Brain and Spinal Tumour

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SUMMARY

This study reviewed the epidemiology of brain and spinal tumours in Sarawak from January 2009 till December 2012. The crude incidence of brain tumour in Sarawak was 4.6 per 100,000 population/year with cumulative rate 0.5%. Meningioma was the most common brain tumour (32.3%) and followed by astrocytoma (19.4%). Only brain metastases showed a rising trend and cases were doubled in 4 years. This accounted for 15.4% and lung carcinoma was the commonest primary. Others tumour load were consistent. Primitive neuroectodermal tumour (PNET) and astrocytoma were common in paediatrics (60%). We encountered more primary spinal tumour rather than spinal metastases. Intradural schwannoma was the commonest and frequently located at thoracic level. The current healthcare system in Sarawak enables a more consolidate data collection to reflect accurate brain tumours incidence. This advantage allows subsequent future survival outcome research and benchmarking for healthcare resource planning.

KEY WORDS:
Brain, spine, tumour, epidemiology, Sarawak

INTRODUCTION

Brain and spinal tumours are relatively rare compared to other tumours. [1] It accounts for 1.95% of all cancers in Malaysia. [2] However, the disease can be debilitating as even benign brain tumours can be fatal due to its location and propensity to malignant transformation.[3] Despite so, the epidemiology of the disease is not well studied in the local setting. Precise information about incidence of disease is essential for many reasons. [4] Comparison of rates across time will provide clues to aetiology and accurate data is needed for informed public health and healthcare resource planning.

MATERIALS AND METHODS

All newly diagnosed brain and spinal tumours patients via neuroimaging from 1st January 2009 till 31st December 2012 were studied. Of all the cases, only cases with tissue (obtained from neurosurgical operation) or prolactin hormonal (obtained from serum) confirmed diagnosis were included. All data on brain and spinal tumours was prospectively collected in Sarawak General Hospital (SGH). The cases were diagnosed and classified where necessary using immunohistochemistry and categorised according to the World Health Organization (WHO) classification.5 The data was analysed using SPSS v.18 to acquire value and comparison.

RESULTS

There was a total of 468 patients included during this period 2009-2012, of which 428 were brain tumours and 40 were spinal tumours. Among the brain tumours, there were 247 females and 181 males. The age ranged from day 11 of life to 83 years old, but paediatric cases were uncommon. The incidence of brain tumours increased with age from approximately 30 years onwards and dropped in those over 70 years old. The peak age group was 40-59 years, accounting for 202 cases (47.2%). There were only 19 cases (4.44%) from the age group of 70-89 years. Figure 1. Majority of the patients were Malay, Chinese and Iban, which was consistent with the racial composition of the state population. Figure 2. According to Department of Statistics Malaysia, Sarawak's total population in 2010 was 2,506,400. Sarawak General Hospital was the main neurosurgery referral centre, covering a total population of 1,085,600 (43.4%), while Sibu Hospital, Miri Hospital and Bintulu Hospital population coverage were 695,700 (27.8%); 463,600 (18.5%) and 261,500 (10.4%) respectively. The number of brain tumour cases picked up from Sarawak General Hospital were 54.0%, Sibu 25.0%, Miri 15.0% and the least from Bintulu hospital 6.0%. Figure 3. Table I shows types of for brain tumours categorised according to the (WHO) classification.

The commonest adult brain tumour was meningioma with 138 cases. This accounted for 32.2% of all the brain tumour cases. Meningioma commonly occurred in middle aged group, with a peak in the fourth and fifth decades. There was a marked female preponderance, giving rise to a female to male ratio of 3:1 (104 females and 34 males). The ratio peaks at 5.3:1 in the patients 30-39 years of age. Figure 4. There were 129 benign and 9 atypical subtypes, none were malignant. Meningothelial WHO grade I was the most common variant. Figure 5. There was no significant racial composition difference in this meningioma group.

Glioma was the second commonest adult brain tumour with 93 cases. This accounted for 21.7% of all brain tumour cases. There were 83 astrocytomas, 7 ependymomas, 2 oligodendrogliomas and 1 oligoastrocytoma. There was no

This article was accepted: 26 September 2014
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Table I: Cases of Brain Tumours in Sarawak (2009-2012)

WHO* Brain tumour classification	Year				Total (n)
	2009 (n)	2010 (n)	2011 (n)	2012 (n)	
Neuroepithelial	19	30	30	34	113
Meningeal	34	42	35	39	150
Tumours of cranial and paraspinal nerves	5	7	6	2	20
Lymphoma and haemopoietic cells	5	5	4	5	19
Germ cell tumours	6	1	5	1	13
Sellar region tumours	11	12	10	9	42
Metastatic tumours	12	13	20	21	66
Unclassified	0	1	0	4	5

* WHO – World Health Organization

Table II: Cases of Brain Tumours in paediatric age group (<12 years old) in Sarawak (2009-2012)

		Year				Total (n)
		2009 (n)	2010 (n)	2011 (n)	2012 (n)	
Tumorus of neuroepithelial tissue	Astrocytoma	1	1	4	2	8
	Ependymal – Ependymoma	0	0	0	1	2
	Ependymal – Subependymoma	1	0	0	0	
	Embryonal – Medulloblastoma	2	2	4	1	9
	Embryonal – Atypical teratoid/ rhabdoid tumour	1	0	0	0	1
	Neuronal-glial – Ganglioglioma	1	0	0	0	1
	Neuronal-glial – Dysembryoplastic neuroepithelial tumour	0	0	0	1	1
	Pineoblastoma	0	1	0	0	1
Lymphomas and haemopoietic neoplasms		0	1	0	0	1
Germ cell tumours	Germinoma	0	0	1	0	1
	Teratoma	2	0	1	1	4
Unclassified		0	0	0	1	1

Table III: Brain Tumour incidence per 100,000 population Crude incidence (CR) and Age-standardised incidence (ASR), by gender and ethnicity, Sarawak 2012

Ethnic group	Brain tumour incidence per 100,000 population Crude incidence (CR) and Age-standardised incidence (ASR), by gender and ethnicity, Sarawak 2012							
	Male				Female			
	No. of cases	% (n)	CR (n)	ASR (n)	No. of cases (n)	%	CR	ASR
All ethnics	43	100.0	1.7	1.8	72	100.0	2.9	3.2
Iban	19	44.1	2.6	2.8	18	25.0	2.5	2.8
Chinese	7	16.3	1.1	1.2	17	23.6	2.6	3.0
Malay	7	16.3	1.3	1.3	24	33.3	4.3	4.8
Bidayuh	6	14.0	3.0	3.0	4	5.6	2.0	2.2
Others	4	9.3	1.1	1.3	9	12.5	2.5	2.7
All ethnics	Both gender (Male and female)							
	No. of cases		CR		ASR	Cumulative rate (lifespan 0-74 years)		
	115		4.6		5.1	0.5%		

significant gender preponderance. Of all the astrocytoma, Glioblastoma multiforme (GBM) was the most common subtype which accounted for 39 cases (47.0%). GBM manifested at any age from neonates to elderly (day 11 of life to 83 years old), but preferentially affected adults, with a peak incidence at 40-59 age range. Glioblastoma is slightly more common in the female group. There were 22 females and 17 males.

Metastatic brain tumours had shown a rising trend, whereby cases doubled from 12 to 21 in 4 years. Lung carcinoma was found to be the most common primary, accounted for about one third (38.0%) of the metastatic brain tumours; followed by breast cancer (9.0%), thyroid cancer (6.0%), malignant melanoma (3.0%) and others (27.0%). There were 14 males and 11 females who had primary lung cancer. Adenocarcinoma was the commonest subtype. Figure 6.

Table IV: Brain tumour age specific incidence per 100,000 population, by ethnicity and gender, Sarawak 2012.

Gender	Ethnicity	Age Group, years																Cumulative
		0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	≥75	rate (lifespan 0-74 years)
Male	All ethnics (100%)	0.5	1.2	0.4	0.4	0.8	3.3	0.6	1.2	4.3	0.7	5.0	4.1	2.7	5.4	0.0	3.8	0.2%
	Iban (29%)	0.0	1.4	1.4	1.4	1.5	4.9	2.0	0.0	6.4	0.0	8.5	3.5	4.6	18.6	0.0	0.0	0.3%
	Chinese (26%)	0.0	0.0	0.0	0.0	1.6	0.0	0.0	4.5	2.4	0.0	0.0	7.8	5.1	0.0	0.0	0.0	0.1%
	Malay (22%)	2.1	3.6	0.0	0.0	0.0	2.2	0.0	0.0	2.8	0.0	3.8	4.6	0.0	0.0	0.0	0.0	0.1%
	Bidayuh (8%)	0.0	0.0	0.0	0.0	0.0	11.9	0.0	0.0	15.4	8.6	10.3	0.0	0.0	0.0	0.0	0.0	0.2%
	Others (15%)	0.0	0.0	0.0	0.0	0.0	3.2	0.0	0.0	0.0	0.0	5.5	0.0	0.0	0.0	0.0	25.4	0.04%
Female	All ethnics (100%)	0.5	0.4	0.0	0.0	0.4	2.4	2.9	1.7	4.9	5.5	6.6	14.3	10.7	9.0	3.6	5.7	0.3%
	Iban (29%)	0.0	0.0	0.0	0.0	1.5	1.6	0.0	2.0	2.1	4.7	8.5	17.6	9.2	12.4	0.0	0.0	0.3%
	Chinese (26%)	0.0	0.0	0.0	0.0	0.0	1.8	6.8	2.2	7.1	0.0	3.2	11.8	5.1	0.0	6.9	22.0	0.2%
	Malay (22%)	2.1	1.8	0.0	0.0	0.0	4.3	2.7	0.0	8.4	12.5	11.3	13.9	18.2	16.3	8.2	0.0	0.5%
	Bidayuh (8%)	0.0	0.0	0.0	0.0	0.0	0.0	7.3	0.0	7.7	8.6	0.0	12.7	0.0	0.0	0.0	0.0	0.2%
	Others (15%)	0.0	0.0	0.0	0.0	0.0	3.2	0.0	3.9	0.0	4.6	5.5	13.6	17.8	12.0	0.0	0.0	0.3%

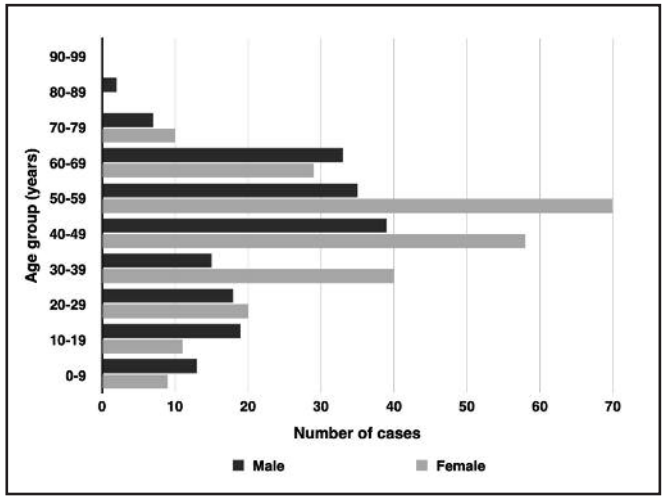

Fig. 1: Brain tumour cases according to age group and gender (2009-2012).

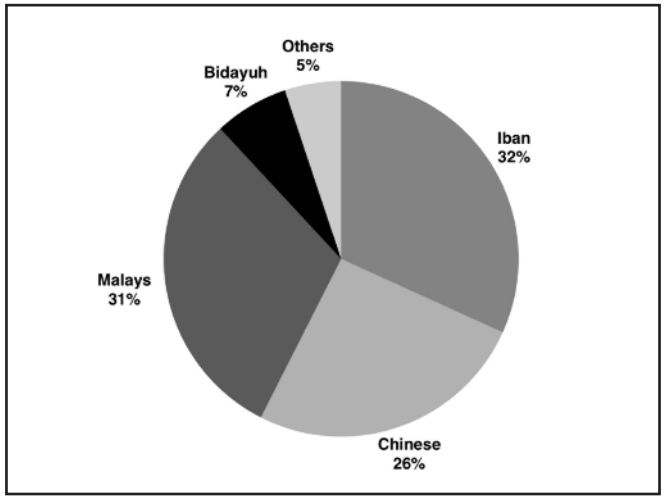

Fig. 2: Number of brain tumour cases according to ethnicity.

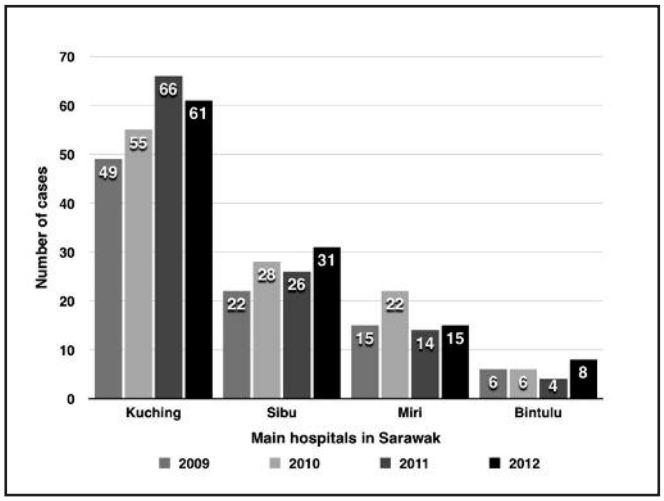

Fig. 3: Number of brain tumour cases according to four main hospitals in Sarawak (2009-2012).

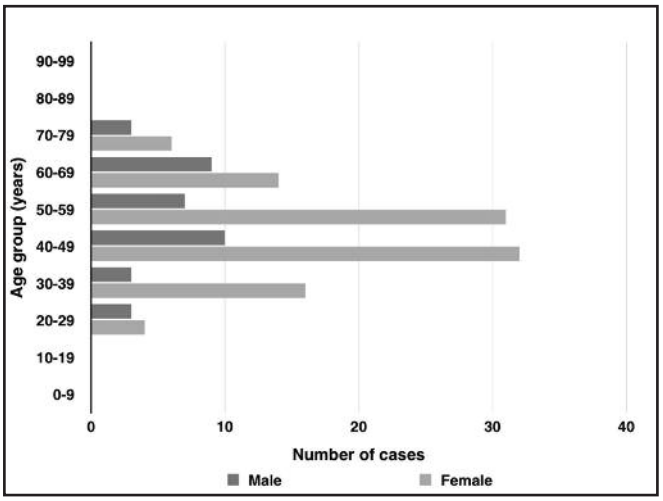

Fig. 4: Meningioma according gender (2009-2012).

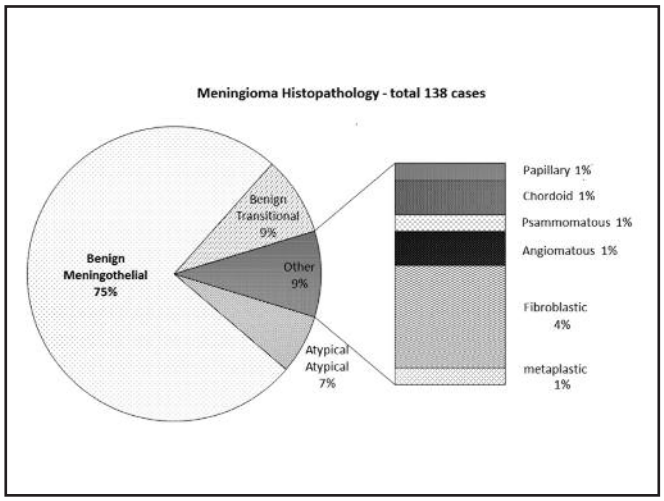

Fig. 5: Meningioma according to histopathology (total 138 cases).

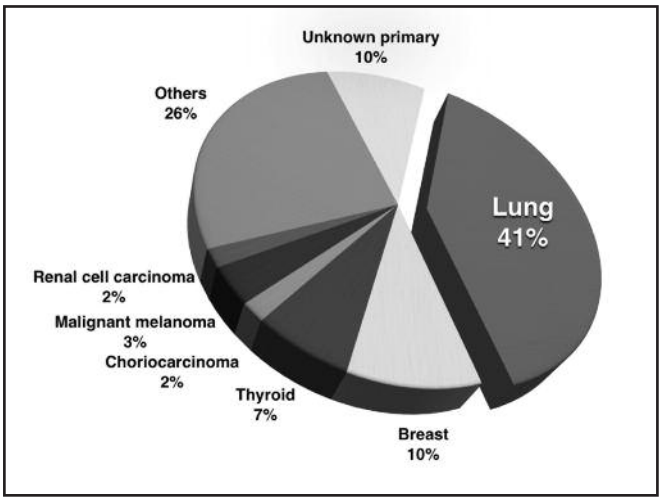

Fig. 6: Brain metastases according to primary (2009-2012).

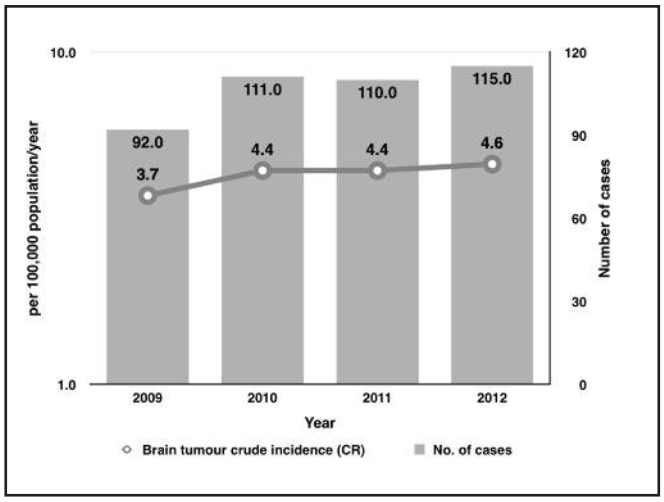

Fig. 7: Brain tumour crude incidence (CR) and number of cases (2009-2012).

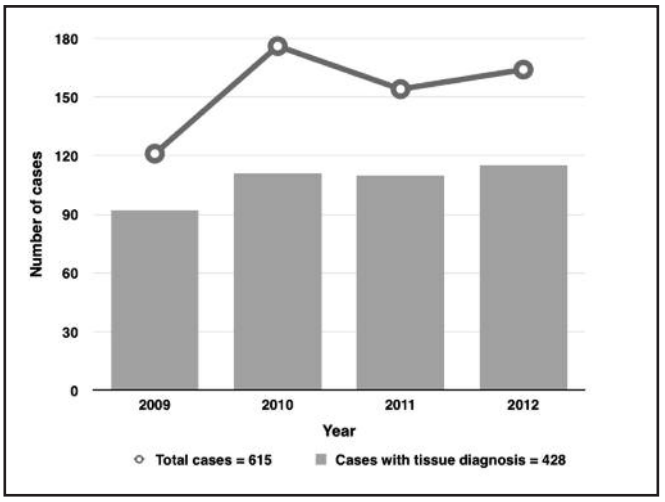

Fig. 8: Total radiologically diagnosed brain tumours and brain tumours with tissue diagnosis.

Cerebellopontine tumours accounted for 25 cases of all brain tumour (5.8%). There were 14 females and 11 males. 80% of those cases presented with sensorineural hearing loss and 32% had headache with tinnitus. Schwannoma was the commonest histopathology which accounted for 19 cases, followed by four cases of meningioma, one epidermal cyst and one endolymphatic sac tumour. 18 of 25 cerebellopontine tumours size were more than 3cm and none were intracanalicular type. As for seller region tumours, pituitary adenomas accounted for 37 cases of all brain tumours (8.6%). There were 16 females and 19 males. 36 cases were macro adenoma with two females diagnosed acromegaly by clinical and biochemical tests. There was only one pituitary microadenoma in a female who had cushing's disease. Two prolactinomas were included in this data. Majority (92%) presented with headache 41% had visual field defect. Occurrence of lymphoma/ haemopoietic cells tumours were consistent in the four years with approximately 4-5 cases per year. There were none of the confirmed lymphoma cases were positive for HIV test.

There were 30 paediatric primary brain tumours (age less than 12 years old) with 17 males and 13 females. Medulloblastoma and astrocytomas were the commonest (30.0% respectively), followed by germ cell tumours (16.7%), ependymal tumour (6.7%), neuronal and mixed neuronal-glial tumours (6.7%), pineoblastoma, atypical teratoid/ rhabdoid tumour and lymphoma (3.3% respectively). Majority of the tumours were from the Malay group with 13 out of 30 cases (43.0%). The youngest paediatric primary brain tumour was 11 days old who had an intraventricular glioblastoma multiforme. The other rare case of 7 year old girl with glioblastoma multiforme had drop metastases to spine. Table II.

As for the 40 spinal tumours, there were 28 intradural, seven extradural and five spinal metastases. There were only two paediatric spinal tumours, one Ewing's sarcoma (7 years old) and one metastatic adenocarcinoma (9 years old). Majority of the intradural spinal tumours were extramedullary and benign in nature. Among the intradural tumours, there were 14 males and 13 females (one being recurrent tumour at level T6 and T9). Age ranged from 13 to 75 years old. Twenty were extramedullary and eight were intramedullary. These intradural tumours were most frequently localised along the neuraxis at the thoracic level (n=11), lumbar (n=6), thoracolumbar (n=4), cervical (n=3). Others were at the thoracolumbosacral (n=2), cervicothoracic (n=1) and sacral (n=1). Schwannoma was the commonest intradural tumour which accounted for 13 cases (46.4%). Others were six meningioma, four myxopapillary ependymoma, two astrocytoma, one haemangiopericytoma, one haemangioblastoma and one epidermoid cyst.

DISCUSSION

Neurosurgery service in Sarawak General Hospital was established in 1988. It is the only main referral centre which receives cases from Kuching and other divisions in Sarawak. Sarawak does not have brain tumour registry and the exact tumour burden of such diseases goes under-reported and under-estimated. Thus, appropriate database of brain and spinal tumours is essential to ascertain neurosurgical healthcare infrastructure and estimation of local disease load.

The incidence of brain tumours in developed countries ranged from 10-19.89 per 100,000 population/year .[1,6,7,8] The increasing numbers of primary brain tumours reported in recent decades needed to be interpreted with caution,[3] as studies in Norway and the USA revealed that this trend over time is likely to be an artefact of improved diagnosis and clinical practice. [9] Yusoff *et al.* reported the incidence of brain tumour among Kelantan and Terengganu population in 1996 was 0.44 per 100,000 population/year, whereas from the Institute of Neurology Kuala Lumpur was 1.4 per 100,000 population/ year .[10] The most recent report of National cancer registry (2003-2005) revealed that the crude incidence of brain tumours and other nervous system (including spinal and peripheral nerve tumours) in Peninsular Malaysia was 2.7 for male and 2.2 for female per 100,000 population/ year.[11] Meanwhile, Globocan 2012 estimated Malaysia brain tumours and other nervous system age standardised incidence to be 2.8 per 100,000 population/year with cumulative rate 0.3% .[12] In Sarawak, we noted similar trend in our centre, whereby the calculated brain tumour only incidence was 3.7 per 100,000 population/year in 2009 and it has steadily risen to 4.6 per 100,000 population/year in 2012 (Figure 7). Its age standardised incidence was 5.1 per 100,000 population/year with cumulative rate (lifespan of 0-74 years) of 0.5% in 2012. Table III and IV. The age standardised incidence was comparable to India, Hong Kong and Taiwan data.[11]

The main factor is the improvement of access and availability to diagnostic radioimaging service in selected hospitals apart from Sarawak General Hospital. The diagnosis of brain tumour is very much dependent on radioimaging. It has dramatically advanced over the last few decades and provides highly accurate information about intracranial structures, especially computed tomography imaging of brain, with very little risk.[4] Following the introduction and commercialisation of computed tomography and magnetic resonance imaging, it has significantly resulted in higher detection rates and better differential diagnosis of brain tumour which were previously misdiagnosed as strokes. [6] CT scan is widely available and it is useful in detection of brain tumours.

Before 2009, CT scan machine in the public sector was only available in Sarawak General Hospital and Sibu Hospital. Currently, radioimaging service (CT scan) is also available in Miri Hospital and Bintulu Hospital. This allows the potential cases to be sent to the nearest selected hospital (based on the area of coverage) by primary healthcare practitioners for diagnostic radioimaging. All the diagnosed cases will eventually be referred to Neurosurgical department of Sarawak General Hospital with the help of Malaysia teleprimary care service[13] which was introduced to Sarawak since 2010. Teleconsultation enables instant browse of radioimagings and immediate neurosurgical consultations can be done without delay in patient health care. Those diagnosed cases that require neurosurgical intervention will be transferred to Sarawak General Hospital via air or land

transportation. The sole public neurosurgery healthcare system in Sarawak has made this database more robust with a more consolidated and complete registry, thus giving rise to a seemingly higher incidence rate than Peninsular Malaysia. Yet, we believe that the incidence could be even greater as we only included cases with histopathological diagnosis. Cases with only radiological diagnosis were excluded. They were either not operable or refusal from the patient or family members. Figure 8 shows the overview of total radiologically diagnosed brain tumours (615 cases) versus cases with tissue diagnosis obtained (428 cases), approximately 70%. The Sarawak neurosurgery public service generally received 90% of majority primary and secondary brain tumour cases. However, it was a different situation in metastatic spine tumours as most cases did not come to us like brain tumour cases did, let alone ones not referred for surgical opinion either neurosurgery or orthopaedic team.

We compared the four main hospitals and found that incidence of brain tumours in proportion to Kuching population was higher at about 54%. This was likely due to the fact that neurosurgery service was actively functioning in Sarawak General Hospital and annual local neurosurgical update campaign to boost the knowledge and awareness among health personnel in particularly paramedics. In Bintulu, the brain tumour incidence proportionate to its local population was extremely low, accounting for 6%. This was because Bintulu Hospital was the last among the four public hospitals in Sarawak to receive CT scan machine, most patients were channelled to Sibu or Kuching for radioimaging prior to that. We believe and foresee the increase of Bintulu pick-up rate in coming years. Incidence of brain tumours in Sibu and Miri were almost proportionate to its local population, 25% and 16% respectively.

The incidence of brain tumours increased with age and formed a bell's curve, peaked at the age group of 50-59 years. There was significant drop in the trend in the age group 70 years and above. The similar finding were described by most authors. [3,10,14] This is due to the fact that brain tumours were less likely to be investigated and detected in elderly. Conservative approach was usually used in this age group.

There were more females (57.7%) who had brain tumours than males (42.3%) in our study. McKinney *et al.* and Yusoff et al. reported that males were more preponderant in brain tumours overall. [3,10] It is certain that meningioma occurred more frequently in female than in male. [6,10,13,15] Meningioma was the most common adult brain tumour in our series. It accounted for about 30-36 % of all brain tumours. Wong et al reported meningioma made up 35% of all brain tumours at the same centre in 2002. [16] These data clearly showed that benign meningioma tumour load was consistent for the past 10 years in Sarawak. Claus *et al* reported that the incidence of meningioma in the United States had remained fairly constant from 1985 to 1994. [14] Gliomas were the second commonest brain tumours in our series with no gender preponderance. Most authors reported that it was the commonest brain tumours, especially in males. [1,10,17] This data and others showed that glioblastoma multiforme was the commonest primary malignant brain tumours that affected all age group and races from all walks of life. [1,6,10,17] It was slightly preponderant in female in our series.

Brain metastases cases in our four year study had increased tremendously following the change of clinical practice in Sarawak General Hospital, this included easy access to clinic appointment and ease of getting CT scan. Sarawak General Hospital's Pathology unit also provides almost a complete set of immunohistochemical stains to enable further detail immunohistochemical staining for diagnosis of primary source. Nonetheless, surgical resection continues to play a crucial role in diagnosis of brain metastases in our centre. Lung cancer was the main cause of brain metastases followed by breast and thyroid cancer. Johnson *et al.* and Nakagawa *et al.* reported lung cancer was the commonest though they tend to encountered more cases of malignant melanoma. [18,19] Despite the increasing number, the incidence of intracranial metastases was still largely underestimated. [20] The reason being that brain metastases itself reflected the advanced stage of disease and most of the time, palliative care was the main aim whereby small lesions and asymptomatic patients were treated conservatively and were not referred to the neurosurgical department.

Brain tumour is the third commonest paediatric cancer in Malaysia after leukaemia and lymphoma. [11] In paediatric age group under 12 year old, we had equal brain tumour cases of medulloblastoma and astrocytoma. Ayushi *et al.* and Rickert *et al.* reported histological profile that favoured astrocytoma. [7,21] In general, brain tumours in paediatric age group were more malignant in nature.

CONCLUSION

The incidence of brain tumours in Sarawak is 4.6 per 100,000 population/year, higher than national statistics. Meningioma is the commonest brain tumour, accounting for 32.3%. Meningiothelial is the most frequent subtype. This was followed by astrocytoma. Lung carcinoma was the commonest primary in brain metastases. In the paediatric group, medulloblastoma and astrocytoma were more common. Intradural spinal tumour frequently localised at thoracic level and schwannoma being the commonest. This study provides the very first profile of the spectrum of brain and spinal tumours among the population in Sarawak. Accurate data is needed to guide future research, benchmarking and for healthcare resource planning.

ACKNOWLEDGEMENT

We thank Madam Chung Ee Wee and Madam Oui ling ling at Histopathology lab Sarawak General Hospital for their assistance in the technical aspect of this study. Also, to Dr. Sutenn and all the staff especially neurosurgery nurses in our hospital who have worked hard to care for these patients.

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