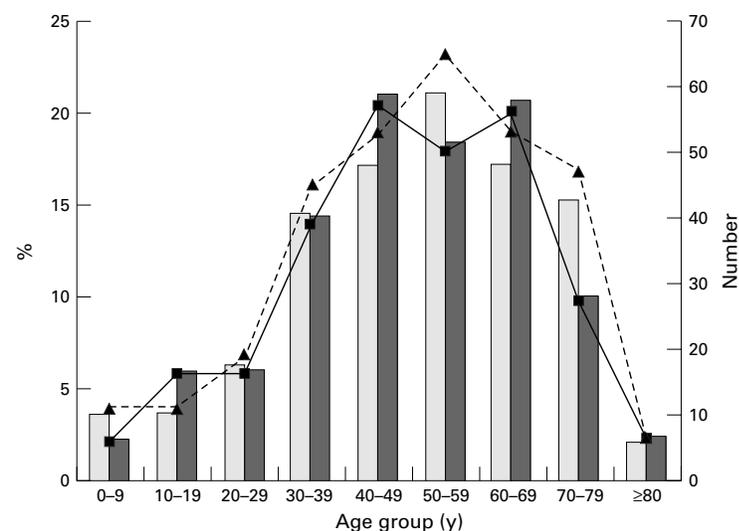
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Table 1 Distribution of CNS tumours by histology and sex

	Males	Females	Total (%)
Tumours of neuroepithelial tissue:			
Astrocytic tumours			
Pilocytic astrocytoma (WHO grade I)	11	8	19 (3.3)
Astrocytoma (WHO grade II)	9	5	14 (2.4)
Anaplastic astrocytoma (WHO grade III)	7	12	19 (3.3)
Glioblastoma (WHO grade IV)	31	23	54 (9.3)
Subependymal giant cell astrocytoma	1		1 (0.2)
Oligodendroglial tumours			
Oligodendroglioma	7	3	10 (1.7)
Anaplastic oligodendroglioma	2	1	3 (0.5)
Ependymal tumours	1	4	5 (0.9)
Mixed gliomas	3		3 (0.5)
Neuroepithelial tumours of uncertain origin			
Gliomatosis cerebri	1		1 (0.2)
Choroid plexus tumours			
Choroid plexus papilloma	1	2	3 (0.5)
Neuronal and mixed neuronal-glioma tumours			
Ganglioma	1	1	2 (0.3)
Central neurocytoma	1	1	2 (0.3)
Tumours with neuroblastic or glioblastic elements (embryonal tumours)			
Primitive neuroectodermal	1	3	4 (0.7)
Neuroblastoma	2	1	3 (0.5)
Tumours of the sellar region			
Pituitary adenoma	45	24	69 (11.8)
Craniopharyngioma	6	4	10 (1.7)
Haematopoietic tumours			
Lymphoma			
B cell	9	6	15 (2.6)
T cell	1	1	2 (0.3)
Germ cell tumours			
Germinoma	3	1	4 (0.7)
Teratoma	2		2 (0.3)
Tumours of the meninges			
Benign meningioma	52	133	185 (31.7)
Atypical meningioma	6	8	14 (2.4)
Malignant meningioma	3	3	6 (1.0)
Non-meningothelial tumours of the meninges			
Malignant mesenchymal			
Hemangiopericytoma		4	4 (0.7)
Tumours of uncertain histogenesis			
Haemangioblastoma	4	9	13 (2.2)
Tumours of cranial and spinal nerves	28	27	55 (9.4)
Local extensions from regional tumours			
Paraganglioma		1	1 (0.2)
Chordoma	1		1 (0.2)
Metastatic neoplasms			
Adenocarcinoma	20	13	33 (5.7)
Squamous cell carcinoma	2		2 (0.3)
Metastatic carcinoma	15	8	23 (4.0)
Unclassified tumours			
Haemangiioendothelioma		1	1 (0.2)
Total	276	307	583 (100)

(47.3%) giving a male:female ratio of 1:1.1. Data on the histology of symptomatic newly diagnosed CNS tumours with pathological verification are outlined in the table.



Age distribution by sex. Light bars % women; dark bars % men; triangles number of women; squares number of men.

The most commonly encountered tumours were meningiomas, which comprised 35.1% of all newly diagnosed tumours in our series with 9.8% of those initially diagnosed being of the atypical or malignant variety. Atypical meningiomas demonstrated hypercellularity, patternless or sheet-like growth, and brisk mitotic activity, and malignant meningiomas demonstrated brain invasion. The second largest group of 69 cases (11.8%) were pituitary adenomas. In order of decreasing frequency, the remaining most often reported histologies were secondary neoplasms (10%), tumours of the nerve sheath (9.4%), glioblastoma multiforme (9.3%), astrocytomas including anaplastic, diffuse, and pilocytic (9.2%), primary CNS lymphomas (2.9%), oligodendrogliomas (2.2%), haemangioblastomas (2.2%), craniopharyngiomas (1.7%), embryonal tumours (1.2%), germ cell tumours (1.0%), ependymomas (0.9%), neuronal tumours (0.6%), choroid plexus tumours (0.5%), and chordomas (0.1%). When histological subtypes were categorised according to ethnicity, no significant differences in the distribution of tumour subtypes among the different ethnic groups were seen.

Females had a higher incidence of benign meningiomas than males, with a male to female ratio of 1:2.3 ( $p > 0.001$ ). However, no significant differences in sex predominance were noted for either the atypical or malignant meningiomas. Although neuroepithelial and pituitary tumours occurred slightly more often in men than women, this difference was again not significant.

The median age at presentation was 51 years (range 0.58 to 87 years) with no significant difference between men and women ( $p = 0.330$ ). This cohort's age distribution is outlined in the figure. The incidence of CNS tumours increased from the 4th to the 7th decade. Of the various tumour types progressively higher grade astrocytic tumours presented in progressively older patients with median ages of 20.0 years for grade I astrocytomas, 31.5 years for grade II astrocytomas, 34.5 years for grade III astrocytomas, and 55 years for grade IV astrocytomas.

## Discussion

Our report examines the different subtypes of all symptomatic and pathologically proved CNS neoplasms at a single institution, reflecting the selection bias that is inherent in any hospital series. We estimate that our cohort of 655 tumours from 583 patients includes 50% of all CNS tumours diagnosed in this country over a 5 year period from 1994 to 1998. Previously, differences in histological subtypes among ethnic groups living in the same geographical region have implicated racial factors in the pathogenesis of CNS tumours.<sup>4</sup> The problematic classification of numerous histological categories and lack of consensus on diagnostic criteria complicates the comparison of tumour incidence across regions.<sup>5</sup> Nevertheless, we compared our series with others in an attempt to ascertain if unique trends in histological subtypes were present in this part of south east Asia. Whereas astrocyto-

mas are the most common primary tumour type in other series from Japan, Thailand, United States, and the previous USSR,<sup>9</sup> meningiomas seem to be proportionately more common in our series. In population based studies from the west, neuroepithelial tumours account for 40% to 67% and meningiomas for 9% to 27% of CNS tumours<sup>7</sup> compared with respective rates of 24.5% and 35.1% in our series. This finding is consistent with several reports of non-white ethnic groups showing higher rates of meningiomas, including males from Asia and the Middle East residing in Victoria, Australia,<sup>8</sup> African-Americans,<sup>9</sup> and series from China<sup>10</sup> and Hong Kong.<sup>11</sup> In many series only 5% of meningiomas are atypical or malignant, whereas in our series 9.8% are atypical or malignant.<sup>12</sup> These findings are likely to be explained at least in part by genetic factors. Tumours of the pituitary and tumours of the cranial and spinal nerves which account for 11.8% and 9.4% of reported histologies were more common than other series, in which these tumours account for 8% and 6.5% of tumour types.<sup>13</sup> Tumours diagnosed by neuroimaging but without histological confirmation were excluded. This exclusion might produce a pathological bias in that tumours of the cranial nerves detected on neuroimaging studies are often treated without biopsy. As the Singapore Cancer Registry does not record the incidence rates for benign brain tumours, the population incidence rates cannot be provided. We cannot conclude that the increased proportion of certain tumour subtypes found in our series reflects an increased population incidence rate for meningiomas in Singapore. To really explore such incidence rates will require further examination in future cancer registry studies.

Brain tumours are thought to occur more often in males than in females.<sup>7</sup> A comparison using international data of the incidence of primary intracranial tumours of all histological types results in an average male to female ratio of 1.4:1 (range 0.9–2.6) across geographical areas.<sup>14</sup> However, the sex ratio varies considerably by histological type. Gliomas are higher in males with a male to female ratio of 1.5:1 and meningiomas are higher in females with a sex ratio of 0.65.<sup>15</sup> The lower male to female ratio of 1:1.1 in our study may be due to the female preponderance of meningiomas. Reports on pituitary adenomas from the United Kingdom show a constant and sizeable predominance of

females for all ages and especially among women of childbearing age.<sup>16</sup> By contrast, in our series males had a higher predominance of pituitary adenomas with a male to female ratio of 1.88:1. This finding is surprising and the reason for this male predominance of pituitary adenomas is difficult to explain.

Our series of symptomatic brain tumours inclusive of all histologically confirmed tumours over a 5 year period highlights a preponderance of meningiomas. Higher than expected percentages of reported brain tumours include tumours of cranial and spinal nerves and pituitary tumours. Glioblastoma multiforme occurred less often. Genetic and environmental factors may be responsible for our histological findings and further study is required to identify these factors.

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