PRESENTATION OF INTRACRANIAL MENINGIOMAS IN JOHANNESBURG (A 12-MONTH PROSPECTIVE STUDY AT CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL AND CHRIS HANI BARAGWANATH HOSPITAL)

by

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A research report submitted to the

Faculty of Health Sciences

University of the Witwatersrand, Johannesburg

in partial fulfillment of the requirements for the degree of

Master of Medicine in the specialty of in Neurological Surgery

Johannesburg, 2011

DECLARATION

I, Dr Kaunda Emeka Ibebuike, declare that this research report is my own work. It is being submitted for the degree of Master of Medicine in the University of the Witwatersrand, Johannesburg. It has not been submitted in part or in full for any other degree or examination at this or any other University, nor has it been submitted elsewhere for publication.

…… ……..

…25th...day of…October…2011

DEDICATION

This research report is dedicated to:

The Almighty God through whom all blessings come

My family, especially my wife, for her patience, understanding and support since the first time we met.

PRESENTATION ARISING FROM THIS STUDY

1. Intracranial meningiomas in Johannesburg

Presented at the 21st Biennal Congress of the Society of Neurosurgeons of South Africa, Johannesburg, 19-22 September, 2010

SESSION EIGHT 21st September 2010

TOPIC: Tumours **TIME:** 16h30 – 18h00pm (1½ hour)

Chairperson: Prof. HB. Hartzenberg **Panel:** Prof. A Kaye, Dr. S. Nadvi

TIME ACTIVITY/TOPIC PRESENTER

16:30 – 16:50 Management of giant pituitary tumours Prof P Semple

16:50 – 17:00 Extracranial Ependymoma Dr T Kuruvilla

17:00 – 17:15 Surgical treatment of pineal region tumours: Our experience of 9 cases

DrVN Bikmullin

17:15 – 17:25 Review of pituitary tumours over 10 years Dr K Matshana

17:25 – 17:35 Intracranial meningiomas in Johannesburg Dr KE Ibebuike

17:35 – 17:45 A1 segment aneurysm presenting as pituatory apoplexy Dr OA Labeodan

17:45 - 18:00 DISCUSSION

ABSTRACT

The study aimed at determining the relative frequency of intracranial meningiomas among primary brain tumours; age, gender, ethnic distributions and their mode of presentation.

This was a 12-month prospective study of 48 consecutive patients with histologically proven intracranial meningiomas seen at CMJAH and CHBH.

Meningiomas accounted for 33.8% of all primary brain tumours. The mean age of patients was 45.7 ± 10.1 years with a female-to-male ratio of 3.8:1. The peak age range at presentation was in the fifth (41.7%) and sixth (27.1%) decades. The highest frequency was in Blacks (75%) and Sotho ethnic nationality (27.1%). The mean duration of symptoms and signs was 24.4 ± 26.5 months. The commonest presentations were headache (87.5%), visual impairment (64.6%), seizures (43.8%), motor deficit (37.5%), convexity meningiomas (25%), meningothelial subtypes (39.6%) and WHO grade I tumours (81.3%).

This study showed that meningiomas are the most common primary intracranial tumours among adults in our environment.

ACKNOWLEDGMENTS

I thank the Almighty God for giving me good health and life, and for guiding me all through this work.

I am profoundly grateful to my supervisors, Dr. John Ouma and Dr. Pascale Willem, for their help and relentless guidance with this study. My very special thanks to my head of department, Prof. Rasik Gopal, whose encouragement and support since I commenced this work remained a great source of strength during several challenging moments in the course of the study. I also wish to express my appreciation to the entire consultants and registrars in the Department of Neurosurgery for their encouragement, understanding and inputs. I am grateful to the consultants, registrars and staff of Histopathology Department, Charlotte Maxeke Johannesburg Academic Hospital and Chris Hani Baragwanath Hospital, for their assistance, support and encouragement. My special thanks to the Faculty Research Office for the various research/statistical workshops and writing skills that helped in guiding me through this study. I am grateful to Mr. Sass Starlen, who helped with the installation of useful statistical software for data analysis, and to Mrs Junia Mthombeni who helped me with secretarial assistance whenever I needed her support. I am immensely grateful to the Imo State Government of Nigeria and the Imo State University Teaching Hospital, Orlu, for providing me with research grant to enable me weather the financial challenges for the study

Finally, I remain indebted to my wife, Mrs. J. E. Ibebuike, my children (David, John, Ruth and Caleb), my parents, siblings, and in-laws whose encouragement, understanding and support remain sources of inspiration to me.

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NOMENCLATURE

CT scan	-	Computed tomography scan
MRI	-	Magnetic resonance imaging
USA	-	United States of America
US	-	United States
USSR	-	Union of Soviet Socialist Republics
CMJAH	-	Charlotte Maxeke Johannesburg Academic Hospital
CHBH	-	Chris Hani Baragwanath Hospital
GCS	-	Glasgow Coma Score
FNS	-	First Noticed Symptoms
NCS	-	Neurosurgical Consultation Symptoms
CP Angle/CPA	-	Cerebello-pontine angle

1.0 INTRODUCTION

Meningiomas are tumours that develop from meningothelial cells of the arachnoid layer. Although they are a common central nervous system neoplasm and have an interesting long history which predates modern neurosurgery, they remain under-studied and under-reported (1, 2). Meningioma was first described in 1614 by Felix Paster (1, 3), and one hundred and sixty years afterwards, Louis (1, 4) published a series on the pathology of a "fungating tumour of the dura mater". The 18th century witnessed attempts at surgical resection and in 1887, W.W. Keen performed the first successful excision of a meningioma in the United States (1, 5, 6).

Later in the 20th century Harvey Cushing (1, 5, 7, 8) adopted the term meningioma as a single description for the different pathological types of tumours which arise from the meninges. Since then there has been increasing scientific and surgical interest in meningiomas. In 1922, Cushing wrote: "There is today nothing in the whole realm of surgery more gratifying than the successful removal of a meningioma with subsequent perfect functional recovery, especially should a correct pathological diagnosis have been previously made. The difficulties are admittedly great, sometimes insurmountable, and though the disappointments still are many, another generation of neurological surgeons will unquestionably see them largely overcome" (1, 7, 8). These words are very much fulfilled today.

Advances in neuroimaging have made the preoperative diagnosis of a meningioma almost certain. However, some meningiomas with an aggressive course, potential for recurrence or resistance to available treatment modalities are still a dilemma. The biologically

complex nature of meningiomas together with the challenges they present clinically and surgically, coupled with the rewarding potential for cure make them of immense interest to neurosurgeons and neuroscientists (9).

An overview of the descriptive epidemiology and presentation of this most intriguing disease will be presented in the literature review.

1.1 LITERATURE REVIEW

1.1.1 Incidence

Meningiomas are the most common primary intracranial neoplasms in adults (10). Though early combined results from several large hospital-based brain tumour studies showed that the incidence of meningiomas is approximately 20% of all intracranial tumours (11, 12), they are estimated to constitute between 13 and 26% of all intracranial neoplasms (13). Cushing (7, 12, 14) in 1938 found 13.4% while Zimmerman (12, 15) in 1969 reported 27.3% prevalence rate for meningiomas. The highest incidence of meningiomas was noted by Percy et al (12, 16) in a population based review of records from 1935 to 1958. In their study meningiomas accounted for 38% of primary intracranial tumours, though this contrasts with another population based clinical study performed in Manitoba, Canada from 1980 to 1985 where meningiomas accounted for 22% of primary intracranial tumours (7, 12, 17). The overall incidence of meningiomas in the Manitoba study was 2.3/100,000 (7, 12)

More recent studies show consistently high incidence of meningiomas, accounting for 25% of all intracranial neoplasms diagnosed in the United States (18), approximately 20% of all intracranial tumours in males and 38% in females (12, 18, 19). The estimated prevalence of meningiomas was approximately 97.5/100,000 in the United States (18, 20). A recent study in Nigeria, West Africa by Idowu et al (21) supports earlier findings that meningiomas are the most common primary intracranial neoplasms in adults with an incidence of 35% in their study.

1.1.2 Sex

Whereas intracranial tumours as a whole show a predominance in men (12, 21), meningiomas have a 2:1 female-to-male ratio in adults (7, 12, 13, 22). Interestingly, the Manitoba meningioma study showed no predominance in women in their fourth decade of life (7, 12, 17). Female predominance was noticed only after the fifth decade, and when readjusted after the sixth decade was 1:1 (7, 12, 17). Other studies, however, show that the difference is greatest in the older age group (23-25). An interesting finding among African groups in early reports was equal gender distribution or a male predominance (12, 26). However, recent African based studies are not in keeping with that (21, 27, 28).

1.1.3 Race

The prevalence of intracranial meningiomas displays racial/ethnic differences as can be seen between Caucasians, Africans and African-Americans. Meningiomas are more common in Africa than in America and Europe (29, 30) and accounts for nearly 30% of all primary intracranial tumours (29). In a Los Angeles County population-based study, Africans had a higher incidence than the Caucasian Americans(average, 3.1/100,000 compared to 2.3/100,000 respectively) (12, 31, 32). In this study, Asians were found to have the lowest rates though the differential rates between Asians and whites was less particularly among women (12, 31). On a larger scale, this is supported by a comparison of relative frequency of intracranial meningiomas in different countries including USA, Sweden, Iran, India, Japan and Germany (33). India had the lowest rate of 10.3% of meningiomas while Iran had the highest rate(29%) (33).

1.1.4 Age

The incidence of meningiomas increases with age (11, 12, 18). The annual incidence per 100,000 people ranges from 2 to 7 for women and from 1 to 5 for men (11, 12). In a study by Rohinger et al (12, 34), the incidence for males peaked in the seventh decade at 6.0/100,000 and for females in the eight decade at 9.5/100,000. Idowu et al (21) in their study noted that meningiomas accounted for 23% of all intracranial tumours in all age groups, and 35% in adults. Meningiomas are rare in children (7, 29, 35) and even more rare in infants (7, 12, 29). They account for 1-4% of all childhood (<18 years) primary brain lesions (7, 12, 35). They differ from those in adults and the childhood tumours in several respects including equal distribution between boys and girls (7, 35) or a male predominance (71%) especially in infants (7, 12). The average age at presentation is 10.9 years compared to 5.5 years for other Paediatric brain tumours (12). The incidence of intraventricular (17%) and posterior fossa (19%) meningiomas are higher in childhood than in adults as well as a significantly higher incidence (32% compared to 10%) of tumour calcification, sarcomatous elements and recurrence (7, 12). They, however, show similarities with adult meningiomas or other Paediatric brain tumours in the frequent (23%) association of neurofibromatosis with multiple intracranial tumours as well as clinical manifestations of increased intracranial pressure, visual disturbance, cranial nerve involvement or seizures (7, 12).

The incidence of intracranial meningiomas has also been noted to increase with time (12, 36). However, these increased rates may reflect improved diagnostic imaging modalities and increasing life expectancy of the general population (2, 10, 12)

1.1.5 Presentation and Magnitude of the Problem

Meningiomas are slow growing, usually benign and can remain clinically asymptomatic for years (29, 37). They challenge the neurosurgeon at every step and management decisions in asymptomatic presentations may be difficult (1). In some locations in the brain, meningiomas are problematic neoplasms which are difficult, disabling and ultimately fatal (1).

The mean duration of symptoms is approximately 15 months and 30% of complaints are less than 3 months in duration (38). They are associated with distressful clinical symptoms including loss of vision, dementia, headaches and seizures (1, 18). The relatively slow rate of growth for some meningiomas may lead to subtle losses of neurological function over time including speech difficulties such as finding words, changes in concentration abilities and paralysis of an arm or leg causing problems with writing, or walking (1, 18). It is reported that up to 30% of meningioma patients cannot read, write, drive or think at the same level as before their diagnosis (1). This highlights the subtle disabling outcomes associated with meningiomas. It is therefore important to identify means of defining individuals at risk as well as potential areas for rehabilitation services for such patients (18).

Though most meningiomas are benign, about 20% demonstrate clinically aggressive features which leads to significant morbidity and mortality (2). These categories of meningiomas frequently recur and expose patients to multiple surgical resections (39). In addition to the burden of suffering related to its disabilities and the attendant loss of productivity, meningiomas therefore constitute a major socioeconomic problem as well as

an important neurosurgical problem. And although intracranial meningiomas are usually benign and often cured after complete surgical excision, they still exhibit significant diagnostic and treatment challenges (9, 22, 40).

1.2 JUSTIFICATION FOR THE STUDY

Though meningiomas are common intracranial neoplasms, they remain under-studied and under-reported with comparatively limited research in the past regarding their epidemiology (2, 10). However, over the years there has been growing interest in meningiomas with new questions and challenges especially in epidemiology, radiology, pathology, genetics and treatment (9, 10).

Worldwide there has been consistent increase in the incidence of meningiomas and; also studies confirm increase in incidence with age as well as a female preponderance (18, 21). In several industrialised countries in the late 1970s and early 1980s there was an observed increase in the incidence of meningiomas (38). In Denmark, Finland, Norway and Sweden, the combined incidence increased from 1.4 to 1.9 per 100,000 among men and 2.6 to 4.5 per 100,000 among women (38) confirming an increase with age and a female preponderance. In a study by Elia-Pasquet (41) in Gironde, France, the incidence of intracranial meningiomas was 4 per 100,000 in those younger than 50 years and 7 to 10 per 100,000 in those older than 50 years. Christensen et al (36) in a 55 year study in Denmark reported 3.9 fold increase in the incidence of meningiomas from 1943 to 1997. In contrast, the incidence of gliomas increased by 1.7 fold during the same period. They noted in their study that improved diagnostic modalities have reached their maximum for gliomas. But

the same was not observed for meningiomas, and this may be an indication that under reporting of meningiomas is still present.

In addition to more sensitive diagnostic tools, the increased incidence of meningiomas may be related to increased exposure to environmental risk factors (10). It is reported that the high incidence of meningiomas in Iran (29%) is thought to be partly due to the late effects of mild doses of radiation of the scalp that some patients received in early childhood for treatment of ring worm of the scalp (33). Hence with increased life expectancy and availability of modern diagnostic tools, the incidence of meningiomas is expected to increase.

However, the advent of better imaging techniques has enabled earlier identification of these tumours in asymptomatic patients or patients with only a mild seizure as the presenting complaint(1), hence aiding reduction in morbidity and mortality. Whereas these new diagnostic tools including computed tomography scan (CT scan) and magnetic resonance imaging (MRI) are available in our environment, these tumours remain under reported. A closer look at the presentation of this disease in our environment is therefore considered worthwhile. This will increase awareness of this slow growing, mostly benign, potentially curable and highly prevalent disease among clinicians to aid early detection, treatment and subsequent reduction in morbidity and mortality associated with late presentation in our environment.

The information relating to the highest incidence of meningioma being in Africa (12, 30) adds to the challenge for a closer look at the presentation of this disease. This is in addition to the observation of a lack of such study in our environment. As our population ages due

to increase in our life expectancy, a closer look at this disease is therefore justified. Meningioma presents geographical and ethnic differences (18, 30). South Africa being peculiarly multiracial and multiethnic presents an ideal environment for studying the presentation of intracranial meningiomas. It is hoped that this will help in the advancement of knowledge for intracranial meningiomas both in South Africa and in the Southern Africa subregion. This may also aid health planners in their search for information about disease patterns, particularly about the prevalence of those conditions likely to make a high demand on hospital services.

Currently, there is growing interest in prospective studies on meningiomas (10). It is therefore hoped that this prospective study on the presentation of intracranial meningiomas in Johannesburg will be a worthwhile contribution to the renewed research endeavour on meningiomas. It is also probable that this research endeavour will eventually translate into better understanding and improved survival prospects for the few sufferers of the clinically aggressive and malignant forms of this disease.

It is hoped that with the increase in awareness of intracranial meningiomas expected from this study, there will be early detection and early treatment of intracranial meningiomas in our environment with resultant improved quality of life and survival rates in our patients.

1.3 STUDY OBJECTIVES

1.3.1 General Objectives

The aim of the study is to determine the presentation of Intracranial Meningiomas as seen at the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) and the Chris Hani Baragwanath Hospital, Johannesburg (CHBH).

1.3.2 Specific Objectives

1. To determine the relative frequency of intracranial meningiomas among primary intracranial tumours.
2. To determine the age, gender, racial and ethnic distribution at presentation in patients with intracranial meningiomas.
3. To determine the mode of presentation of intracranial meningiomas in Johannesburg.
4. To note and make comparison with intracranial tumours that satisfied the criteria for inclusion in this study of intracranial meningiomas but which had negative biopsies.

2.0 METHODS

2.1 Research Design

A descriptive prospective study design was used.

2.2 Place and Period of Study

This prospective study was carried out at the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) and the Chris Hani Baragwanath Hospital (CHBH), Johannesburg, over a period of 12 months from 13th July 2009 to 12th July 2010. Approval for the study was obtained from the Human Research Ethics Committee (Medical).

2.3 Patient Selection

Consecutive patients seen at the CMJAH and CHBH, Johannesburg with histologically proven intracranial meningiomas over a 12 month period were recruited into the study.

2.4 Inclusion Criteria

Criteria for inclusion in the study were as follows:

a) Patients with clinically and radiologically suspicious intracranial meningiomas. However, 5 patients with intracranial tumours clinically and radiologically not suspicious for meningioma but with histological diagnosis of meningioma were entered for the study.

b) Patients with biopsies of intracranial tumours positive for meningioma.

2.5 Exclusion Criteria

a) Patients with intracranial tumours whose clinical and radiological features were not suspicious for meningioma.

b) Patients with intracranial tumours whose clinical and radiological features were suspicious for meningioma, but who either declined operative intervention or did not have their tumours resected whatever the reason for such decision.

2.6 Limitations

a) Clinical and radiological diagnostic features of intracranial meningiomas are clear. However, management decisions excluded some patients from operative intervention. These patients, in addtion to patients who declined operative intervention limited the number of patients with biopsies positive for meningioma.

b) In addition, patients with clinical and radiological features of intracranial meningioma who died before a final diagnosis also limited the number of patients with biopsies positive for meningioma.

2.7 Instrument

An investigator-administered questionnaire (Appendix A) designed to record details of patient's personal record and clinical data as well as findings from relevant investigations was used. Every new patient was clerked by the author following the order on the pro forma after obtaining informed consent (Appendix C). The patient was then investigated following the standard investigative protocol for intracranial neoplasms including CT scan

and or MRI. Following clinical and radiological assessment treatment was instituted. Treatment was on outpatient basis for some patients on account of age and mild symptoms such as seizures and, which are amenable to control with drugs. Patients who required neurosurgical operative intervention were treated as in-patients. All specimens removed at operative intervention were subjected to histology for a final diagnosis.

2.8 Data Analysis

The data obtained was analyzed by the use of computer aided statistical analysis of the variables. Epi Info™ 2008 was used to analyze variables. Epi Info is a Database and Statistics Program for epidemiology on microcomputers designed for Public Health Professionals. It was developed by the Center for Diseases Control and Prevention (CDC), Atlanta, Georgia. Simple statistical calculations such as mean, median, frequency, percentages and standard deviation of variables were worked out. Statistical diagrams such as tables and figures were created to highlight relevant findings.

3.0 RESULTS

During the 12 months study period, 69 patients were initially entered for the study at the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) and the Chris Hani Baragwanath Hospital (CHBH), Johannesburg. All patients were seen as in-patients. Fourty eight of these patients had histologically confirmed intracranial meningioma with the hospital distribution as 27 patients at CHBH and 21 patients at CMJAH.

Table 3.1: Initial assessment of intracranial neoplasms entered for the study

Diagnosis	Number of patients	Percent
Meningioma	64	92.8%
Pituitary tumour	3	4.3%
Glioma	1	1.4%
Haemangiopericytoma	1	1.4%
Total	69	100%

Sixty four patients (92.8%) were initially assessed during preoperative work up as meningiomas, 3 (4.3%) as pituitary tumours and 1 (1.4%) each as glioma and haemangiopericytoma.

Table 3.2: Patients initially assessed as meningioma but with biopsies negative for meningioma

Histological Diagnosis	Number of patients	Percent
Metastatic tumour	3	33.3%
Haemangioblastoma	1	11.1%
PCNSL	1	11.1%
Myeloma	1	11.1%
Meningeal haemangiopericytoma	1	11.1%
Pituitary tumour	1	11.1%
Mycobacterial infection	1	11.1%
Total	9	100%

Patients initially assessed as meningioma after clinical and radiological assessment but with biopsies negative for meningioma were nine in number. Metastaic tumours were 3 (33.3%) whereas the rest were 1 (11.1%) each including mycobacterial infection.

Table 3.3: Reasons for non-operative intervention

Reasons for Non-operative Intervention	Number of patients	Percent
Patient declines operative intervention	4	33.3%
Elderly + clinical debilitation from primary diseae	2	16.7%
Clinical debilitation from extensive primary diseae	1	8.3%
Elderly + mild symptoms amenable to medications	1	8.3%
Elderly + clinical debilitation from co-morbidities	1	8.3%
Asymptomatic incidental finding on CTB	1	8.3%
Extensive recurrent intracranial meningioma	1	8.3%
Death before operative intervention	1	8.3%
Total	12	100%

The reasons why some patients with clinically and radiologically suspicious intracranial meningiomas did not have operative intervention showed that 4 (33.3%) patients declined surgical removal of their brain tumour, 2 (16.7%) were elderly patients who were clinically debilitated from the brain tumour and therefore were not fit for surgical operation. The other reasons (1 (8.3%) patient each) for non-operative intervention are as shown in table 3.3.

Table 3.4: Relative frequency of intracranial meningiomas among primary intracranial tumours

Diagnosis	Number of patients	Percent
Meningioma	48	33.8%
Pituitary adenoma	35	24.6%
Glioma	32	22.5%
Craniopharyngioma	4	2.8%
Ependymoma	4	2.8%
Medulloblastoma	4	2.8%
Schwannoma	3	2.1%
Myeloma	3	2.1%
Lymphoma	2	1.4%
Epidemoid cyst	2	1.4%
PCNSL	1	0.7%
Meningeal haemangiopericytoma	1	0.7%
Haemangioblastoma	1	0.7%
Atypical teratoid/rhabdoid tumour	1	0.7%
PNET	1	0.7%
Total	142	100%

Fourty eight (33.8%) patients had histologically confirmed intracranial meningioma during the study period, 35 (24.6%) had pituitary adenomas and 32 (22.5%) had gliomas. The rest of the intracranial tumours seen during the study period are as shown in Table 3.4.

Table 3.5: Age of patients at presentation

Age group in years	Number of patients	Percent
Both genders		
21-30	4	8.3%
31-40	9	18.7%
41-50	20	41.7%
51-60	13	27.1%
61-70	2	4.2%
Total	48	100%
Males		
21-30	3	30%
31-40	2	20%
41-50	2	20%
51-60	2	20%
61-70	1	10%
Total	10	100%
Females		
21-30	1	2.6%
31-40	7	18.4%
41-50	18	47.4%
51-60	11	29.0%
61-70	1	2.6%
Total	38	100%

The mean (range) age of patients with intracranial meningiomas was 45.7 ± 10.5 (23-67) years with a median age of 46.5 years. The mean (range) age for male patients was 39.3 ± 13.5 (23-61) years while that of female patients was 47.4 ± 9.0 (27-67) years.

The peak age range was in the age group 41-50 years accounting for 41.7% of patients with meningiomas and corresponding to the fifth decade of life. The age group 51-60 years accounted for 13 patients (27.1%). Four patients (8.3%) were less than 30 years and only 2 patients (4.2%) were over 60 yeaars of age. No patient was seen below 23 years. The relative frequency for males peaked in the third decade with 3 (30%) patients and for

females in the fifth and sixth decades with 18 (47.4%) and 11 (29.0%) patients respectively.

Table 3.6: Gender, Race and Ethnic Nationality (Home language) distribution

Variable	Number of patients	Percent
Gender		
Male	10	20.8%
Female	38	79.2%
Total	48	100%
Race		
Black	36	75%
White	6	12.5%
Coloured	4	8.3%
Indian/Asian	2	4.2%
Total	48	100%
Ethnic Nationality (Home language)		
Sotho	13	27.1%
Afrikaans	6	12.5%
English	5	10.4%
Zulu	5	10.4%
Tshwana	5	10.4%
Xhosa	5	10.4%
Foreign National	4	8.3%
Pedi	3	6.3%
Tshivenda	1	2.1%
Shangane	1	2.1%
Total	48	100%

Thirty eight (79.2%) patients were females and 10 (20.8%) were males. Thirty six (75%) patients were blacks, 6 (12.5%) were whites, 4 (8.3%) were coloured and 2 (4.2%) were Indians. Thirteen (27.1%) patients were of the Sotho ethnic nationality, 6 (12.5%) were Afrikaans and 5 (10.4%) patients accounted for English, Tshwana, Zulu and Xhosa ethnic nationalities. Three (6.3%) patients were Pedi and 1 (2.1%) each was Shangane and Tshivenda. There were 4 (8.3%) foreign nationals from neighboring Southern African countries.

Table 3.7: Presenting symptoms and signs

Symptoms/signs	Number of patients	Percent
Headache	42	87.5%
Visual impairment	31	64.6%
Seizures	21	43.8%
Generalized	15(71.4%)	
Focal	6(28.6%)	
Motor deficit	18	37.5%
Dizzziness	17	35.4%
Memory loss	12	25.0%
Personality/behavioural changes	12	25.0%
Other cranial nerve deficits	8	16.7%
Affected cranial nerves		
VII	4(50.0%)	
Multiple	3(37.5%)	
VI	1(12.5%)	
Decreased GCS	9	18.8%
Loss of smell	7	14.6%
Gait problem	6	12.5%
Vomiting	5	10.4%
Hearing loss	5	10.4%
Language problem	4	8.3%
Neck stiffnes	4	8.3%
Proptosis	4	8.3%
Sensory loss	3	6.3%
Extracranial mass/swelling	2	4.2%
Cerebellar symptoms	2	4.2%
Epistaxis	1	2.1%

The order of prevalence of the presenting symptoms and signs of the patients is as shown in table 3.7. Headache (87.5%), visual impairment (64.6%), seizures (43.8%), motor deficit (37.5%), dizziness (35.4%), memory loss (25%), personality/behavioural changes (25%) and decreased GCS (18.8%) were noted in that order. These were followed by other cranial nerve deficits (16.7%), loss of smell (14.6%), gait problems (12.5%), vomiting (10.5%), hearing loss (10.5%), language problems (8.3%), neck stiffness (8.3%), proptosis (8.3%),

sensory loss (6.3%), extracranial mass (4.2%), cerebellar symptoms (4.2%) and epistaxis (2.1%).

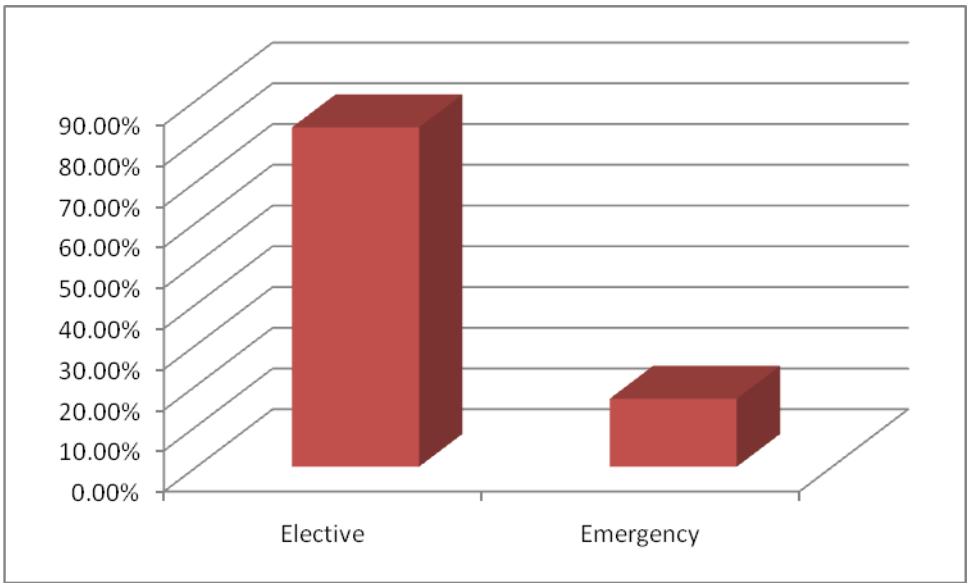

Figure 3.1: Mode of admission

Forty patients (83.3%) were admitted as elective cases while 8 (16.7%) patients presented as emergencies.

Table 3.8: Characteristics of symptoms and signs at presentation and their duration

Variable	Number of patients	Percent
First noticed symptoms (FNS)		
Headache	20	41.7%
Visual impairment	7	14.6%
Loss of smell	5	10.4%
Seizures	4	8.3%
Personality/behavioural changes	3	6.3%
Motor deficit	3	6.3%
Proptosis	3	6.3%
Decreasing LOC	1	2.1%
Cranial nerve palsy	1	2.1%
Extracranial mass/swelling	1	2.1%
Neurosurgical consultation symptoms (NCS)		
Visual impairment	14	29.2%
Motor deficit	8	16.7%
Seizures	4	8.3%
Personality/behavioural changes	4	8.3%
Proptosis	4	8.3%
Headache	3	6.3%
Decreasing LOC	3	6.3%
Uncontrollable seizures	2	4.2%
Extracranial mass/swelling	1	2.1%
Memory loss	1	2.1%
Blindness	1	2.1%
Cranial nerve palsy	1	2.1%
Vomiting	1	2.1%
Shortness of breath	1	2.1%
Duration of FNS in months		
<1	3	6.3%
1-12	20	41.7%%
13-24	13	27.1%
25-36	5	10.4%
37-48	1	2.1%
49-60	1	2.1%
>60	5	10.4%

Duration of NCS in months		
<1	19	39.6%
1-12	25	52.1%
13-24	2	4.2%

The duration of symptoms varied widely, ranging from 1-120 months with a mean of 24.4 ± 26.5 months. On the average symptoms lasted for more than 24 months. Twenty patients (41.7%) first noticed their symptoms (FNS) within 12 months while three patients (6.3%) noticed their symptoms within a month. The rest (25 patients) had symptoms longer than 12 months. Headache (41.7%) was the first symptom to be noticed followed by visual impairment (14.6%) and loss of smell (10.5%).

On the other hand, the duration of symptoms that necessitated neurosurgical consultation (NCS) were all within 24 months with 25 (52.1%) patients presenting within 12 months, 19 (39.6%) within a month and only 2 (4.2%) patients presented in the second year. Visual impairment (29.2%) was the commonest symptom followed by motor deficit (16.7%) in that order.

Table 3.9: Anatomic location of intracranial meningiomas

Radiological findings	Number of patients	Percent
Anatomic Location		
Convexity	12	25.0%
Olfactory groove	8	16.7%
Sellar/suprasellar	7	14.6%
Sphenoid wing	6	12.5%
Falx	5	10.4%
Spheno-orbital	3	6.3%
Orbital	1	2.1%
CP angle	1	2.1%
Convexity-extracalvarial	1	2.1%
Parasagittal	1	2.1%
Intraventricular	1	2.1%
Tentorial	1	2.1%
Foramen magnum	1	2.1%
Total	48	100%
Multiple meningiomas	4 (8.4%)	
Spheno-orbital	2	
Sellar/suprasellar	1	
Olfactory groove	1	
Compartmental location		
Supratentorial	45	93.8%
Infratentorial	3	6.3%

All forty eight patients carried out CT scan and/or MRI of the brain as part of their pre-operative investigation and work up. MRI had better definintion for these tumours and was able to detect somes cases with multiple tumours and dural tail. The anatomic location of the tumours is as shown in table 3.9. Convexity meningioma accounted for 25% of cases, olfactory groove 16.7%, sellar/suprasellar 14.6%, sphenoid wing 12.5%, falx 10.4% and spheno-orbital 6.3%. All spheno-orbitally located meningiomas presented with proptosis.

Meningiomas located at the cerebello-pontine angle (CPA), convexity-extracalvarial, parasagittal, intraventricular, tentorial and foramen magnum were found in 1 (2.1%) patient each. Four patients, however, had multiple tumours. Of these, two belonged to the spheno-orbital meningiomas, one each for sellar/suprasellar and olfactory groove meningiomas. The locations indicate the resection sites from which tissue biopsies were obtained. Supratentorially located tumours were the commonest (93.8%).

Table 3.10: Radiological findings in patients with intracranial meningioma

Variable	Number of patients	Percent
Radiologic findings		
Enhancement	48	100%
Mass effect	36	75%
Oedema	30	62.5%
Midline shift	24	50.0%
Hydrocephalus	15	31.3%
Hyperostosis	11	22.9%
Dural tail	8	16.7%
Bone destruction	5	10.4%
Side of location		
Left	22	45.8%
Midline	15	31.3%
Right	11	22.9%
Size of tumour		
1-2cm	2	4.2%
2-3cm	4	8.3%
3-4cm	13	27.1%
4-5cm	7	14.6%
>5cm	22	45.8%
Component of tumour		
Solid	27	56.3%
Solid + calcification	11	22.9%
Solid + necrotic	4	8.3%
Solid + cystic + necrotic	3	6.3%
Solid + cystic	1	2.1%
Solid + calcification + becrosis	1	2.1%

Solid + haemorrhagic	1	2.1%

The order of prevalence of diagnostic radiological findings as well as tumour effects in the brain is as shown in table 3.10. Enhancement (100%), mass effect (75%), oedema (62.5%), midline shift (50%), hydrocephalus (31.3%), hyperostosis (22.9%), dural tail (16.7%), bone erosion (10.4%) were noted in that order. Tumour location on the left side of the brain was seen in 22 (45.8%) patients, midline location in 15 (31.3%) patients while 11 (22.9%) patients had their tumours located at the right side of the brain. The size of the tumours ranged from between 1-2cm in diameter to more than 5cm in diameter with the largest tumour sizes of >5cm in their longest dimension accounting for 45.8% of all the tumours. There were no tumours below 1cm in size among the resected cases except for those incidentally detected in the MRI of some of the patients with multiple tumours. Solid tumours constituted the highest (56.3%) in tumour component whereas among the mixed components, mixed solid tumour and calcification accounted for 22.9%. Mixed solid and haemorrhagic (acute haemorrhage) component was found in the only patient who presented in pregnancy.

Table 3.11: Histological subtypes and grading of intracranial meningiomas

Variable	Number of patients	Percent
Histology result		
Meningothelial	19	39.6%
Fibroblastic	7	14.6%
Mixed meningiomas	7	14.6%
Angiomatous, microcystic	2 (28.6%)	
Angiomatous, microcystic, secretory	1 (14.3%)	
Fibroblastic, fibroblastic, rhabdoid features	1 (14.3%)	
Meningotheliomatous, fibroblastic, microcystic	1 (14.3%)	
Transitional, meningothelial, fibroblastic	1 (14.3%)	
Transitional, fibroblastic, meningothelial and angiomatous	1 (14.3%)	
Transitional	4	8.3%
Atypical	3	6.3%
Anaplastic	2	4.2%
Psammomatous	2	4.2%
Chordoid	1	2.1%
Clear cell	1	2.1%
Microcystic	1	2.1%
Secretory	1	2.1%
WHO classification		
Grade I	39	81.3%
Grade II	6	12.5%
Grade III	3	6.3%

Meningothelial meningioma accounted for 39.6% of cases followed by fibroblastic meningioma (14.6%), mixed meningiomas (14.6%), transitional (8.3%), atypical (6.3%), anaplastic (4.2%) and psammomatous meningiomas (4.2%) in that order. Chordoid, clear

cell, microcystic and secretory meningiomas accounted for 2.1% each. WHO classification grade I tumours were the commonest (81.3%). Though there were only 2 (4.2%) anaplastic tumours, the mixed meningioma with rhabdoid morphology confered to that tumour WHO grade III classification, hence the 3 (6.3%) WHO grade III tumours in this study.

4.0 DISCUSSION

There are few prospective studies on histologically proven intracranial meningiomas in the literature. This study therefore serves as a useful baseline study on intracranial meningiomas in our environment. Although the number of cases seen during the period of study remains the highest among the literatures reviewed and compared to in this study, the study is limited by the short period of 12 months. Hence the results were displayed in descriptive terms for comparison with other published data.

4.1 Relative Frequency

Meningiomas are estimated to constitute between 13-26% of primary intracranial neoplasms (42), though early combined results from several large hospital-based brain tumour studies showed that the incidence of meningiomas is approximately 20% of all intracranial tumours (11, 12, 22). In this study meningiomas accounted for 31.8% of all intracranial neoplasms and 33.8% of primary intracranial neoplasms. The findings in this study (33.8%) compares with a recent study by Idowu et al (21) in Ibadan (35%) and Idowu and Apemiye (43) in Lagos (30%) which showed high relative frequency of meningiomas among primary intracranial neoplasms in adults. It also compares with a recent study (44) in the United States (US) in which meningiomas accounted for 33.8% of all primary brain and central nervous system tumors reported in the United States between 2002 and 2006. The findings also compares with a study by Das et al (45) in Singapore

(35.1%). The findings in this present study show that meningiomas are the most common primary intracranial tumours among adults in our environment. This, however, contrasts with reports indicating gliomas as the most common primary intracranial neoplasms in other series from Japan, Thailand, United States, and the previous USSR (45).

When adjusted for number of patients per year, the findings (48 patients per year) in this study rates highest compared to that of Das et al (45) in Singapore (41 patients per year), Fynn et al (27) in Pretoria (17.3 patients per year), Gasparetto et al (46) in Brazil (15.6 patients per year), Quiñones-Hinojosa et al (47) in US (9.6 patients per year), Francis (48) in India (6.9 patients per year) and Jaggon and Char (49) in Jamaica (5.3 patients per year). Although this may indicate a high trend in the relative frequency of intracranial meningiomas in our environment, it may also be the result of the improved detection rate through the increasing availability of modern diagnostic neuroimaging facilities in our environment.

4.2 Sex

Meningiomas affect women more often than men with a male-to-female ratio ranging from 1:1.4 to 1:2.8 (29). This study showed a female-to-male ratio of 3.8:1 and compares with the findings of Idowu et al (21) which revealed a female-to-male ratio of 4.2:1 in both age group, and 4:1 in the adult population. It, however, contrasts with the findings of Jaggon and Char (49) in Jamaica (2.8:1), Fynn et al (27) in Pretoria (2.5:1) and Gasparetto et al (46) in Brazil (2:1). It is also a sharp contrast to Francis (48) in India (1.6:1) and Odebode et al (28) in Ibabdan (1.3:1). The findings in this study also differs from earlier observations in the literature (12, 29, 50), which reports equal gender distribution or a male

predominance among Africans. However, the female-to-male ratio of 1:3 in the third decade of life in this study is in keeping with reports in the literature which showed no predominance in women in their fourth decade and below (7, 12, 17).

4.3 Race/Ethnicity

Racial/ethnic differences in the prevalence of intracranial meningioma have been reported between Caucasians, Africans and African-Americans (29). The high frequency of intracranial meningiomas among the black race (75%) in this study may reflect the predominantly black population in our environment. However, among the other races, Indians had the lowest rate and there was no Asian, in keeping with the findings in other studies elsewhere (12, 31-33). In a recent US study (44), reported rates for Black Non-Hispanics are slightly higher (6.67) than for White Non-Hispanic and Hispanics (5.90 and 5.94, respectively).

Meningiomas constituted 30% of brain tumors in Bantus in Africa (38). This compares with the high prevalence among Sotho ethnic nationality (27.1%) noted in our environment, despite the dominant ethnic group in Johannesburg being Zulu (10.4%). These findings may partly be explained on the influence of genetic factors on the prevalence of intracranial meningiomas in Johannesburg. The relative contributions of risk factors including environmental, hormonal or genetic factors to this sociodemographic variation are yet to be determined in our environment.

4.4 Age

Meningiomas have a tendency to occur from the third to sixth decades of life (22, 38) and with peak incidence between the age of 40-60 years (51). Meningiomas are rare in patients younger than 20 years (38). This compares with the findings in our study which showed the peak age range in the fifth (41.7%) and sixth (27.1%) decade for both gender. Females showed similar peak age incidence of 47.4% and 29% respectively, whereas males had a fairly equal spread with the highest incidence in the third (30%) decade of life. There was no meningioma in infancy and childhood in this study. This is in keeping with the rarity of meningiomas in infants and children (7, 11, 22), though the short study period may have influenced this finding as well.

The incidence of meningiomas increases with age (29). In this study, the youngest patient was 23 years old; the median age was 46.5 years while the mean age was 45.7 ± 10.1 years. This corresponds with the findings of Jaggon and Char (49) in Jamaica where the mean age of patients with intracranial meningiomas was 45 years. Fynn et al (27) in Pretoria found similar mean age (47 years) in their series. A lower mean age of 40 years was noted by Odebode et al (28) in Ibadan, though this may have been influenced by the low number of patients (n=35) in their study. A higher mean age of 52.7 years was noted in the study by Quiñones-Hinojosa et al (47) in the United States. However, their study assessed pre-operative factors affecting resectability of giant intracranial meningiomas (≥ 5cm in the longest dimension). From their study, one can infer the likelihood of a shift towards older age group in large sized meningiomas. Large sized meningiomas are more likely to reflect long standing disease for these slowly growing tumours, and therefore their likely occurrence in the older age group.

When compared to other studies, the age range (23-67 years) in this study differs from that of Fynn et al (27) in Pretoria (2-83 years), Odebode et al (28) in Ibabdan (9-77 years), Jaggon and Char (49) in Jamaica (13-80 years) and Francis (48) in India (18-75 years). It compares to the findings of Gasparetto et al (46) in Brazil (23-81 years), in not having any patient in the paediatric age group but contrasts with it in not having any patient from the eight decade upwards. The absence of intracranial meningiomas in the paediatric age group in this study may have been influenced by the short study period, which may have limited the possibility of identifying patients in the paediatric age group within the study period. And the absence of intracranial meningiomas among patients from the eight decade upwards in this study may reflect a cautious approach to operative intervention among the elderly, as was reflected in the elderly constituting 33.3% (table 3.3) of patients among the reasons for non-operative intervention.

4.5 Clinical Presentation

The mean duration of symptoms for intracranial meningiomas has been reported to be approximately 15 months with 30% of complaints within 3 months in duration (38). This contrasts with the findings in this study where the mean (range) duration of symptoms and signs is 24.4 ± 26.5 (1-120) months with 6.3% of patients presenting within 1 month duration and 41.7% of patients within 12 months duration. The remaining 52% of patients presented after 12 months of symptoms. It is also a sharp contrast to the study by Quiñones-Hinojosa et al (47) where the median (range) duration of symptoms prior to diagnosis was 6 (2- 12) months, though it compares with the findings by Odebode et al (28) with a mean (range) duration of symptoms of 18 (2-60) months. One had expected a

longer duration of symptoms in the series by Quiñones-Hinojosa et al (47) on account of the larger tumour size (≥5cm) observed in their study which could reflect long standing lesions. This was, however, not the case. This may support the observation in the literature that late presentation and diagnosis remain serious issues in developing countries when compared to developed countries (28, 43). Probable reasons for this fact may be cultural and religious beliefs as well as self medication, financial constraints, low health education and low level of awareness even among clinicians (28, 43). However, large sized meningiomas, especially in the frontal lobes, can exist with few symptoms (38, 52) and this may contribute to the early presentation in the series by Quiñones-Hinojosa et al (47) despite the large tumour size.

The primary complaints of patients include focal deficit, seizures, psycho-organic syndrome, and headaches (38). The most common symptoms and signs reported in the literature (53) are headache (36%), paresis (22%) and change in mental status (21%). This contrasts with the findings in the present study which showed headache (87.5%), visual impairment (64.6%), seizures (43.8%), motor deficit (37.5%) and dizziness (35.4%) as the commonest symptoms. The findings in this study, however, compares with that of Odebode et al (28) where the most common symptoms and signs were headache (91%), decreased visual aquity (85.7%), focal neurological deficits (59%), seizure (34.0%) and features of increased intracranial pressure other than headaches (32%). The high frequency of visual impairment in the present study differs from reports that visual loss is rare in olfactory groove, parasagittal, falx and convexity meningiomas but with a high association in sellar/suprasellar meningiomas because of close proximity of the latter to the optic nerves or chiasm and consequent pressure on the nerves (28). The high prevalence of

visual impairment in this study despite the wide distribution of the meningiomas throughout the cranium (table 3.9) may suggest the involvement of other influencing factors. The high prevalence of larger tumour size (45.8%), mass effect (75%), perifocal oedema (62.5%), and hydrocephalus (31.3%) (table 3.10) and, the resultant intracranial hypertension in addition to late presentation may act singly or in combination (28) as possible reasons for the high visual impairment noticed in this study. The symptom of epistaxis noticed in this study was in a HIV positive patient and may therefore be related to the systemic debilitation asssociated with HIV/AIDS symptomatology.

Seizure activity is reported as one of the most common first presenting symptoms, with a frequency of 26% among patients with intracranial meningioma (10). In contrast when adjusted for First Noticed Symptom (FNS), headache (41.7%) was the first noticed symptom at presentation in our environment. This is closely followed by visual impairment (14.6%), anosmia (10.4%) and seizures (8.3%). This may have partly contributed to the issue of late presentation in our environment as the above symptoms are readily controlled on self-medication by patients, and as well easily misdiagnosed at initial presentation to primary care physicians as representing flu or refractory problems as the case may be.

Further probing of the patients' history in this study showed that the duration of symptoms that necessitated neurosurgical consultation (Neurosurgical Consultation Symptoms-NCS) were all within 24 months. Nineteen (39.6%) patients presented within 1 month of NCS while 25 (52.1%) patients presenting within 12 months and only 2 patients presented in the second year. Deterioration in vision (29.2%) was the commonest symptom followed by motor deficit (16.7%), seizures (12.5%) and behavioural changes (8.3%) in that order. This

may suggests that presentation to a neurosurgeon is highly influenced by the severity of the symptoms and signs as well as the degree of incapacitation to the patient. It may also give credence to similar observation and the assertion by Nkposong and Lawani (54) in their study on prostate cancer that the African has greater tolerance of symptoms. However, from personal observation noted by the author, the waiting time for diagnostic neuroimaging at public hospitals also contributes to some of the delays at presentation to neurosurgeons when radiodiagnostic requests are made by clinicians.

4.6 Neuro-radiology

The majority of focal extra-axial masses are meningiomas. In plain radiographs, their characteristic markers are hyperostosis, increased vascular markings and calcifications (13, 53). No attempt was made in this study to use plain radiographs due to the availibility of modern neuroimaging in the two centres choosen for the study. The preferred investigation of choice for the diagnosis of intracranial meningioma is MRI because it has superior image resolution and can show more clearly the dural origin of the tumour in most cases (10, 52). Though CT scan remained the first choice in our environment because of the ease of accessibility and being more economical as a preliminary investigation for patients with neurological symptoms, MRI was employed where necessary to clear doubts on the radiological diagnosis.

In 80% to 90% of cases, meningiomas have characteristic imaging appearances which guide diagnosis with confidence. The main diagnostic challenges include the distinction from dural metastasis, cerebral lymphoma, haemangiopericytoma, and extra-axial inflammatory conditions and infections such as sarcoidosis and tuberculosis; more rarely

gliomas and primitive neuroectodermal tumors may masquerade as meningiomas (10, 52). This was reflected in the findings in this study (table 3.2) which showed nine patients who were initially assessed as having meningiomas but who later had negative histology for meningiomas. The findings in this study show that metastatic tumour is the commonest differential diagnosis for intracranial meningiomas (33.3%) in our environment. Others include lymphoma (11.1%), myeloma (11.1%), tuberculosis (11.1%) and other primary intracranial neoplasms depending on the tumour location including haemangiopericytoma (11.1%).

Some meningiomas show atypical features such as ring enhancement, central cystic degeneration or have an associated cyst that can mimic malignant intra-axial tumours (10, 52). On the otherhand, meningioma can also be a differential diagnosis of other intracranial neoplasms depending on the location. Five of the patients in this study (table 3.1) were initially diagnosed with other types of intracranial neoplasms. The only case which was initially diagnosed as glioma but with histological diagnosis showing meningioma was the youngest patient (23 years) in this study. He presented as an emergency with severe clinical debilitation and a reduced GCS. CT scan showed a large (8.8cm in longest dimension) intra-axial left fronto-parietal inhomogeneously enhancing mass with areas of central necrosis and mild perifocal oedema. However, the histological diagnosis was a meningothelial meningioma (WHO grade I). The study shows that meningioma is a strong differential diagnosis for tumours thought to be pituitary tumours as well as a rare differential for some intra-axial tumours in our environment. However, MRI clearly distinguishes meningioma from other intracranial neoplasms in most cases by showing the presence of a dural-tail in meningiomas (52). Although dural tail is not pathognomonic, it

is possibly the best diagnostic sign (10, 53). Diagnosis of intracranial meningiomas can also be aided by the identification of anatomic interfaces (pial vascular structures, hypointense dura, cerebrospinal fluid clefts) between the tumor and brain surface. Cerebrospinal fluid clefts have high intensity on T2 weighted image and are therefore best for its visualization. Haemangiopericytoma is often confused with malignant meningioma (10). This is in keeping with the finding of haemangiopericytoma in this study (tables 3.1 and 3.2). It featured both as a possible differential diagnosis of intracranial meningioma as well as meningioma being a differential diagnosis of haemangiopericytoma. Diagnostic differentiation is of clinical importance because haemangiopericytoma is associated with a more aggressive clinical course. Important features that are suggestive of haemangiopericytoma over meningioma include absence of calcification, lack of hyperostosis, bone destruction, and lobulated contour (10).

Supratentorially located meningiomas constitute 85-90% with 5-10% infratentorially located (10, 53). This compares with the present study (93.8% and 6.3% respectively), Jaggon and Char (49) (87% and 4% respectively), Odebode et al (28) (94.3% and 5.7% respectively), and Quiñones-Hinojosa et al (47) (87% and 13% respectively). The sites for infratentorial meningioma include along the tentorial free edge, clivus, foramen magnum, petroclival ligament, and petrous ridge (10). The 3 infratentorially located meningiomas in this study were situated along the tentorial free edge, CPA and the foramen magnum and contrasts with the findings by Quiñones-Hinojosa et al (47) which were either along the cerebellar hemispheres or the CPA. It also contrasts with that of Jaggon and Char (49) which were attached to the falx cerebelli. The differences in the location of infratentorial

meningiomas in the different studies may be related to the rarity of meningiomas in this location.

The most common locations include the convexity/parasagittal (45%), sphenoid ridge (15-20%) and olfactory groove/planum sphenoidale (10%) (10, 53). This compares with the findings in this present study with convexity/falx/parasagittal accounting for 39.6%, sphenoid wing/spheno-orbital 20.9% and olfactory groove 16.7%. The findings of Fynn et al (27) and Jaggon and Char (49) also supports the above distribution of intracranial meningiomas in their studies. The prevalence of multiple meningiomas (5-40%) reported in the literature (29) also compares with the findings of multiple intracranial meningiomas (8.4%) in this present study. All the patients with spheno-orbital tumour location in this study in addition to the only orbitally located meningioma presented with proptosis, with one of the patients presenting with bilateral proptosis due to bilateral spheno-orbital meningioma. Intracranial meningioma should therefore be considered a strong differential diagnosis for proptosis in our environment. Meningiomas are reported to account for 6% to 17% of diseases producing proptosis of the eye (55). Intracranial meningiomas of the greater and lesser wing of the sphenoid cause proptosis by different mechanisms including direct encroachment on the orbital cavity, by reactive hyperostosis of the inner orbital wall or by interfering with venous or lymphatic drainage (55). Classical optic nerve meningiomas results in proptosis devoid of ophthalmoplegia, visual failure, optic atrophy or papilloedema (55, 56).

Meningiomas typically demonstrate intense enhancement after contrast administration both on CT scans and MRI (27, 46) and with the majority enhancing avidly and homogeneously

(10). This is in keeping with the findings in this study where all the meningiomas demonstrated enhancement (100%) with accentuation in over 56.3% of the cases and heteregeneous in the rest. This may be a possible reflection of the late presentation in our environment and the consequent large tumour sizes, long standing lesions and the attendant degenerative changes in the tumours. Gasparetto et al (46) noticed 83% and 64% respectively in their study.

Meningiomas may also be associated with cystic components and calcification in some cases (27, 53). Peritumoral oedema, haemorrhage and central cystic degeneration may also be seen (52, 53). Hydrocephalus is uncommon because of the convex calvarial dural attachment of intracranial meningiomas, with the exception of intraventricular and posterior fossa locations (38). In addition, most meningiomas show a characteristic dural tail sign (35-80%) and hyperostosis which though uncommon in convexity meningiomas occurs in nearly 50% of skull-base tumours (10, 52, 53). On the otherhand, calvarial invasion may manifest with radiologic appearances of destruction and lysis. It is important to identify bone invasion as it guides decisions on treatment modality. Although bone invasion is thought to signify aggressive tumor behavior, it does not always correlate with the histologic morphology of meningiomas (10).

The few cases of hyperostosis (22.9%) and dural tail (16.7%) in this study may be due to the low number of skull-base meningiomas and the limited use of MRI respectively. Bone destruction resulting from bone invasion was seen in 10.4% of cases in this study including the only patient with convexity-extrcalvarial meningioma. Contrary to reports in the literature, hydrocephalus was not uncommon (31.3%) in this study. The large (≥ 5cm in

longest dimension) size (45.8%) of meningiomas in this study and the associated marked mass effect (75%) in most cases, peritumoral oedema (62.5%), midline shift (31.3%) resulted in ventricular entrapment and hence hydrocephalus. These are all evidence of late presentation in our environment. Symptoms resulting from tumour haemorrhage are infrequent (38). The only patient who presented with tumour haemorrhage in this study was a post partum patient. She first presented to the obstetricians with pregnancy induced hypertension at 33 weeks of pregnancy. The development of fetal distres resulted in an emergency caesarean section being performed. She had a persistently reduced GCS postoperatively, necessitating an urgent CT scan of the brain which showed a large haemorrhagic (active haemorrhage) right frontal lobe mass. She subsequently had an emergency craniotomy and tumour excision afterwards which revealed an atypical meningioma. This supports the observation that meningiomas tend to have a more rapid growth rate during the later stages of pregnancy (10, 18, 57). It also supports reports in the literature noting the difficult clinical problem presented by the co-existence of brain tumour in preganacy because of their similar symptoms including headache, vomiting and visual impairment (58). Even convulsions caused by a brain tumour as well as rising blood pressure and reduced GCS (both resulting from raised intracranial pressure) may be erroneously attributed to pregnancy (58).

The majority of the tumours in this study were located in the left side of the brain (45.8%), closely followed by midline location (31.3%) and the least being on the right side (22.9%). The implication is that our patients will be prone to tumour related morbidity and an attendant early presentation for neurosurgical consultation. The findings in this study showed significant tumour related mobidity including symptoms and signs of intracranial

hypertension (dizziness-35.4%, decreased GCS-18.8%, vomiting-10.4%), visual impairment (64.6%), seizures (43.8%), motor deficit (18%) and cranial nerve palsies (16.7%) among others (table 7). However, presentation to neurosurgeons was late and only 16.7% of patients in this study were admitted as emergencies (table 8). The rest (83.3%) were admitted through the neurosurgical out-patient clinic. While this may add further credence to the observation by Nkposong and Lawani(54) that the African has greater tolerance of symptoms, it may also be related to low index of suspicion and consequent high level of misdiagnosis of intracranial meningiomas by most clinicians who see the patients first before referral for specialist care.

4.7 Neuro-pathology

The most commonly used grading system for meningiomas is that of the World Health Organization (WHO). The WHO classifies meningiomas into 3 grades: benign (WHO grade I), atypical (WHO grade II), and anaplastic or malignant (WHO grade III) and these constitute about 88-94%, 5-7% and 1-3% of cases respectively (10, 38, 52, 53). Therefore most meningiomas are benign tumours with the potential for cure after complete surgical excision. There is a range of subtypes based on their histological characteristics. However, the clinical behavior and outcomes correlate with the WHO grade, rather than the histological subtype. The grading of meningiomas is controversial, and accordingly there is a high incidence of interobserver variability (45). In this study WHO grade I constituted 81.5% of cases followed by WHO grade II (12.5%) and WHO III (6.3%) in that order and contrasts with the rates reported in the literature. While this may reflect the influence of interobserver variability in the grading of meningiomas, it may also indicate a real

difference in the histological characteristics of meninigiomas between blacks and the rates reported in the literature. This may also indicate a need for a genome wide study of meningiomas in our environment likely to reveal valuable information at a high genomic resolution. In particular, it would be of value to assess copy number aberrations associated with the respective histological subtypes (typical, atypical, anaplastic) and with differing grade of tumors, in comparison to other published data (22). The findings in this study compares to that of Quiñones-Hinojosa et al (47) in the United States which showed 73% of tumours being WHO grade I, 19% WHO grade II and 7% WHO grade III. However, the restriction of their study to larger sized tumours (≥ 5cm) may have influenced their findings. The findings of Das et al(45) in Singapore (WHO grade I. 90.2%, grade II, 6.8% and grade III, 3% respectively) were in agreement with rates in the literature. Jaggon and Char (49) in Jamaica found 94% of tumours to be WHO grade I lesions and 6% of WHO grade III lesions in their study. While their findings may be interesting and reflect the role of genetic and environmental factors in tumour epidemiology across differing world regions, the difficulties in characterization of various histological subtypes and lack of consensus on diagnostic criteria may also play a role in their findings (45).

Histological subtypes constituting WHO II include atypical, clear cell and chodoid subtypes and for WHO III they include the rhabdoid, anaplastic and papillary subtypes (53). WHO grade I meningiomas may have a variety of appearances, with the meningothelial, fibroblastic, and transitional variants occurring most commonly (10, 53). This is similar to the findings in this study (table 13). Similar findings were also noted by Odebode et al (28) and Jaggon and Char (49) in their studies.

5.0 CONCLUSION

Although this study did not aim at establishing the incidence of intracranial meningiomas in Johannesburg, it has shown that intracranial meningioma is not uncommon in Johannesburg. In fact, the relative frequency of intracranial meningiomas among primary intracranial neoplasms found in this study is one of the highest, and compares with other reports in the literature. Also the findings in this study agree with the observation that the highest incidence of intracranial meningiomas is in Africa when compared to other published data.

The high relative frequency of intracranial meningiomas among primary intracranial neoplasms during the study period might be the result of the improved detection rate through the increasing availability of modern diagnostic neuroradiology in our hospitals.

The peak age range at presentation of intracranial meningiomas in this study was in the fifth and sixth decades and is in agreement with most other studies. The female-to-male ratio of 3.8:1 is in keeping with the previous reports of female preponderance in intracranial meningiomas.

Despite the high prevalence of intracranial meningiomas in our environment, patients presented late to neurosurgeons and tended to present when the symptoms and signs appear to be worsening, unbearable or incapacitating. This may reflect the observation in the literature that the African people have a greater tolerance of symptoms.

The majority of tumours were large in size with associated marked mass effect, peritumoral oedema and degenerative changes in most of the tumours. WHO grade I tumours were the commonest with meningothelial, fibroblastic and transitional histologic subtypes commonest as well, all in keeping with reports in the literature.

Continuation of this prospective study and the expansion of the objectives to include genetic aspects of intracranial meningiomas, the methods of management and outcome in our environment need to be carried out to arrive at wide ranging conclusions.

6.0 RECOMMENDATION

Genetic and environmental factors may be responsible for some of the findings in this study and therefore further study is required to identify these factors. Preferably a multicentre study in different cities in South Africa may help to have a clearer picture of the racial/ethnic epidemiology of this tumour in our environment.

A much longer prospective study is strongly recommended to give the data stronger power for definite conclusions that will arise from the findings.

Greater awareness of intracranial meningiomas should be created through widespread mass information of our population including clinicians.

Visual problems and headache should be given serious consideration for diagnostic neuroimaging where symptoms remain unrelieved with basic care and medications. New onset headache and other symptoms and signs of brain tumours should raise a high index of suspicion in pregnant women as well.

New onset seizures and motor deficits should remain absolute indications for diagnostic neuroimaging and accorded urgent status by neuroradiologists.

A high index of suspicion for intracranial neoplasms should be given to neurologic symtoms and signs at presentation to clinicians and should also be considered urgent by neuroradiologist to reduce the waiting time by such patients for neuroimaging diagnosis.

APPENDIX A

PRESENTATION OF INTRACRANIAL MENINGIOMAS IN JOHANNESBURG (A 12-MONTH PROSPECTIVE STUDY AT CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL AND CHRIS HANI BARAGWANATH HOSPITAL, JOHANNESBURG)

PRO FORMA OF STUDY

BY

DR IBEBUIKE, KE

DATE: …..... HOSPITAL NUMBER: ……

A. DEMOGRAPHIC DATA (BASIC EPIDEMIOLOGY)

NAME & INITIALS: …… SERIAL NUMBER: …….....

1. Age at presentation ☐
2. Sex ☐
    1. Male
    2. Female
3. Race (Population Group)
    1. Black
    2. Coloured ☐
    3. Indian
    4. White
    5. Others (please specify).....
4. Home language
    1. Afrikaans
    2. English
    3. Pedi
    4. Sotho

5. Tswana
6. Swati
7. Xhosa
8. Zulu
9. Tshivenda
10. Xishonga
11. Ndebele
12. Others (please specify)……

5. Occupation
   1. Class I - Professionals and Business men
   2. Class II - Lesser professionals, traders and teachers
   3. Class III N - Skilled non-manual e.g. clerical staff
   4. Class III M - Skilled manual e.g. electrician, lorry drivers
   5. Class IV - Semi-skilled manual e.g. machine operators, farm workers
   6. Class V - Unskilled manual to the unemployed e.g. Labourers

6. Religious affiliation
   1. Christian
   2. Hindu
   3. Muslim
   4. Jehovah's Witness
   5. Jewish
   6. None
   7. Others (please specify)

7. Marital Status
   1. Single
   2. Married

3. Widow/er
4. Divorced
5. Separated

8. Place of Domicile
    1. Urban
    2. Periurban (townships)
    3. Rural

B. CLINICAL PRESENTATION

1. Headache
2. Seizures
    1. Focal
    2. Generalised
3. Neurological deficit
    1. Cranial nerves
    2. Long tracts
    3. Mixed
    4. Others (please specify).....
4. Associations (please specify)……..
5. Others (please specify)……
6. Duration of symptoms
7. Mode of admission
    1. Elective
    2. Emergency

C. RADIOLOGY

1. Location

2. Size
3. Enhancement ☐
4. Oedema
    1. Widest margin less than tumour size
    2. Widest margin equals to tumour size ☐
    3. Widest margin greater than tumour size
    4. No oedema ☐
5. Relationship to surrounding vascular structures ☐
    1. Displacement of vessels
    2. Encasement of vessels
6. Association with other intracranial pathology (please specify)….
7. Others relevant findings (please specify).....

E. **HISTOLOGY**

1. Histological diagnosis
2. WHO classification
3. Benign
4. Malignant

APPENDIX B

PATIENT INFORMATION SHEET

Title of study: Presentation of Intracranial Meningiomas in Johannesburg (A-12 month Prospective Study at Charlotte Maxeke Johannesburg Academic Hospital and Chris Hani Baragwanath Hospital)

Principal Investigator: Dr. K.E. Ibebuike

Institute: Department of Neurosurgery, University of the Witwatersrand, Johannesburg

Introduction:

I am Dr. K.E. Ibebuike from Department of Neurosurgery, University of the Witwatersrand, Johannesburg and doing a research on the presentation of intracranial meningiomas in Johannesburg. Since your brain scan shows that you are a patient likely to be suffering from this disease, I would like to invite you to join this research study.

Background information

Meningioma is a common brain tumour in the world and it is said to be commonest in Africa. It causes headache and many other symptoms depending on where it is located in the brain. The cause is not known for sure but there are some risk factors like previous exposure to x-rays, use of hormones as in oral contraceptives and even altered genes in our

body. There are many forms of management including surgery, radiotherapy and observation.

Purpose of this research study

The purpose of the study is to find out how common meningioma is in Johannesburg, how it is distributed in our population and the type of symptoms it causes in our patients.

Procedures

In this study, all patients from children to adults, presenting at the clinic or through emergency admission with brain tumour highly suspicious for meningioma will be considered for the study. A record of their demographic data, their symptoms including findings on brain scan will be kept for the study. As part of treatment some of the patients may undergo an operation where pieces of the tumour or even the whole tumour will be removed. The removed tumour will be sent to the histology laboratory in this hospital to be tested by scientists and doctors. This can help them diagnose your medical condition.

Possible risks or benefits

Collection of information is by our standard protocol in the routine assessment and care of our patients. No extra demands will be made on you.

There is no direct financial or other benefit for the participant of the study. However, any investigation which is specific for the study will be done free of cost to the patients.

Right of refusal to participate and withdrawal

You are free to choose to participate in the study. You may refuse to participate without any loss of benefit which you are otherwise entitled to. You will receive the same standard care and treatment which is considered best for you irrespective of your decision to participate in the study. You may also withdraw any time from the study without any adverse effect on your management. You may also refuse to answer some or all the questions if you don't feel comfortable with those questions.

Confidentiality

The information provided by you will remain confidential. Nobody except the investigator will have access to it. Your name and identity will also not be disclosed at any time. However the data may be seen by Ethical review committee and may be published in journal and elsewhere without giving your name or disclosing your identity.

Available Sources of Information

If you have any further questions you may contact the Investigator (Dr. K.E. Ibebuike), department of neurosurgery, University of the Witwatersrand, Johannesburg on the following phone number 0764931321.

What do I have to do?

You will need to give your written consent by signing an authorization.

APPENDIX C

INFORMED CONSENT FORM

Title of study: Presentation of Intracranial Meningiomas in Johannesburg (A-12 month Prospective Study at Charlotte Maxeke Johannesburg Academic Hospital and Chris Hani Baragwanath Hospital)

Principal Investigator: Dr. K.E. Ibebuike

Institute: Department of Neurosurgery, University of the Witwatersrand, Johannesburg

Introduction:

I am Dr. K.E. Ibebuike from Department of Neurosurgery, University of the Witwatersrand, Johannesburg and doing a research on the presentation of intracranial meningiomas in Johannesburg. Since your brain scan shows that you are a patient likely to be suffering from this disease, I would like to invite you to join this research study.

Background information

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body. There are many forms of management including surgery, radiotherapy and observation.

Purpose of this research study

The purpose of study is to find out how common meningioma is in Johannesburg, how it is distributed in our population and the type of symptoms it causes in our patients.

Procedures

In this study, all patients from children to adults, presenting at the clinic or through emergency admission with brain tumour highly suspicious for meningioma will be considered for the study. A record of their demographic data, their symptoms including findings on brain scan will be kept for the study. As part of treatment some of the patients may undergo an operation where pieces of the tumour or even the whole tumour will be removed. The removed tumour will be sent to the histology laboratory in this hospital to be tested by scientists and doctors. This can help them diagnose your medical condition.

Possible risks or benefits

Collection of information is by our standard protocol in the routine assessment and care of our patients. No extra demands will be made on you. There is no direct financial or other benefit for the participant of the study. However, any investigation which is specific for the study will be done free of cost to the patients.

Right of refusal to participate and withdrawal

You are free to choose to participate in the study. You may refuse to participate without any loss of benefit which you are otherwise entitled to. You will receive the same standard care and treatment which is considered best for you irrespective of your decision to participate in the study. You may also withdraw any time from the study without any adverse effect on your management. You may also refuse to answer some or all the questions if you don't feel comfortable with those questions.

Confidentiality

The information provided by you will remain confidential. Nobody except the Investigator will have access to it. Your name and identity will also not be disclosed at any time. However the data may be seen by Ethical review committee and may be published in journal and elsewhere without giving your name or disclosing your identity.

Available Sources of Information

If you have any further questions you may contact the Investigator (Dr. K.E. Ibebuike), department of neurosurgery, University of the Witwatersrand, Johannesburg on following phone number 0764931321.

AUTHORIZATION

I have read and understand this consent form, and I volunteer to participate in this research study. I voluntarily choose to participate, but I understand that my consent does not take

away any legal rights in the case of negligence or other legal fault of anyone who is involved in this study. I further understand that nothing in this consent form is intended to replace any applicable laws.

Participant's Name:

Date:

Participant's/Informant's Signature or thumb impression:

Date:

Principal Investigator's Signature:

Date:

Signature of Person Obtaining Consent:

Date:

REFERENCES

1. Black PM. Meningiomas. Neurosurgery. 1993;32(4):643-57.
2. Lusis E, Gutmann DH. Meningioma: an update. Current Opinion in Neurology. 2004;17(6):687-92.
3. Netsky M, Lapresle J. The first account of meningioma. Bull Hist Med. 1956;30:465-8. Cited by (1)
4. Louis A. Memoires sur les tumeurs fungeuses de la dure-mere. Memories de l'Academie Royale de (Paris). 1774;5:1-59. Cited by (1)
5. Al-Rhodan NF, Laws ER. The history of intracranial meningiomas. In: Al-Mefty O, editor. Meningiomas. New York: Raven; 1991. p. 1-7.
6. Bingham WF. W W Keen and the dawn of American Neurosurgery. J Neurosurgery. 1986;64:705-12. Cited by (1,5)
7. Haddad GF, Al-Mefty O, Abdulrauf SI. Meningiomas. In: Winn HR, editor. Youmans Neurological Surgery. Philadelphia: WB Saunders; 2004. p. 1099-131.
8. Cushing H. The meningiomas (dural endotheliomas): Their source, and favoured seats of origin. Brain. 1922;45:282-306. Cited by (1,5)
9. Drummond KJ, Zhu J, Black PM. Meningiomas: Updating Basic Science, Management and Outcome. Neurologist. 2004;10(3):113-30.
10. Campbell BA, Jhamb A, Maguire JA, Toyota B, Ma R. Meningiomas in 2009: Controversies and Future Challenges. A J Clin Oncol. 2009;32(1):73-85.
11. Longstreth WJJ, Dennis LK, McGuire VM, Drangsholt MT, Koepsell TD. Epidemiology of Intracranial Meningioma. Cancer. 1993;72(3):639-48.

12. Bondy ML, Ligon BL. Epidemiology and aetiology of intracranial meningiomas: a review. J Neurooncol. 1996;29(3):197-205.

13. Marosi C, Hassler M, Roessler K, Reni M, Sant M, Mazza E, et al. Meningioma. Critical Reviews in Oncology/Haematology. 2008;67(2):153-71.

14. Cushing H, Eisenhardt L. Meningiomas: Their Classification, Regional Behaviour, Life History, and Surgical End Results. Springfield, IL: Charles C Thomas; 1938. Cited by (7,12)

15. Zimmerman HM. Brain Tumour: their incidence and classification in man and their experimental production. Ann NY Acad Sci. 1969;159:337-59. Cited by (12)

16. Percy AK, Elveback LR, Okaziki H, Kurland LT. Neolpasms of the central nervous system: epidemiologic considerations. Neurology. 1972;22:40-8. Cited by (12)

17. Sutherland GR, Florel R, Louw D, et a. Epidemiology of primary intracranial neoplasms in Manitoba, Canada. Canadian J Neurol Sci. 1987;14(586-592). Cited by (7,12)

18. Claus EB, Bondy ML, Schildkraut JM, Wiemels JL, Wrensch M, Black PM. Epidemiology of Intracranial Meningioma. Neurosurgery. 2005;57(6):1088-95.

19. Central Brain Tumour Registry of the United States (CBTRUS) website. [cited 2009 8 March]; Available from: http://www.cbtrus.org/2002/2002 products.htm.

20. Davis FG, Kupelian V, Freels S, McCarthy B, Surawicz T. Prevalence estimates for primary brain tumours in the United States by behaviour and major histology groups. Neuro-oncol. 2001;3:152-8. Cited by (18)

21. Idowu O, Akang EEU, Malomo A. Symptomatic Primary Intracranial neoplasms in Nigeria, West Africa. Journal of Neurological Sciences (Turkish). 2007;24(3):212-8.

22. Rockhill J, Mrugala M, Chamberlain MC. Intracranial meningiomas: an overview of diagnosis and

treatment. Neurosurg Focus. 2007;23(4).

23. Staneczek W, Janisch W. Epidemiologic data on meningiomas in East Germany 1961-1986: incidence, localization, age and sex distribution. Clin Neuropathol. 1992;11:135-49.

24. Sacko O, Sesay M, Roux F, Riem T, Grenier B, Liguoro D, et al. Intracranial meningioma surgery in the ninth decade of life. Neurosurgery. 2007;61(5):950-5.

25. Helseth A, Mork SJ, Johansen A, Tretli S. Neoplasms of the central nervous system in Norway. IV. A population-based epidemiological study of meningiomas. APMIS. 1987;97:646-54.

26. Fan KJ, Pezeshkpour GH. Ethnic distribution of primary central nervous system tumours in Washington, DC, 1971-1985. J Natl Med Assoc. 1992;84(848-863). Cited by (12)

27. Fynn E, Khan N, Ojo A. Meningioma - a review of 52 cases. SA Journal of Radiology. 2004:3-5.

28. Odebode TO, Akang EE, Shokunbi MT, Malomo AO, Ogunseyinde AO. Factors influencing visual and clinical outcome in Nigerian patients with cranial meningioma. J of Clinical Neurosciences. 2006;13:649-54.

29. Haddad G, Chamoun RB. Meningioma. eMedicine Neurology [serial on the Internet]. Nov 14, 2006 [cited 2009 15 February]: Available from: e-medicine.medscape.com/article/.

30. Ohaegbulam SS. Geographical Neurosurgery. Neurol Res. 1999;21(2):161-70.

31. Preston-Martin S, Henderson BE, Peterm JM. Descriptive epidemiology of central nervous system neoplasm in Los Angeles Country. Annals NY Acad Sci. 1982;381:202-8. Cited by(12)

32. Preston-Martin S. Descriptive epidemiology of primary tumours of the brain, cranial nerves and cranial meninges in Los Angeles County. Neuroepidemiology. 1989;8:283-95.

33. Ameli N, Haddadian A, Kamalian N. Incidence of intracranial tumours in Iran. A survey of 1500 verified cases. Neurosurg Rev. 1979;2(2):67-71.

34. Rohringer M, Sutherland GR, Louw DF, Sima AAF. Incidence and clinicopathological features of meningioma. J Neurosurg. 1989;71:665-72.

35. Al-Mefty O, Heth J. Meningiomas. In: Rengachary SS, Ellenbogen RG, editors. Principles of Neurosurgery. Philadelphia: Elsevier Mosby; 2005. p. 487-500.

36. Christensen HC, Kosteljanetz M, Johansen C. Incidence of gliomas and meningiomas in Denmark, 1943 to 1997. Neurosurgery. 2003;52:1327-33.

37. Greenberg MS. Meningiomas. Handbook of Neurosurgery. New York: Thieme; 2006. p. 426-9.

38. Castillo GC. Meningioma, Brain. eMedicine Neurology [serial on the Internet]. Apr 27, 2007 [cited 2009 15 February]: Available from: emedicine.medscape.com/article/341624-overview.

39. Hoffmann CE, Ament J, Black P. Meningioma and NF 2: A Review. Neurosurgery Quarterly. 2007;17(2):128-31.

40. Chamberlain MC, Blumenthal DT. Intracranial meningiomas: diagnosis and treatment. Expert Review of Neurotherapeutics. 2004;4(4):641-8.

41. Elia-Pasquet S, Provost D, Jaffre A, Loiseau H, Vital A, Kantor G, et al. Incidence of central nervous system tumours in Gironde, France. Neuroepidemiology. 2004;23(3):110-7.

42. Hashiba T, Hashimoto N, Izumoto S, Suzuki T, Kagawa N, Maruno M, et al. Serial volumetric assessment of the natural history and growth pattern of incidentally discovered meningiomas. J Neurosurg. 2009;110:675-84.

43. Idowu OE, Apemiye RA. Delay in presentation and diagnosis of adult primary intracranial neoplasms in a tropical teaching hospital: A pilot study. International Journal of Surgery. 2009;7:396-8.

44. Wiemels J, Wrensch M, Claus EB. Epidemiology and etiology of meningioma. J Neurooncol. 2010;99:307-14.

45. Das A, Chapman CAT, Yap WM. Histological subtypes of symptomatic central nervous system tumours in Singapore. J Neurol Neurosurg Psychiatry. 2000;68:372-4.

46. Gasparetto EL, Leite CC, Lucato LT, Barros CV, Marie SKN, Santana P, et al. Intracranial meningiomas: magnetic resonance imaging findings in 78 cases Arquivos de Neuro-Psiquiatria. 2007;65(3a).

47. Quiñones-Hinojosa A, Kaprealian T, Chaichana KL, Sanai N, Parsa AT, Berger MS, et al. Pre-Operative Factors Affecting Resectability of Giant Intracranial Meningiomas. Can J Neurol Sci. 2009;36:623-30.

48. Francis A. Clinicopathological Analysis of Intracranial Meningiomas [Dissertation]. Karnataka, India: Rajiv Gandhi University of Health Sciences; 2008.

49. Jaggon JR, Char G. Epidemiologic Data on Meningiomas in Jamaica: The First from the Caribbean. The Internet Journal of Third World Medicine. 2007;5(1).

50. Haddad G, Al-Mefty O. Meningiomas: An overview. In: Wilkins RH, Rengachary SS, editors. Neurosurgery. 2nd ed. New York: McGraw-Hill; 1998. p. 833-41.

51. Al-Hadidy AM, Maani WS, Mahafza WS, Al-Najar MS, Al-Nadii MM. Intracranial Meningioma. J Med J. 2007;41(1):37-51.

52. Whittle PR, Smith C, Navoo P, Collie D. Meningiomas. The Lancet. 2004;363(9420):1535-43.

53. Gaillard F. MeningiomaMay 2, 2008 [cited 2010 15 December]: Available from: http://radiopaedia.org/articles/meningioma.

54. Nkposong EO, Lawani J. Primary Carcinoma of the prostate in Ibandan. West African Medical Journal. 1973;6:108-11.

55. Misra M, Mohanti AB, Rath S. Intracranial extension of orbital meningioma-A case report. Indian J Ophthalmol. 1989;37(3):152-3.

56. Housepian EM, Trokel SL. Tumours of the Orbit. In: Youmans JR, editor. Youmans Neurological Surgery. 2 ed. Philadephia: Saunders Company Pub; 1983. p. 3046.

57. Roelvink NCA, Kamphorst W, Van Alphen HA, Rao BR. Pregnancy-related primary brain and spinal tumors. Arch Neurol. 1987;44:209-15.

58. Nishio S, Morioka T, Suzuki S, Takeshita I, Ikezaki K, Fukui M, et al. Primary brain tumours manifesting during pregnancy: presentation of six cases and a review of the literature. Journal of Clinical Neuroscience. 1996;3(4):334-7.